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STRUCTURAL AND FUNCTIONAL CHROMATIN DISTURBANCES IN THE THYROID CELLS IN THE AGING PROCESS

Abstract: Chromosomal instability during aging leads to the appearance of a large number of cells with various quantitative and structural disorders that occur during chromosomal aberrations. The purpose of subsequent cytogenetic analysis experiments is to study chromosomal aberrations that occur in the cells of the thyroid gland during aging. In the study of cytogenetic, mutational and molecular genetic disorders in most cases, it was found that their frequency increases with age.

Keywords: Age, genome, chromatin, thyroid gland, chromosomal aberrations.

Introduction. The aging of the organism is a multifaceted process, it affects the tissue and cellular levels. This process is controlled by the genome and environmental conditions, where the hereditary program of each organism is implemented [1, 26–34]. The mechanisms of aging are manifested in many types of disorders occurring at the molecular level. Aging includes a number of processes that reduce the organism's resistance [2, 27–32]. It is known that the number of chromosomal aberrations is used as a marker DNA damage in aging organisms. Somatic mutations can arise due to the accumulation of steady aberrations and underlie age-related pathology, including malignant tumors [3, 341–349]. An effective method for assessing the influence of environmental factors on the human organism is a cytogenetic analysis of peripheral blood lymphocytes, which allows to determine the level of chromosomal abnormalities in somatic cells [4, 229–231]. The spontaneous level of chromosomal aberrations in human lymphocytes can vary depending on external and internal factors: organism metabolism, hormonal balance, changing during life [5, 21–29; 6, 125–163; 7, 368]. Many scientific studies indicate that with increasing age, spontaneous levels of chromosomal aberrations in human lymphocytes may increase, which is potentially dangerous for health in terms of the development of cancer pathology [8, 80–85; 9, 277–278; 10, 253–258].

The aim of the study was to study the frequency and spectrum of spontaneous chromosomal aberrations in the peripheral blood of lymphocytes of conditionally healthy volunteers of different ages with and without diseases of the thyroid gland.

Material and methods. The material of the cytogenetic study was the lymphocytes of the peripheral blood of the young, middle, senior and elderly (7 people in each age group) age. Blood lymphocytes were cultured according to standard methods [11, 23]. Cytogenetic analysis was performed under a microscope at magnification x1000. The entire spectrum of chromosome aberrations was taken into account according to the international nomenclature [12, 140]. The preparations were stained with 4% solution Romanovsky-Giemsa. The analysis was carried out in the metaphase stage.

Results and discussion. Cellular aging is accompanied by various chromosomal changes: a violation of the number of chromosomes, intragroup variations in the number of chromosomes, structural changes in chromosomes, the appearance of marker chromosome aberrations. Cell aging may be associated with the appearance of spontaneous chromosomal aberrations. Chromosomal instability during aging leads to the appearance of a large number of cells with various quantitative and structural disorders that occur during chromosomal

aberrations. The purpose of subsequent cytogenetic analysis experiments is to study chromosomal aberrations that occur in the cells of the thyroid gland during aging. In the study of cytogenetic, mutational and molecular genetic disorders in most cases, it was found that their frequency increases with age. This concerned chromosomal aberrations, micronuclei, aneuploidy, loss of telomeric repeats, mutations. Structural aberrations of chromosomes are related to the type of genetic abnormalities that undoubtedly contribute to the multifactorial process of aging. Unstable chromosomal aberrations – dicentrics, rings, fragments – lead to cell death, stable – translocations, insertions are known to accompany oncogenesis, and can also affect vital cell functions [3, 341–349]. Based on the results obtained, we concluded that with age the thyroid gland does not undergo any special changes. Analysis of the results showed that the average group frequency of chromosome aberrations significantly increased with an increase in the age of the examined individuals from 19 to 70 years. Comparing the obtained results with literary sources, the following can be noted. According to Polish researchers who used G-differential staining of metaphase chromosomes of peripheral blood lymphocytes of healthy volunteers aged from 21 to 78, an increase in all types of chromosomal aberrations with increasing age was shown [13, 763–772].

However, the presence of one or another pathology of the thyroid gland, perhaps, accelerates the aging process. To confirm the obtained data, we performed a cytogenetic analysis of chromosomal aberrations at the metaphase stage of mitosis of peripheral blood lymphocytes in young people (19 years and 25 years) and elderly people (54, 69 and 75 years). It should be noted that the elderly were with thyroid pathology: 54 years and 79 years with diffuse toxic goiter and 75 years with a nodal euthyroid goiter. In these cultures, we studied the level of spontaneous chromosomal aberrations in peripheral blood lymphocyte cells. The figure shows that at least 100 metaphases with a good chromosome spread were analyzed for each culture. In patients aged 54, the total number of metaphases studied was 123 cells, among which there is 1 cell with one microfragment (0.8%); in patients aged 79, the total number of metaphases studied was 111 cells and one cell with a paired fragment (0.9%). In a 75-year old patient with a nodal euthyroid goiter, the total number of metaphases studied was 156 cells, of which 3 (1.92%) are aberrant cells with paired fragments. The aberrant cells in this patient exceed the number of aberrant cells in the control (19 years and 25 years). We carried out a cytogenetic analysis of the chromosomes of the cells of peripheral blood lymphocytes of elderly people without thyroid gland pathology (59–75 years). Cytogenetic analysis of chromosomes of cells of peripheral blood lymphocytes at the age of 75 years without thyroid gland revealed single asymmetric translocations of chromosomes (Fig. 1). Chromatid translocations represent the exchange between chromosomes and chromatid exchanges within the chromosomes. The figure shows that in this patient cytogenetic analysis revealed the presence of chromatid asymmetric translocation. Chromatid asymmetric translocations lead to the appearance of chromatid dicentric and fragments and lead to cell death.

Cytogenetic analysis of chromosomes of peripheral blood lymphocytes of patients aged 75 years with papillary adenocarcinoma revealed the presence of chromatid breaks and deletions. Based on our data, we concluded that chromosomal aberrations (translocations, fragments, rings, inversions) can lead to aging of the organism and age-related diseases. Cytogenetic analysis of peripheral blood lymphocytes of this patient also revealed the presence of gaps, single and paired fragments. It is known that the localization of the gap in the chromosome may indicate the place of the former gap or the junction of fragments. Gaps are unrealized, potential damage that does not go through the repair process.

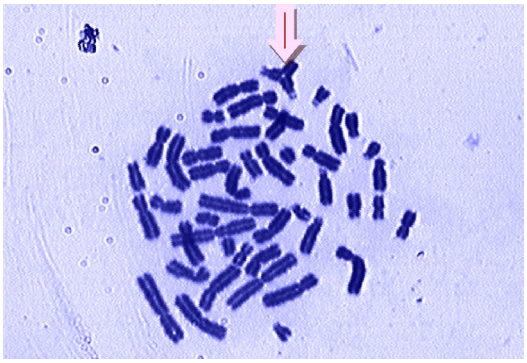

Figure 1. Asymmetric chromatid translocations detected in patients aged 75 years

The resulting fragments devoid of centromeres during asymmetric translocations usually fall into the plasma and lyse, which upsets the gene balance, and such cells die. In this chapter, we also conducted a study of the age dynamics of the frequency of stable chromosomal aberrations in the elderly in normal conditions and in papillary adenocarcinoma. Structural aberrations of chromosomes are considered as the most likely events associated with cell malignancy. This fact

is confirmed by the fact that the vast majority of tumors are characterized by chromosomal rearrangements; many carcinogens induce structural chromosome aberrations; mutations in the genes responsible for DNA repair, for the suppression of oncogenes, for control of the cell cycle increase both the frequency of tumors and the frequency of chromosomal breakdowns. It is known that in old age the likelihood of tumor development increases, therefore, the analysis of the age dynamics of chromosomal aberrations can contribute to an understanding of the mechanisms of carcinogenesis and aging. In the lymphocytes of the peripheral blood of elderly people (age 70, 75 years) without thyroid gland pathology, an age-related increase in the level of chromosomal aberrations in the form of deletions and translocations.

Cellular aging is accompanied by various chromosomal changes: a violation of the number of chromosomes, intragroup variations in the number of chromosomes, structural changes in the chromosomes, the appearance of marker chromosomes – aberrations. Cell aging may be associated with the appearance of spontaneous chromosomal aberrations. Chromosomal instability during aging leads to the appearance of a large number of cells with various quantitative and structural disorders that occur during chromosomal aberrations. Aging can be defined as the increasing likelihood of degenerative diseases (cancer, autoimmune diseases, cardiovascular pathology) and death. Structural aberrations of chromosomes are related to the type of genetic disorders that undoubtedly contribute to a multifactorial process. We performed a cytogenetic analysis of chromosomal aberrations at the metaphase stage of mitosis of peripheral blood lymphocytes in young people (18 years and 24 years) and elderly people (54, 59 and 75 years). It has been established that with a nodal euthyroid goiter in a patient at the age of 75 years, small chromosomal aberrations are observed. It was shown that in patients aged 75 years without thyroid gland, isolated asymmetric translocations of chromosomes were observed.

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DETECTION OF *HELICOBACTER PYLORI* AND GENE CagA WITH USE REAL-TIME PCR IN THE UZBEKISTAN

Abstract: The CagA is one of the virulence factors of *H.pylori,* CagA is important in gastroduodenal disease pathogenesis and affect cure rates and almost 100% of the East Asian strains express CagA. All clinics installed real time PCR amplifiers, not the usual PCR. Therefore, we identificated gene CagA with help Real-Time PCR with sybr green. The detection of *H.pylori* UreC gene by Real- time PCR revealed that 100% of samples were positive. We found that the prevalence of CagA gene was 80% (68) and in addition, found gene CagA all local isolates 132, 142, 1740, 1741, 1742, 1743 *H.pylori*.

Keywords: *H. pylori,* CagA, UreC, peptic ulcer, duodenal ulcer, Real-Time PCR.

Introduction

Helicobacter pylori, a spiral, Gram-negative, micro-aerophilic bacterium, colonizes at more half of the world's human population and is recognized as a major cause of chronic gastritis, peptic ulcer, duodenal ulcers, gastric mucosa lymphoma (MALT lymphoma) and risk factor for gastric cancer [1, 11654–11672; 2, 784–789]. *H.pylori* non-gastroenterological diseases; thrombotic purpura, chronic iron deficiency anemia and vitamin B12 deficiency [3, 646–664; 4, 49–55; 5, 124–128; 6, 674–677; 7, 13434–13441]. In addition, the effects of *H.pylori* on the immune system have been identified [8, 190]. Research by Sentos and other authors points out that *H.pylori* infection causes an epigenetic mechanism, that is, a disorder of gastric epithelial cells DNA and development of congenital anomalies [9, 329–335]. In most cases the *H.pylori* infection is asymptomatic and but he is has been classified as a class I carcinogen in humans by a Working Group of the World Health Organization International Agency for Research on Cancer [10, 1–124]. H.pylori infection is prevalent worldwide with an estimated prevalence of 70–90% in developing countries and 30–40% in industrialized countries [11, 11221–11235; 12, 506]. The risk of gastrological disease risk in a person infected with *H.pylori* includes: the virulence of the infecting strain, human factors such as gene polymorphism and immunity [13, 713–739], environmental factors, such as diet, smoking [14, 372–380; 15, 5–10], alcohol [16, 1381], high-Salt [17, 1–8]. Develop severe disease in the *H.pylori* virulence factors have been suggested to play important roles. *H.pylori* virulence factors strongly associated with gastric and duodenal disease are the cytotoxin associated gene A (CagA), which is encoded by one of the genes located in the cag pathogenicity island (PAI). CagA protein, which is encoded by the CagA gene, is one of the most studied virulence factors of *H.pylori*. The presence of CagA in a strain results in an increased risk of gastric carcinogenesis compared with individuals infected with CagA-negative strains [18, 764–777]. About 60–70% of the western *H.pylori* strains and almost 100% of the East Asian strains express CagA [13, 713–739], but the Central Asian strains are almost not been studied. CagA is associated with epithelial tight junction, as a result destroys cellular junction, CagA leads to gastric epithelial cell proliferation and carcinoma [13, 713–739; 19, 1003–1008].

Methods

2.1. Ethics statement

This study was approved by the Ethics Committee of the Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation of the Ministry of Health of the Republic of Uzbekistan, Institute of Bioorganic chemistry of Uzbekistan Academy of Sciences and Republican Specialized Scientific Center named after Academician V. Vakhidov received a local and obtained all patients signed informed consent, in accordance with the Declaration.

2.2. Sample collection

Gastric biopsy samples were collected from 85 patients diagnosed with stomach ulcer and peptic ulcer at the Republican Specialized Scientific and Practical Medical Center for Therapy and Medical Rehabilitation of the Ministry of Health of the Republic of Uzbekistan between 2016 and 2017. Gastritis was investigated by endoscopy. 85 *H.pylori* infected gastritis patients including 52 men (44 ± 2.2 years) and 33 women (40 ± 1.6 years).

In addition, local isolates 132, 142, 1740, 1741, 1742, 1743 H. pylori were obtained from the Republican Specialized Scientific Center named after academician V. Vakhidov [20, 222]. Biopsy were obtained from the stomach of each patient during endoscopy. DNA of *H.pylori* strain HP-26695 and DNA of venous blood samples (leukocytes) of humans were used as controls. H. pylori strain 26695 was used as a reference strain.

2.3. DNA Extraction

DNA samples were isolated from biopsy samples using the AmpliPrim RIBO-PREP reagent kit (InterLabService, Russia) and Biospin Bacteria Genomic DNA Extraction Kit (Hangzhou Bioer Technology Co., Ltd. China) bacterial DNA in cultural *H.pylori*, according to the manufacturer's instructions. The concentration and purity of the isolated DNA samples were checked on a BioSpec-nano spectrophotometer (Shimadzu Biotech, Japan).

2.4. Detection of H. pylori and cagA gene by Real-Time PCR.

All PCRs were performed by real-time methods using the Step One Real-Time PCR system (Applied Biosystems, USA). The UreC gene (GlmM) to identify *Helicobacter,* and the CagA gene is the main virulence factor of *H.pylori*, and we chose the CagA and UreC genes, in addition, the main goal of our study was to use real-time PCR to detect the pathogenic CagA gene in biopsy specimens from patients with gastrointestinal diseases. The presence of *H.pylori* in the samples was confirmed by PCR using specific primers Forward 5^{I}- AAGCTTTAGGGGTGTTAGGGGTTT -3^{I}, Revers 5^{I}- AAGCTTACTTTCTAACACTAACGC -3^{I}, and Probe FAM–CGATTGGGGATAAGTTTGTGAGCG–RTQ1 of the UreC (GlmM) gene [21, 1–6]. The following reagents were used for real-time PCR amplification of the *H.pylori* CagA gene; final volume of 20 μl containing primers Forward (20 pM) 5^{I}-GATAACAGGCAAGCTTTTGAGG-3^{I} and Revers (20 pM) 5^{I}–CTGCAAAAGATTGTTTGGCAGA-3^{I} (Eurofins genomics, CustomArray. USA) [22, 2274–2279; 23, 3336–3338], 2 mkl 10 x PCR buffer + Sybr green (cat.№ R-402. Syntol, Russian), 2 mkl 2.5 мМ $MgCl_2$, 2 mkl 2.5 мМ dNTP, 0.2 mkl Taq-polymerase (5u/μl) (Syntol, Russian), DNA 5 mkl (50 ng/mkl). For CagA gene evaluation, the PCR program contained 40 cycles of denaturation (95 °C for 4 min), annealing (58 °C for 30 s, extension at 72 °C for 45 s), and one final extension (72 °C for 3 min).

2.5. Data Analysis

Odds ratios and G-tests were used to evaluate the proportion of risk factors in the control and patient groups. The level of significance was set at 95%. Statistical analysis was performed using the Doctor Stat program. A p value less than 0.05 ($p < 0.05$) was accepted as statistically significant.

Results

Our study included 85 patients; they were suffering stomach ulcer and duodenal ulcer. All patients were examined endoscopically and clinically. This study was designed to determine the frequency of *H.pylori* CagA gene in stomach from the Uzbekistan. The detection of *H.pylori* UreC (GlmM) gene by Real- time PCR revealed that 100% of samples were positive. We found that the prevalence of cagA gene was 80% (68) and in addition, found gene CagA all local 132, 142, 1740, 1741, 1742, 1743 H. pylori isolates. *H.pylori*-positive samples, cagA gene was detected. The cagA gene status has shown a significant relationship with gingival status stomach ulcer and duodenal ulcer (Fig. 1).

The presence of CagA gene was associated with a significantly higher frequency of stomach ulcer and duodenal ulcer ($P = 0.001$; $P = 0.0009$). Identification of the CagA *H.pylori* gene by the Real-Time PCR method reduced the time and increased the degree of sensitivity. All clinics installed real time PCR amplifiers, not the usual PCR.

All clinics installed real time PCR amplifiers, not the usual PCR. Therefore, we modified PCR in real time with the help of syber green. Real-time PCR system provides a highly sensitive assessment of CagA type as a new diagnostic tool for the pathogenicity of *H.pylori* infection.

Discussion. In this study, the detection of *H.pylori* and CagA gene was performed by Real-time PCR. Real-time PCR has a higher specificity than other metods. Using Real-Time PCR, Iraqi researchers discovered the CagA gene 75% with gastroduodenal diseases [24, 640–643]. Ruzsovics and others identified the s-region of the Cag and VacA genes using a sybr green probe [25, 369–377], but the difference between the s1, s2 types of the VacA s region cannot be differentiated using sybr green. CagA gene was associated with a significantly

higher frequency of gastritis. The CagA gene was found 81% in gastric and duodenal ulcer in the Iran [26, 1345–1349]. The definition of the *H. pylori* CagA gene using the real-time PCR method is very rare in the literature and is characterized by high renaturation temperature and time taken for the reaction stage.

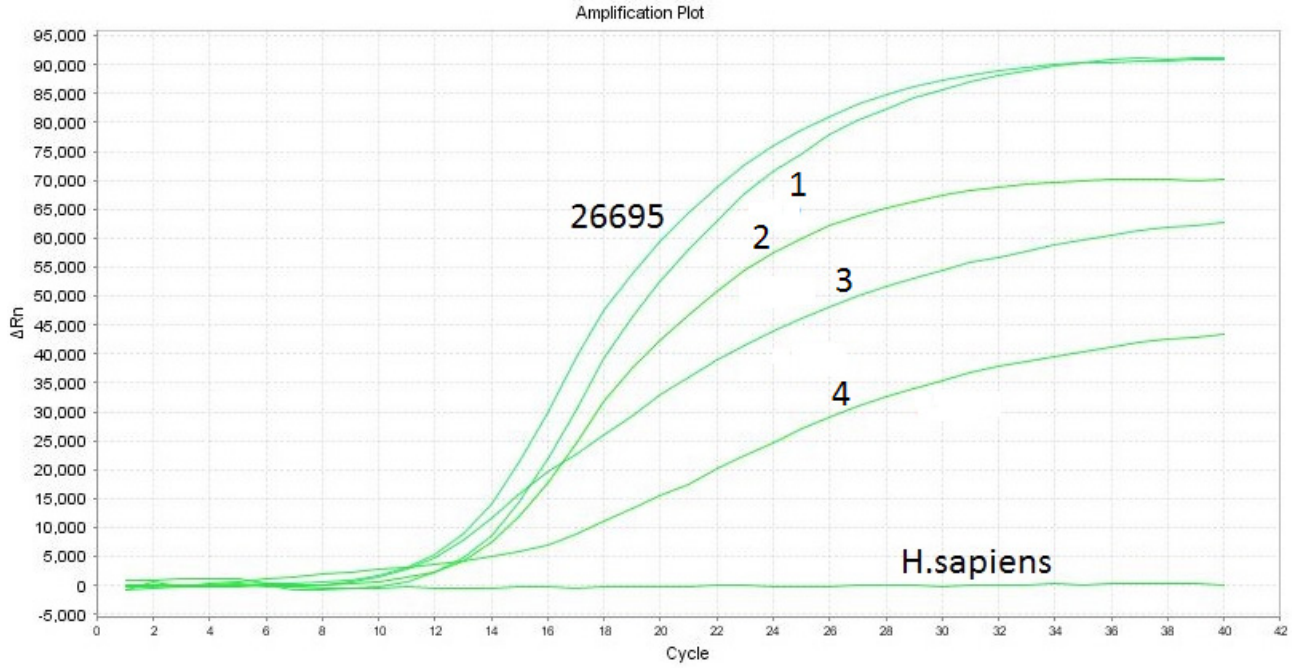

Figure 1. Representative amplification plots of real-time PCR targeting the CagA gene. Curves: 1–4, H.pylori DNA positive specimens; 26695- H.pylori strains DNA positive control, control (*H.sapiens*); broken line, threshold cycle line

In our studies, the reaction stages were modified and the time of the reaction was saved. Based on the results obtained in clinics, the Real-time PCR technique can be used to determine the virulent CagA *H.pylori* gene.

In perspective, we have planned to use the technology of multiplexed Real-time PCR using TaqMan probes, which will reduce costs, increase degree sensitivity and save time analyzing the determination of the of virulence of *H.pylori*.

Conclusions. Frequency of gene CagA occurrence in patients with diseases of gastric ulcer and duodenal ulcer is not different. The CagA gene is associated in these incidence and it can be considered a marker gene.

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ORGANOCHLORINE INSECTICIDE HEXACHLOROCYCLOHEXANE DEGRADATION IN THE SOILS OF KARAKALPAKSTAN

Abstract: The article studies the degradation of organochlorine insecticide in the soils of Karakalpakstan. Research of destructive active microorganisms showed that nine out of ten tested strains could use lindane as their sole carbon source. Tested local active strains-destructors are recommended to be used to create a new biological product that can be used to purify soils contaminated with pesticides-hexachlorocyclohexane in saline conditions.

Keywords: Karakalpakstan, soil, insecticide degradation, lindane.

It is hard to imagine the development of agriculture of the modern era without the chemicals, such as pesticides. According to the data of L. I. Domrachev et al., [3], prudently estimated crop losses that were not treated with pesticides range from 24 to 46%, which leads to high economic losses.

In the Republic of Karakalpakstan, for several decades, crops, such as cotton and rice, were treated with large variety and quantity of pesticides Abdirov et al., [1]; Kurbanov et al., [6].

In addition to their direct positive effects, pesticides have various by-effects (carcinogenic, teratogenic and mutagenic). Pesticides, accumulating in the soil, can widely spread in the environment Melnikov et al., [7]; Shatalov et al., [8].

Organochlorine pesticides are the most hazardous due to their high stability and toxicity. If they remain in the soil, they can get in food chains and, consequently, be eaten by humans resulting in harm to their health Tiemann U. et al., [9]. The amount of banned and expired pesticides landfills are of particular concern in recent years Babkina et al., [2]; Kolesnikov et al., [4]; Ksenofontova et al., [5]. Areas with landfills suffer from extremely slow processes of natural purification and the soil cannot remove the pollution without human interference.

Various methods for soil purification from excessive amounts of pesticides are currently being proposed to solve this problem. Microbiological methods that propose the use of xenobiotic destructors are recognized as one of the most promising, inexpensive and effective ways to detoxify pesticides.

At the present time, a large number of disused pesticides are still stored on the territories of the former farm airfields, pesticides storage sites and landfills. Organochlorine pesticides are of greatest concert, due to the fact that they are persistent and able to accumulate in the natural environment, which are the source of pollution of nearby natural sites. Most predominant organochlorine pesticides are insecticide hexachlorocyclohexane (HCH) and dichlorodiphenyltrichloroethane (DDT). Abovementioned indicates that purification of contaminated areas of the region from pesticides residue is a relevant objective.

To solve this problem, we harvested ten natural bacteria strains from a soil contaminated with hexachlorocyclohexane by a selection method. These strains were conventionally numbered from 1 to 10. The harvested strains were able to grow on a nutrient medium with high pesticide content and use the γ-HCH (lindane) as the sole source of carbon and energy.

With a focus on finding the most active strains of lindane destructors among them, we conducted a study of the degradation of lindane under laboratory conditions under the exposure to the harvested strains.

The first stage of the experiment was devoted to the research of the destructive activity of pure culture bacteria, growing on a nutrient medium, exposed to lindane.

As a result of the research, real quantitative characteristics of γ-HCH-destructive activity of soil bacteria strains were obtained. The results of the chromatogram showed that within 30 days the process of destruction proceeded at different rates. Of the ten tested strains, only four caused the active destruction of lindane in the nutrient medium for a given period of bacterial growth (chromatograms 1, 2, 3, 4). By the end of the first month of incubation of cultures 4, 5, 7, and 10, this specimen was almost completely degraded at its initial concentration in the medium of 100 μg/mg. The destructive activity of the remaining cultures (1, 2, 3, 6, 8, and 9) was not high, as a very slight decrease in the concentration of lindane was noted (by 5–10%) over a given period of time.

Therefore, chromatographic analysis suggests that soil bacteria cultures 4, 5, 7, and 10 have high γ-HCH-destructive activity and are able to degrade lindane in a nutrient medium within one month.

Further research was directed to studying the ability of test crops to use γ-HCH as the sole carbon source. For this purpose, cultures were seeded in synthetic medium M-9,

where the only carbon source was lindane at a concentration of 20 μg/ml.

On the third day after sowing, a weak growth of cultures 2, 7 and 9 was observed in synthetic medium. On the fifth day, growth of other cultures 3, 4, 5, 6, 8 and 10. Culture 1 growth was not observed during the experiment. A moderate growth of cultures 6, 7 and 9 was observed on the mineral medium, while the rest of the cultures had a weak growth.

The results suggest that cultures 4, 5, 6, 7, and 10 are table to assimilate and transform HCH in a synthetic medium without additional organic substrate. Apparently, the studied strains harvested from the plots highly contaminated with pesticides were adapted to these synthetic chemical compounds.

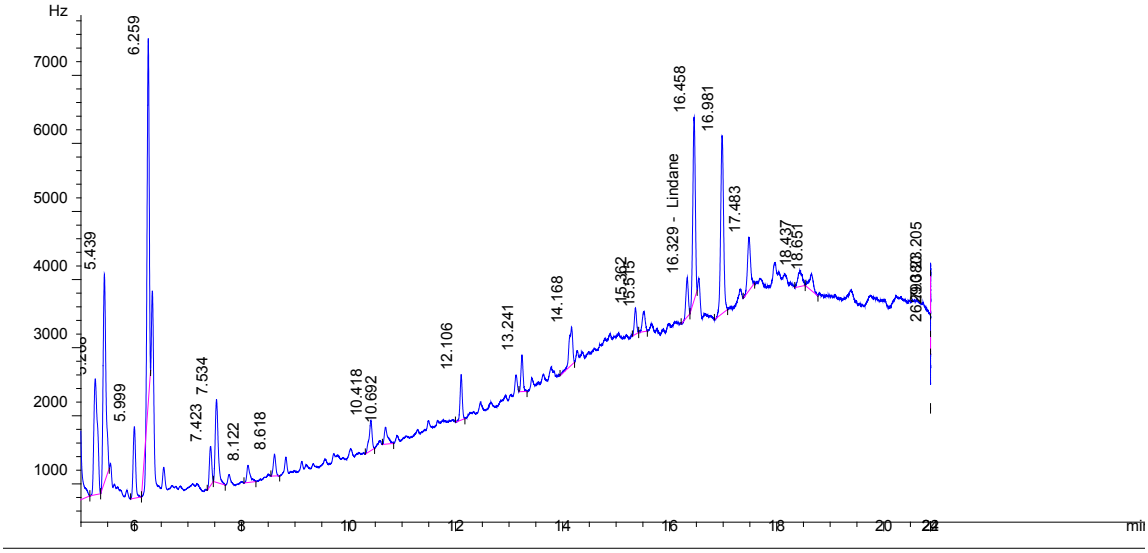

Figure 1. Chromatogram of lindane destruction by strain 4 in a nutrient medium

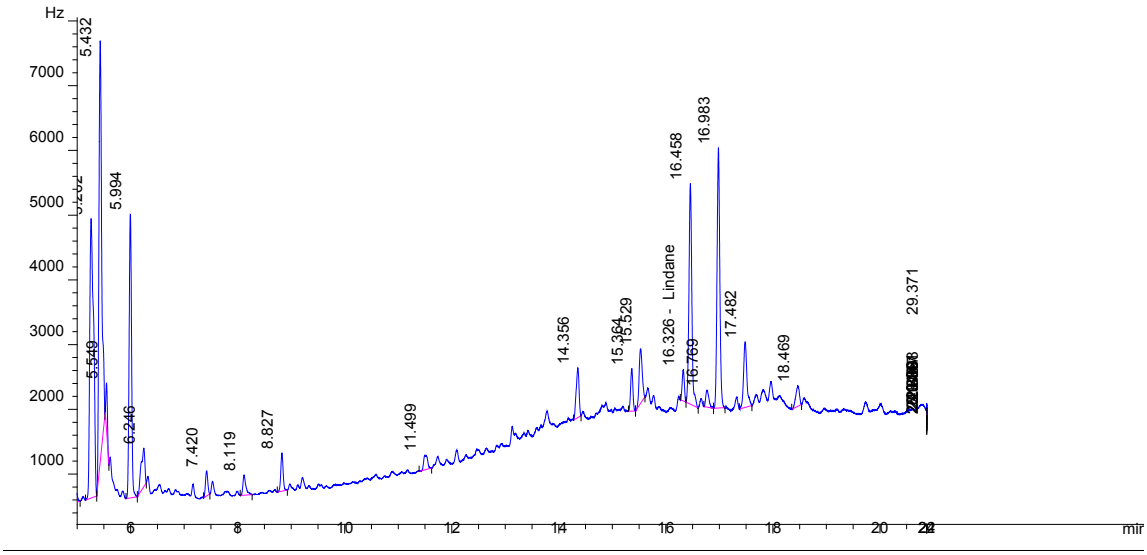

Figure 2. Chromatographic analysis of lindane destruction by strain 5 in a nutrient medium

In summary, a search for active destructive microorganisms showed that nine out of ten strains could use lindane as their sole carbon source.

Along with the work on the destruction of γ-HCH with pure cultures, a research was conducted of the use of γ-HCH by the community of these cultures. It is known fact that the metabolic potential of a consortium of microorganisms is higher and more diverse than that of an individual organism. Added to this is the fact that the association of microorganisms allows the mineralization of pesticides to non-toxic compounds. Given this, our next goal was laboratory research of the microbial lindane destruction by the association of obtained active cultures of bacteria 4, 5, 7 and 10. A modern method was used to carry out the experiment.

It makes possible to determine the distribution of radioactive label between culturing liquid and bacteria cells. The efficiency of accumulation of lindane by bacteria was determined by their ability to absorb a certain amount of this agent in their metabolism. A sterile medium was the test sample.

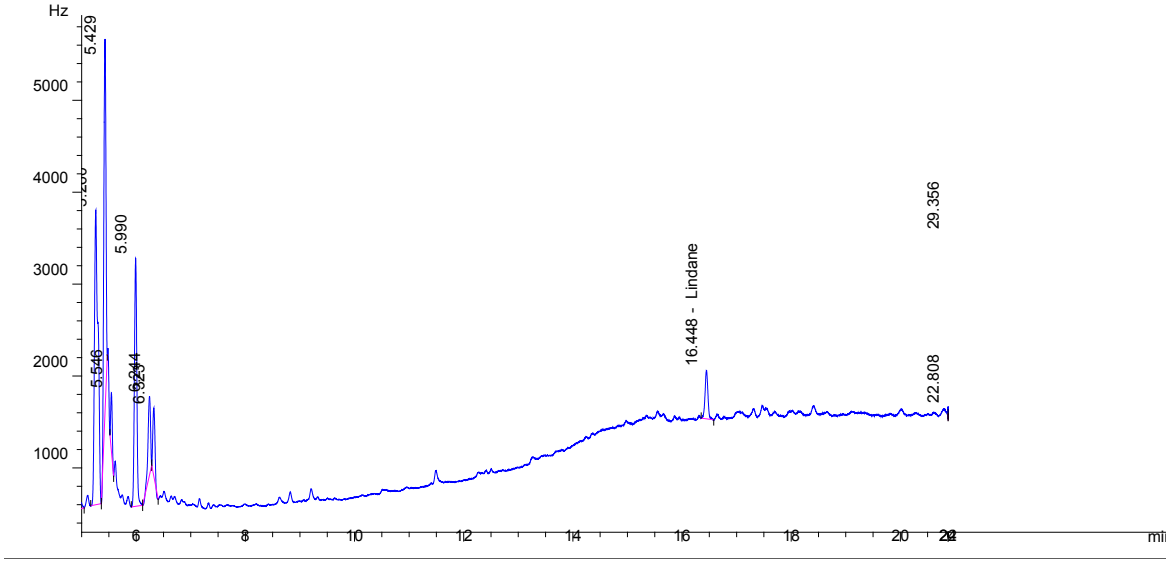

Figure 3. Chromatographic analysis of lindane destruction by strain 7 in a nutrient medium

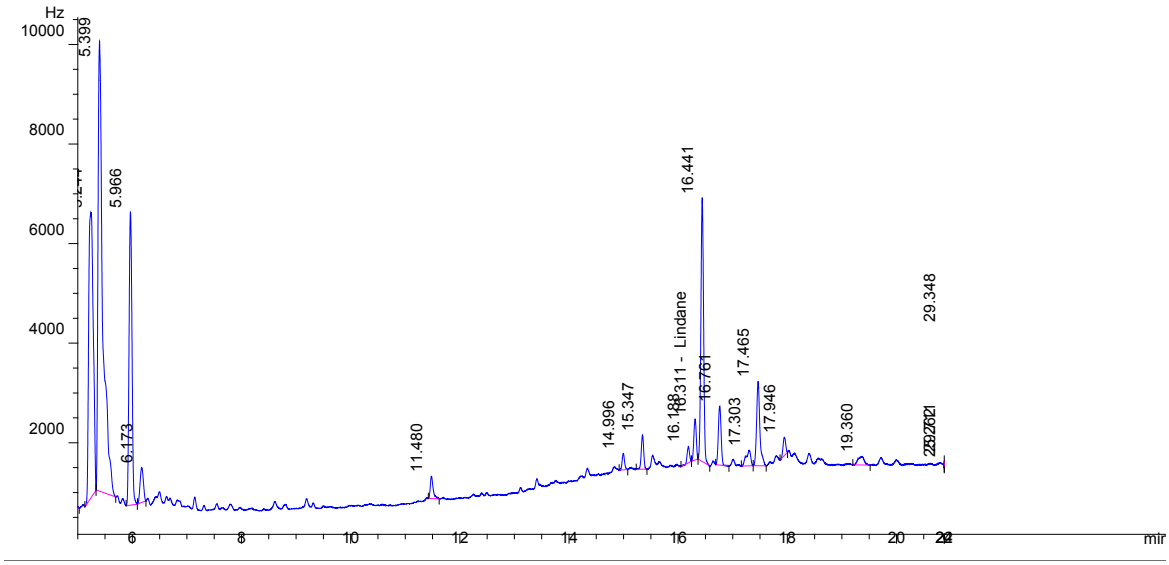

Figure 4. Chromatographic analysis of lindane destruction by strain 10 in a nutrient medium

The results show that experimental cultures associations were efficiently destroying lindane, as evidenced by the percentage of remaining radioactivity. By the end of the 12th day of incubation, a decrease in the initial concentration of tritium-labeled lindane was observed from 100 μg to 45.55 μg.

The total amount of lindane in the sample is 6.83×10^{-2} μg or 26.78% of the radioactive label in bacterial cells, which indicates partial sorption by the surface structures of the cells of the studied strains. The presence of most of the tritium label is 73.22% in the supernatant. It led to the conclusion that lindane destruction was mainly extracellular. The test sample shows no loss of the radioactive label, as evidenced by the 100% detection of radioactivity in the culturing fluid.

In summary, experimental data showed an intensive destruction process of HCH by the association of cultures 4, 5, 7 and 10 in a short span of time, and during this period accumulation of intermediate products of metabolism is unlikely. The results of the research allowed us to select the most active strains that will be used for further research. Subsequently, all four active strains-destructors were selected to determine the species, and based on the study of cultural-morphological and physiological-biochemical characteristics of cultures 4, 5 and

7, they were assigned to the species Bacillus subtilis, culture 10 to the species Micrococcus roseus.

It is known fact that in the natural environment microorganisms in most cases exist in biocenosis and the interactions between the components of them are complex and diverse. One of the types of relationships of microbes in the biocenosis is the process of microbial antagonism, i.e. the phenomenon of active oppression of some microorganisms by others. The success of inoculation of destructive microorganisms into the natural environment depends largely on the survival of microorganisms as they interact in bacterial associations. In this regard, in order to co-cultivate and create in perspective a complex biological product, we were interested in determining the antagonistic relationship of the destructive strains in relation to each other.

The absence of antagonistic action between the tested bacterial strains was determined by theit growth at the contact points of the strokes on the medium. The results of mutual antagonism research of strain-destructors showed that there was no obvious suppression of growth between the strains. When grown on plain agar, B. subtilis 4 culture did not show antagonism to either B. subtilis 7 or M. roseus 10. At the same time, mild antagonism was observed in M. roseus 10 against B. subtilis 7. A weak delay was also observed in development of B. subtilis 5 when co-cultivated with cultures of B. subtilis 4 and M. roseus 10.

The above results show that only B. subtilis 4 and M. roseus 10 did not reveal any inhibitory properties against each other, which indicates the absence of antagonistic interactions between them. In this regard, cultures of bacteria B. subtilis 4 and M. roseus 10 were selected for further research, which allows their joint cultivation to create associative strains.

The next stage of the experiment was supposed to reveal destructive activity of the tested strains in samples of soil contaminated with lindane in the laboratory setting. To research lindane degradation gas chromatography was used, allowing to investigate the decline of lindane. The experiment tested the possibility of lindane degradation in the soil with pure strains of B. subtilis 4 and M. roseus 10 and their association.

To study lindane destruction, sterile, moderately saline soil was used from a natural site, with the addition of lindane in concentration of 100 μg/ml. For inoculation both monocultures and their associations were used. The experiment was carried out for one month.

Model soil experiments showed that the introduction of a bacterial suspension changes the amount of lindane in the soil, whereas in the test sample there were no changes in lindane concentration during the entire experiment (30 days).

The chromatogram data showed that in soil samples with the inoculated strain of B. subtilis 4, there was a decrease in the concentration of lindane from 14.40 to 8.37 μg/ml in a month, which is 41.9% of the initial lindane concentration. Monitoring the state of lindane in the soil with the addition of M. roseus 10 for the same period showed a decrease in the lindane concentration to 5.67 μg/ml of the initial concentration (14.40 μg/ml) or 60.6% of the drug was destroyed.

Later, we studied the degradation of lindane by a consortium of bacteria B. subtilis 4 and M. roseus 10. It was found that lindane destruction by the association of strains is significantly higher than when using pure destructive cultures. These studies showed that the association of the tested strains allowed for a month to reduce the content of lindane from 14.40 μg/ml to 0.08 μg/ml in the soil. Therefore, in thirty days, the percentage of lindane destruction in mixed culture soil (B. subtilis 4 and M. roseus 10) was 99.4%.

Tested strains destructive activity analysis shows that at the end of the test period in samples with inoculated B. subtilis 4 strain, the amount of lindane is 57.8%, and in samples with M. roseus 10 strain – 39.4%. The introduction of the association of strains B. subtilis 4 and M. roseus 10 showed an increase in the degree of lindane destruction to almost 100%.

In summary, this research showed that lindane was efficiently utilized by strains of B. subtilis 4 and M. roseus 10 in soils in laboratory setting, and the use of their association would significantly increase the degree of destruction of the pesticide. Tested local active strains-destructors are recommended to be used to create a new biological product that can be used to purify soils contaminated with pesticides – hexachlorocyclohexane in saline conditions.

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POLYMORPHIZM OF GLIADIN PROTEINS AMONG WHEAT LANDRACES OF UZBEKISTAN

Abstract: Here was described full polymorphism of electrophoretic spectra of gliadines in wheat landraces of Uzbekistan comparing with commercial and newly zoned cultivars. It was conducted work on 21 landraces, 2 new and one commercial commercial variety that it was revealed 40 variation in electrophoretic spectra.

Keywords: traditional wheat landrace, polymorphism, electrophoretic spectra, gliadin.

Introduction. Studying and conservation of the Uzbek wheat landraces is of great importance, since there are cultivars possessing high bread making qualities among them, and this character is genetically determinated and it does not depend on environmental factors met during its growing [1]. Comparative analysis of gliadins (Gliadin is a class of proteins present in wheat and several other cereals within the genus *Triticum*. Gliadins, which are a component of gluten, are essential for giving bread the ability to rise properly during baking) in diverse wheat varieties has revealed numbers of allele blocks on gliadin coding locus. Catalogues of protein constituents of gliadin blocks have been developed for soft bread (*Triticum aestivum* L.) [2] and spring durum (*Triticum durum* Desf.) wheats [3], and using them may allow identifying more than 20 million of genotypes.

Mass screening of the introduced into commercial growing and perspective wheat varieties using electrophoresis of their reserve proteins may purposefully allow to select samples for crossings and develop wide spectrum of variability in hybrid populations, and this could allow select forms having expected properties [4; 5].

Huge polymorphism of gliadin F-spectrum conditioned by the existence of multiple alleles of gliadin coding loci provides with a possibility to easily and effectively differentiate and identify wheat genotypes.

Materials and methods. Material for investigations were soft bread wheat (*T. aestivum*) landraces that have been collected in different regions of Uzbekistan. Analysis of grain reserve proteins (gliadins) have been done using single page electrophoresis in polyacrylamide gel in aluminum lactate buffer with pH 3.1 [2]. Gliadins were extracted from a flour of individual wheat grains by 70% ethanol. 100 grains per landrace variety have been analyzed and intra-varietal heterogeneity for each of varieties have been identified and described. To compile proteins formula, standard clustering spectrum has been used, and 30 gliadin components in that have been divided to α-, β-, γ-, ω-zones.

Results and discussion. Studying wheat landraces is of great interest concerning preservation of gene pool *in vitro* conditions and also as a genetic source of economically valuable traits in breeding process on creation of new varieties adapted well to local condition.

To study landraces of Uzbekistan, their samples have been collected from different regions of Uzbekistan. Morphological characters of samples were identified, and areas of their cultivation have been determined and mapped [6]. Samples were catalogued and characterized by grain quality and reserve proteins [6; 7].

As it has been reported previously [7] several wheat landrace samples under the same name Kyzyl Bugday were collected in mountain areas at altitudes more than 1500 meters above sea-level. All these samples had identical electrophoretic gliadin spectra. Further studies of these samples have revealed that one sample (named Kyzyl Bugday as well) from Saryosiyo district of Surkhandarya region has differed from others by absence of a component in ω-region of the spectrum.

Two more morphologically similar varieties of landraces have varied on their gliadin spectra. One of them named Ak Bugday has been collected in Kashkadarya region, and another one named *Graecum* was collected in Jizzakh region. Both of samples were with white spikes and and white colored grains and belonged to *Greacum* type but their gliadin spectra have been different.

Several samples collected were unnamed because farmers who have cultivated them did not give them any names. These samples have been divided into three groups taking into consideration their morphological and economically valuable characters studied and sites of collection. However, data of electrophoretic analyses have shown that these samples should be divided into two groups, where two samples collected from two sites of the same region have had different spectra (Fig. 1, columns 6 and 7). Landraces Surkhak, Tyuyatish, Kalbugday (awnless), BoysunTura-2 and Kyzyl Sharq were polymorphic as well each having two or three spectra.

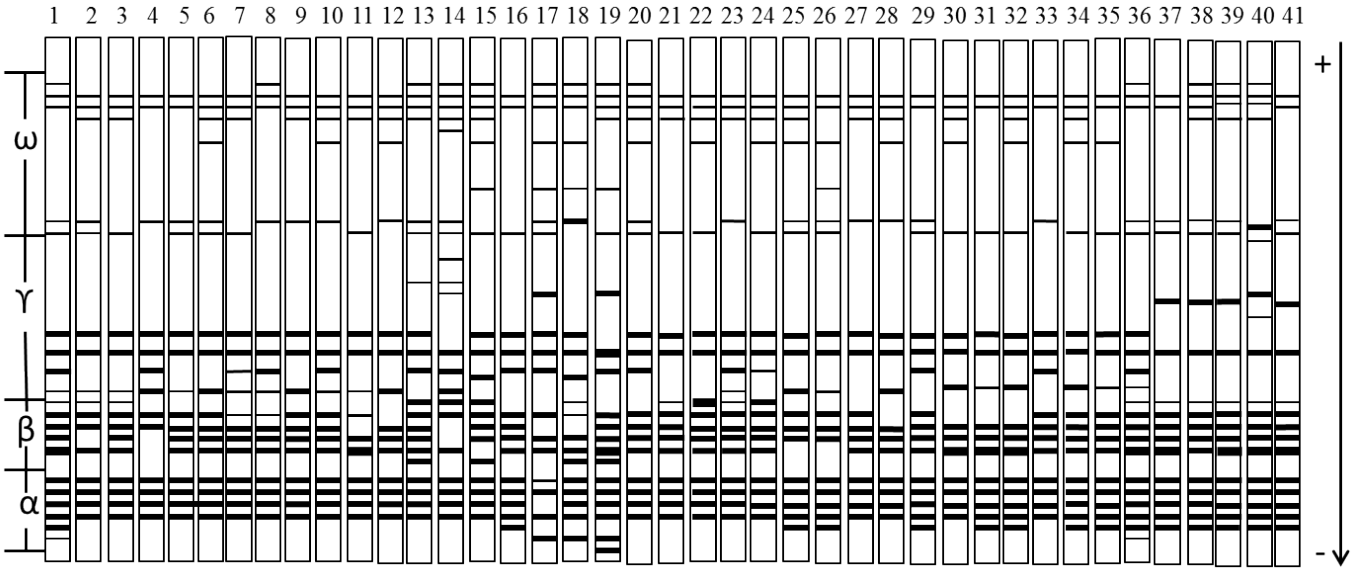

Figure 1. Polymorphism of electrophoretic spectra of gliadins

1 – Bezostaya-1 6– Unknown–(Terakli) 11–12– Tuyatish 20– Kyzyl unumli 29–Ok boshoq 37–38–Ok marvarid; 2 – Kyzyl bugday 7– Unknown–(Kyzyltom) 13–14–15– Kalbugdoy 21–22– Kyzyl Sharq 30–Pashmak 39–40–41–Bardosh; 3 – Kyzyl bug(Oltinsoy) 8– Surkhak (Uzun) 16 – Boysun Tura-1 23–24–Tuyatish 31–32–Hivit; 4 – Ok bugday 9– Surkhak (Baxmal) 17–18 – Boysun Tura-2 25–26–Korakiltik 33–34–35–Boboki; 5 – Greacum 10– Surkhak(Udamali) 19 – Qayroqtosh 27–28–Muslimka 36–Krasnodar-99

We have developed a Project aimed to collect and restore existed landraces endangered to be lost, to multiply them and bring back them to farmers for further cultivation. So, variety Kayraktash, drought tolerant, containing high amount of gluten, with medium-size plant height and moderate resistance to yellow rust, has been restored successfully. This landrace has been sown on 0.3 ha of unirrigated dryland area and 800 kgs of seeds were produced in 2014. These seeds have been cleaned and treated with fungicides. Seeds were delivered to farms for cultivation in drylands in Boysun and Altynsay dirsticts of Surkhandarya region. This restored new variety Kayraktash has been submitted to the State Variety Testing center for testing in dryland conditions. This variety had a homogenous electrophoretic spectra, having enriched components in α- and β-regions (Fig. 1, column 19).

Landrace of the durum wheat named Kara-Kiltik could be found seldom, and differed from other landraces by long, black awns, small spikes and relative compactness. Two biotypes of this landrace have been determined that differed by intensity of expression of one component in γ-region and absence of another component in ω-zone. An interesting landraces are Pashmak and Khivit having very long periods of vegetation. Pashmak has preserved its monomorphity but Hivit had two variables in electrophoretic spectra, differing by two minor components in ω-zone.

Commercial wheat variety Surkhak is cultivated in many regions of Uzbekistan where spring wheat is usually grown. It has been created in 1940's by selection amongst local landraces. It is relatively tolerant to drought and high temperatures. Its awned spikes, white, fuzzy glumes, and red seeds correspond to botanical characteristics of *Erythrospermum*. Electrophoretic analysis of reserve gliadin proteins of this variety has revealed four types of spectra, and polymorphism has been mainly in *α*- and *β*-regions.

Electrophoretic spectrum of Krasnodarskaya 99 variety is close to spectra of standard variety Bezostaya 1. Electrophoretic spectra of Ok-Marvarid and Bardosh had 2 and 3 types of electrophoregrams in *α*-region, respectively.

Conclusions. Thus, we have characterized full polymorphisms based on electrophoretic spectra of gliadins of Uzbeki-

stan wheat landraces and compared them with those of commercial varieties and newly introduced into practice cultivars. 21 landraces, two new and one commercial varieties have been analyzed and 40 electrophoretic spectra were revealed. Ten of analyzed varieties were monomorphic and 14 ones were polymorphic. Many landraces cultivated at private farms of remote regions were monomorphic, but commercial varieties cultivated on large area were revealed to be polymorphic.

As a rule, during introduction of new varieties into commercial growing practice, attention is given mainly to their productivity, resistance to adverse factors, and bread-making quality of grain. All new varieties are high productive but they luck having good of bread-making quality. Wheat landraces cultivated in Uzbekistan and other Central Asian countries cannot compete with commercial varieties on productivity. However, these wheat landraces are extremely valuable as genetic source for improving grain quality, and these genotypes could be used in development of new varieties enriched with nutritious microelements and other ingredients beneficial for human's health.

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A MODERN STATE OF PLANTS AND POPULATIONS OF RARE AND ENDEMIC SPECIES OF THE NORTHERN PART OF FERGANA VALLEY

Abstract: It has been established that the plant communities of the study area are in an man-induced dynamic state, which is characterized by a gradual increase in the number of adventive and invasive species, a decrease in the composition and phytocenotic abundance of natural dominants and subdominants, a decrease in layering, changes in the ratio of life forms towards the prevalence of ephemera.

Keywords: rare and endemic species, juniper, badlands, Fergana valley, anthropogenic landscape**.**

Currently, the territories transformed by human, represented in residential areas and agro-landscapes, occupy more than 70% of the Uzbek part of Fergana Valley, covering almost all the bottom of the intermountain trough and the foothill zone (Fig. 1). They are well identified in satellite images (Fig. 2). Herbarium collections analysis, literatures and other data show that in the first quarter of the twentieth century, existed populations of species such as *Allium anisotepalum* Vved., *A. elegans* Drobow, *A. ferganicum* Vved., *Asparagus ferganensis* Vved., *Iris oxypetala* Bunge, *I. narynensis* O. Fedtsch., *Ixiolirion ferganicum* Kovalevsk. & Vved., *Fritillaria karelinii* Poljak., *Tulipa ferganica* Vved., *Astragalus austroferganicus* Kamelin, *Dorema microcarpum* Korovin et al., extinct at present.

Figure 1. Badlands in the northern foothills of Fergana valley

Conditionally indigenous landscapes are still preserved within the limits of Uzbekistan in the bands of the northern foothills of Fergana Valley and they used mainly as pastures and having an average degree of anthropogenic transformation. This is often so-called "badlands" with plastered and saline soils (Fig. 1), there are endemic and rare species as *Acanthophyllum albidum* Schischk., *Anthochlamys tianschanica* Iljin ex Aellen, *Lamyropappus schakaptaricus* (B. Fedtsch.) Knorr. & Tamamsch., *Mogoltavia sewerzowii* Korovin et al. After 2000, a lot of new species were described from the foothills of Fergana Valley (*Allium chorkessaricum* F. O. Khass. et Tojibaev, *A. haneltii* F. O. Khass., *A. kuramense* F. O. Khass. et Friesen, et R. M. Fritsch, *A. michaelis* F. O. Khass. et Tojibaev, *A. orunbaii* F. O. Khass. et R. M. Fritsch, *A. scharobit-*

dinii F. O. Khass. et Tojibaev, *Tulipa scharipovii* Tojibaev and *T. intermedia* Tojibaev et J.J. de Groot) and most of which are narrow endemics [5]. Nevertheless, local populations of these and other species are in the zone of risk. Development of these landscapes is increasingly intensified as a population grows that leads to a reduction not only individual populations, but also plant communities. Thus, a comparison of current data with geobotanical maps of the 1970's [3; 4] shows a significant reduction in shrub areas (*Amygdalus spinosissima* Bunge, *Cerasus erythrocarpa* Nevski, *Rosa ecae* Aitch.), wormwood (*Artemisia tenuisecta* Nevski, *Botriochloa ischaemum* (L.) Henr.) and wormwood-ephemeroid phytocenosis and expansion of anthropogenic landscapes in the foothills of Chatkal and Qurama ranges.

Figure 2. territories of Yangiqurgan, Chartak and Kasansay districts of Namangan region is almost completely occupied by anthropogenic landscape, which is well identified in the CPT

Ecosystems with a relatively low degree of anthropogenic transformation in the Uzbek part of Fergana Valley are preserved in the upper high-altitude zones of Qurama Range, in Shakhimardan administrative enclave on the northern slope of Alay Range, and in the foothill zone only in strictly protected border areas (Fig. 3). These territories are habitats of many threatened, rare and endemic species. In recent years, several new species of science have been found from these areas (*Allium tatyanae F. O. Khass. & F. Karim., Iris austrotschatkalica Tojibaev, F. Karim. & Turgunov* etc.) and a number of new additions for Uzbekistan flora. However, in these territories the vegetation cover is markedly degraded, as evidenced by low projective cover (on average 30–40%), the prevalence of ephemera and a rather significant abundance of non-fed species such as *Euphorbia ferganensis B. Fedtsch*. was marked on almost all trial plots in the foothills zone.

An important characteristic that helps to identify poorly transformed areas in a satellite image is the degree of coverage of trees, shrubs and herbaceous plants, however, for their reliable selection, quite large-scale field studies were required. It was found that nowhere in the study area did not survive closed wood-shrub communities.

Based on the test of the presence of threatened plant species' populations, listed in IUCN RL, KK RUz, national and local endemics (Appendix B), key botanical territories (IPA) were identified in areas of Fergana Valley with a relatively low and moderate degree of anthropogenic transformation. A description has been published for some of these areas [6].

As far as it was found that a significant part of the investigation area is currently occupied mainly by the anthropogenic landscape, more detailed studies have focused on the remaining relatively few disturbed areas.

In Chust district, we studied thoroughly the northeastern part that on the vegetation map of 1977 [3] is marked by profiles № 17 – *Eremurus-iris-shrub* association, indicating

such dominant species as *Rosa ecae* Aitch dog rose. wild cherry (Cerasus erythrocarpa Nevski), prickly almonds (*Amygdalus spinniksissima* Bunge), Sogdian iris (*Iris sogdiana* Bunge) and *Sogdian shirat* (*Eremurus sogdianus* (Regel) Franch.) and № 18 – Eremurus bog, *Eremurus sogdianus* (Regel) Fran. *Rosa ecae, Eremurus sogdianus*) (Fig. 3, 4).

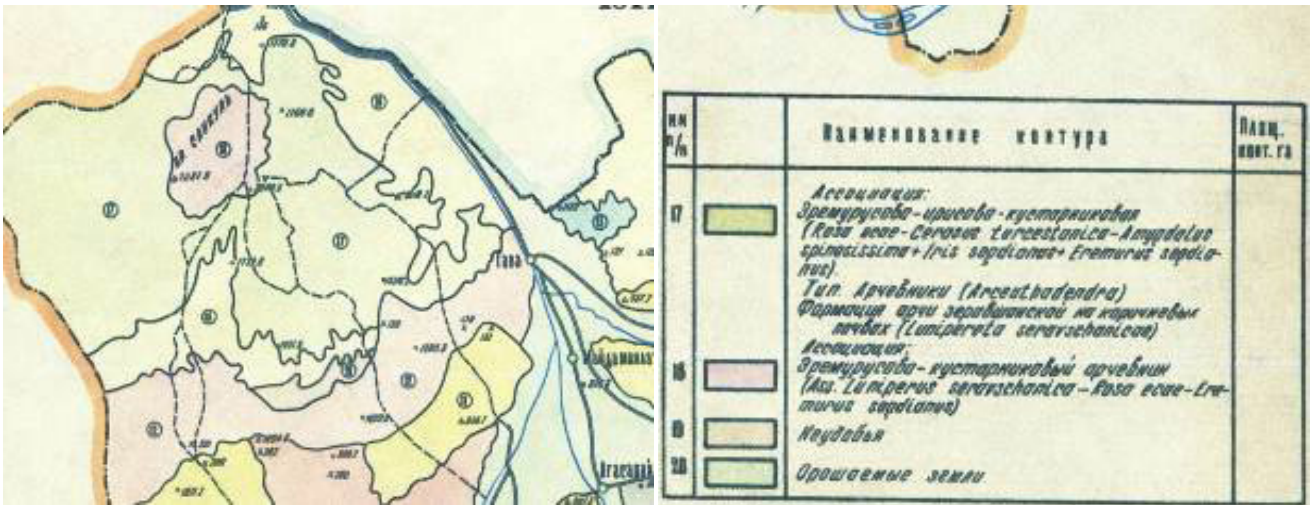

Figure 3. North-Eastern part of Chust district and the legend on vegetation map (Vernik, Rakhimova, 1977)

These associations concerned to xerophytic or xerophilous shrub vegetation type (Xerothamna) and Juniper (Juniperetum or Arcetodendra) according to "Plant cover of Uzbekistan" [8]. In the conditions of Uzbekistan, dominant species of the first of these types are prickly almond and the accompanying bushes, first, wild roses. According to the data of R. S. Wernick and T. T. Rakhimova, the main companion species in Namangan region is the Echison rosehip. This contour is located in the zone of high foothills and the lower zone of mountains (Fig. 4). In profile № 18, the dominant species, according to the data of 1977 [3], should be the Zeravshan juniper (*Juniperus polycarpos* var. *seravschanica* (Kom.) Kitam.), and abovementioned *Rosa ecae* and *Eremurus sogdianus.*

Figure 4. General view of the landscape on the profile № 17 "Vegetation maps of the Chust district of Namangan region"

We have found that nowhere in the northeastern part of Chust district, juniper forests with even 0.3 were not preserved, juniper is found sparsely, single trees that do not form a tree layer, the fullness of plantations does not exceed 0.1. It should be noted that for juniors throughout the entire area of their distribution is characterized by fragmentation and low

livestock. The average closeness of juniors in the Uzbek part of the Western Tien Shan usually does not exceed 0.3 [1]. This is primarily due to the centuries-old anthropogenic pressure. Juniper and other forests have long served the local population as sources of wood, firewood and charcoal. The forests have been used and continue to be used with excessive load as distant pastures. Unauthorized logging and unregulated cattle grazing prevent natural reforestation, lead to degradation of soil and vegetation and reduce forest area. Great damage was inflicted and continues to inflict forest fires (which often arise due to careless handling of fire). As a result, the modern forests of the Uzbek part of the Western Tien Shan are represented by fragmentary and mostly sparse stands; their composition and structure are disturbed. More or less preserved forest areas are located in remote tracts far from populated areas.

These profiles have attracted our attention for the following reasons:

As one of the background species, Sogdian Iris is indicated – *Iris sogdiana* Bunge, (now priority name is *Iris halophila* var. *Sogdiana* (Bunge) Grubov). In Central Asia, the species range includes the Zaisan basin, Kazakh low-hill marshland, the Balkhash and Aral deserts, the Karakum (Repetek), Saur, the Dzungarian Alatau, Tien Shan, Pamir-Alay, Badhyz, Kopet-Dag. In the mountain system of the Western Tien Shan, the closest growing area (to this site) is the Akhangaran River Basin (the northern slopes of the Qurama Range and the southwestern spurs of Chatkal Range). The phytocenotic optimum of the species is observed in the region of Chimgan Mountains, as well as in Western Pamir-Alai, where this species often forms local thickets. This plant is practically not eaten by livestock and in the conditions of overgrazing behaves like a pasture weed, although this fact is not mentioned in the references.

Eremurus sogdianus (Regel) Franch. Range – Tien Shan (on the periphery of the West and South Tien Shan), Pamir-Alai (on the periphery, penetrates only along Zeravshan River), Uzbekistan, Tajikistan, Kyrgyzstan, Afghanistan. It is a usual type of foothills, in Pamir-Alai rises in the lowlands.

During the field studies, Sogdian iris on the indicated contours was not detected. The studies were conducted in two seasons, including the time of species flowering and fruiting. The reasons for the absence may be the following factors:

1. The species extinction from these profiles due to an anthropogenic factor – overgrazing, collecting plants for household needs (for example, as medicinal raw materials), collecting flowers of ornamental plants, developing territories (building roads, communications), etc.

2. Confusion in the species identification. In the practice of field botany, there is often a confusion of some species with others, most often of taxonomically close species. Many types of tulips, onions, etc. can confirm this. Perhaps with field and office identification, the view was replaced by another type of iris.

According to the dominant geobotanical principles [7], the names of the identified plant associations indicate the most common (background) species and the name of the corresponding syntaxon is formed from the names of the dominant species. Therefore, the type indication in the name of the association indicates its abundance in the territory. It is this provision that reduces to "no" the first of the reasons we have indicated. The impact of anthropogenic factors (primarily grazing) could not destroy all individuals of the species in this area. Even with a strong pasturing, individual bushes of different age conditions (vegetative, generative) in various ecotopes (primarily, in hard-to-reach for livestock) remain. Rugged relief, the construction of housing, characterizes the territory or communications here has a very small scale.

Analyzing the species composition of irises of Uzbekistan or the Western Tien Shan (the study area belongs to the southern branches of Western Tien Shan), the second reason we have indicated is also in doubt. The most likely species is Dzhungar iris. However, the species range does not cover the foothill and lowland strip of Western Tien Shan. Other representatives of the genus (in the broad sense of the genus Iris L.) belong to other taxonomic sections, which is difficult to confuse with the Sogdian iris. Therefore, the fact of the disappearance of the species (using reference data) in this area, we can count on the results of subsequent field studies.

The same situation can be observed with *Eremurus sogdianus*. As already stated, the species is considered to be foothill-lowland. Rather, the dominant species for this band was Tien Shan Shyrach, which is still widespread in the mountainous part of the north Fergana Valley. Many species of this genus in Central Asia (*Eremurus kaufmanniana, E. olgae, E. regelii*, and others) are pasture weeds. Because livestock do not eat them, populations develop and cover an increasing area.

Note that *Eremurus sogdianus* was noted as one of the subdominants in Yangikurgan district territory on the profile designated № 7 (the ephemeral – wormwood association, littered with acantholimone), № 8 (*Halothamnus – winterfat – wormwood*, littered with *acantholimone*), № 12 (*wormwood* littered with *eremurus* and *euphorbia*).

Based on the conducted research, it can be concluded that the plant communities of these profiles are in an anthropogenically dynamic state. This stage is characterized by a gradual increase in the number of adventive and invasive species, a decrease in the composition and phytocenotic abundance of natural dominants and subdominants of the species (eaten willingly), a decrease in layering, changes in the ratio of life forms towards the prevalence of ephemers etc. (Fig. 5)

Plant type – Xerophytic semi shrubs, various combinations of wormwood.

The predominant type of human impact – overgrazing of livestock

The main dominant species in indigenous communities – wormwood, ephemera, geophytic onions, forbs.

The main dominant species in the secondary communities – are wormwood species, eremurus species, and adventive annuals, grazing weeds with a wide ecological and geographical amplitude

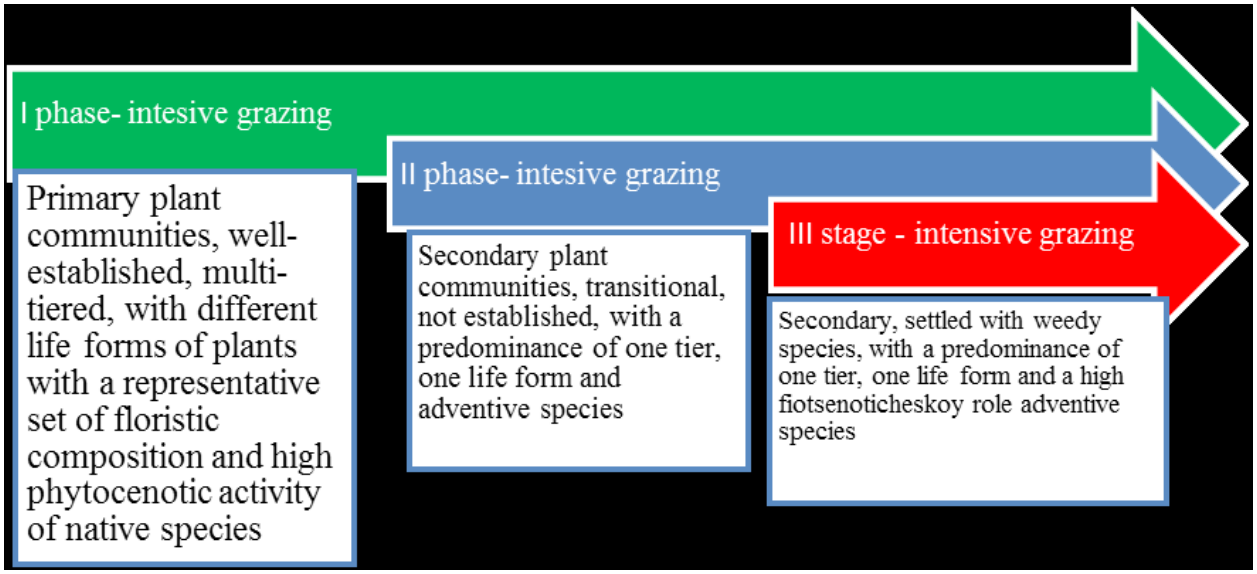

Figure 5. Diagram showing possible pathways of succession processes in communities of xerophytic semi-shrub plant in the presence of a directed anthropogenic factor

More than 50 geobotanical descriptions were compiled according to the research results on this profile. Floristic diversity reflects collected herbarium material represented by more than 150 samples.

In Yangiqurgan administrative district that according to botanical-geographical regionalization of Uzbekistan belongs to Fergana district of the Central Asian province, the following difference is observed from Chust district plants that belongs to West Tien Shan district [9]. As mentioned above, here a significantly larger percentage of the territory is occupied by a synthetic landscape. Secondly, the territory belongs mainly to the foothill zone and a significant role in the plant cover is played by wormwood and hatching and wormwood-ephemeral-ephemeroid associations (*Artemisia sogdiana* Bunge, A. *namanganica, A. tenuisecta Nevski, Salsola orientalis, Carex pachystilis, Poa bulbosa* L.). The communities of xerophilous shrubs and dry grassland steppes occupy an extremely small area (mainly on Ungortepa in the northern part of the region) (profiles № 16 and 17 on the reference map). Wonderful species of the region flora are the relict Central Asian endemic *Allium oreoscordum* Vved. and the only representative of the relict monotype of the Central Asian genus *Lamyropappus schakaptaricus* (B. Fedtsch.) Knorr. & Tamamsch. From here, two new species in science were found (*Allium tatyanae* F. O. Khass. & F. Karim. and *Iris austrotschatkalica* Tojibaev, F. Karim. & Turgunov) and a number of new additions for Uzbekistan flora. Thus, on the slopes of Ungortepa and in the vicinity of the Nanai village, new species for the flora of Uzbekistan were collected – *Eremurus altaicus* Steven, with habitats in Altai, Tarbagatai, Dzhungars Ala-Tau and Northern Tien-Shan and central Tien Shan *Iris alberti* Regel, as well as *Corydalis paniculigera* Regel et Schmalh., that within Uzbekistan was registered only from the administrative enclave of Shakhimardan.

Relic Mountain Middle Asian species of onion (*Allium oreoscordum* Vved.), mentioned above, is one of the primitive species of the *Rhizirideum* Don., the area of which is located mainly in Kyrgyzstan, on Chatkal and Uzun-Akhmat ridges. In "Flora of Uzbekistan" [10] it was included due to the collection from Ungortepa. Now, more than 70 years later, populations of this onion were found near the Ungortepa Mountain, and a new location of the species was found in the Karatag Mountains near Kasansay city.

Of great interest is the only representative of the monotypic Central Asian genus of inhabitant of the variegated strata of Lamyropappus schakaptarsky (*Lamyropappus schakaptaricus* B. Fedtsch.) Knorr. & Tamamsch., Asteraceae). The species was described in 1909 as *Cirsium schakaptaricum* O. Fedtsch. & B. Fedtsch. on a copy collected by B. Fedchenko in 1902 from the outskirts of Shakaftar kishlak in the valley of

Sumsar river (currently it is the territory of Kyrgyzstan, near the border with Uzbekistan). In 1954, according to the results of taxonomic revision, the species was transferred to the monotypic genus Lamyropappus, which belongs to the relics of Central Asian flora. The species range includes the southwestern part of Balkhash deserts and mountains in the middle course of Narin River. However, over the past 50–60 years, the habitats of the species in the northern foothills of the Fergana Valley have been almost completely developed, and the local populations of the species in the territory of Uzbekistan were considered extinct. However, in 2015, the *L. schakaptaricus* population was found in Namangan region, on adyrs to the northeast of Chartak village, in Sassiksay tract.

In addition, the rare endemic of the northern foothills of Fergana Valley, *Allium haneltii*, was found in Sassiksay boundary, which was described from Chust-Pap adyrs and was considered a narrow endemic of this region. As our field work have shown, in Chartak adyrs, the species is represented by normal populations with a density of up to 12–15 plants per 100 m^2. The list of flora of Uzbekistan was also completed by *Astragalus spryginii* Popov, *Cousinia knorringiae* Bornm. and *Pseudosedum ferganense* Boriss., found in Chartak adyrs.

Another no less important find is the discovery of another extraordinary rare species in Chartak adyrs – gypsum tick trefoil (*Hedysarum gypsaceum*). Korotkova from the territory of Kyrgyzstan described the species. In "Flora of Uzbekistan" [10] the species was included, apparently, on the basis of a single collection of M. M. Nabiyev, made in 1951 in Chartak district in the vicinity of Naritan valley. All other herbarium specimens stored in TASH belong to the territory of Kyrgyzstan. The population of the species, discovered in 2015 in the Sassiksay boundary, has about 150 of different-aged plants, seed regeneration is observed, which is due to the lack of grazing in the border zone.

To determine alterations in the flora composition, an important role is played by the initial data. However, as a rule, detailed information on this parameter is not available in geobotanical descriptions or plant maps. The composition of the species is represented by either the main species or only the dominant species. In the first case, for a particular community, a small number of species are given. For example, in the work of R. S. Wernik and T. T. Rakhimova for adyr vegetation of Namangan region [2] is given from 12 to 20 species (pp. 20–24). At the same time, in these conditions, taking into account the full composition of the flora (for different seasons and years) will give significantly more indicators. It is important that when conditions change or under the influence of a long-term certain anthropogenic factor, the composition of rare or small-numbered species be first transformed. The absence of a valuable source material does not allow fixing this fact.

On the other hand, the results of new research allow us to fix the opposite phenomenon, i.e. a large number of new floral findings – an indication of those species that were missed in previous studies. This fact quite takes place among the scientific results obtained, since they have not yet been made public or completely absent. According to the results of research in Chust district, new findings were also found. Some of them (the most significant) are listed below.

Astragalus ferganensis (Popov) B. Fedtsch.– a rare subendemic of Fergana Valley. In the collection of Central Herbarium of the Institute of the Gene Pool of Flora and Fauna of AS of Uzbekistan there are a total of 21 herbarium specimens of this species (out of 12.000 specimens of the species of astragalus in general). There is one collection from the study area – "Fergana Valley. On the way from the villages Chust and Gavasay № 1036. 05.25.1952. Arifkhanova and Gringoff", dated 1952. Another collection refers to the adjacent territories – "Fergana Valley. Yangi-Aryk irrigation region. At 1 km from the railway to the south near the village Dzandzal № 414. 06.20.1928. A. F. Ioffe". Our collections were carried out throughout Chust Pap Adyr.

Another interesting finding relates to *Campanulaceae* family. On the territory of profile № 17, we found *Cylindrocarpa sewerzowii* (Regel) Regel. In Central Asiaт Plant Identifier, this species was indicated for the Talas Alatau, Karatau, Ugam ridges within the Western Tien Shan and Turkestan, Zarafshan within the Pamir-Alay. Previously, we indicated the new location of the species on the Kuramin ridge in Chadaksay river valley. Populations of this interesting representative of Karatau-Kuchistan monotypic genus *Cylindrocarpa* were also found here. This find once again underlines the intermediate position of the Qurama Range and its connection with the Pamir-Alai flora. At the same time, this fact can serve as an argument for the belonging of the Qurama Range to the system of mountains of the Western Tien Shan. Our research shows that local populations of the species are distributed throughout the South-Western Tien Shan, because several locations were found on the Qurama Ridge (Chadaksay, northeast of the Chust district), in western Chatkal (Besharal, in the vicinity of Chimgan), upstream of Pskem river (Chiralma, Oygaing). The discovery of new populations fills a gap between the West Tien Shan and Kuchistan flora, linking the Qurama ridge with both the rest of the Western Tien Shan and the floras of the Kuchistan district of Pamir-Alai.

New discoveries relate not only to the elements of mountain floras. The foothills of the northern side of Fergana Valley are also surprised by the findings from the desert flora. So in 2015, populations of a typical Kyzyl-Kum *Bunge whole-leaf* (*Haplophyllum bungei* Trautv.) With a distribution area along the Muyunkum and lower reaches of the Chu and Sarysu

rivers were found in the adyrs between Chust and Pap; Valley Syrdarya river, Ustyurt, Mangyshlak, Pri-Karatau Plain, Kyzyl-Kum, valley of Amu Darya river, Mirzachul, valley of Zarafshan river, Karnabchul, Karshi Steppe, in the sands of Sundukli, a valley of Surkhandarya river, Shirabad valley, Karakum desert, Small and Big Balkhan and Badkhyz. This finding demonstrates the influence of the conditions of the Turan province on the composition and structure of the vegetation on the southern slopes of the Qurama Range.

In addition, several plant species of environmental interest were found within the field research. These include:

Onosma gmelinii Ledeb. (Gmelin Onosma) is an extremely rare plant for Qurama Range;

Spiraea pilosa frach. (Villous ipecac) is a typical West Tien Shan species not previously indicated for these areas.

Pistacia vera L. (Pistachio natural) – in all literary sources, local populations of the species from this territory were not indicated. Within the profile № 17 found several trees of natural origin. All individuals need protection, because grazing and cutting of trees and shrubs can lead to the destruction of a species in the area.

As far as endemic and rare species can serve as an important indicator of phytocenoses state in general, and are used in IPA allocation, during the project a special attention was paid to mapping of populations of these especially threatened plant species. In particular, they include Astragalus pseudo biflorate (*Astragalus pseudodianthus* Nabiev) – a rare plant on the southern slopes of Qurama Range, the southern spurs of Chatkal Range, endemic to Uzbekistan; prickly thrift of Nabiyev (*Acantholimon nabievii* Lincz.) is an endemic of Fergana Valley, with the main growing areas in Kyrgyzstan. On reference cards [3; 4], it is erroneously listed as *Acantholimon compactum* (endemic to the Alai Range). The studied populations of the species are located in Chust district (Mashat, Agasaray), Kasan district (Karatag) and Yangiqurgan district (adyrs in the eastern part of the district near the villages Araaryk and Pishkaran).

Thus, it was found that in the study area of the northern part of Fergana Valley, compared with the 70s of the last century, the area of man-induced transformed landscapes significantly increased, and the juniper and shrub communities strongly degraded. On the other hand, conditionally indigenous communities and populations of endemic and rare plant species of great conservation interest are still preserved in the strictly protected border area, as well as in areas with heavily dissected topography. It has been established that the plant communities of the study area are in an man-induced dynamic state, which is characterized by a gradual increase in the number of adventive and invasive species, a decrease in the composition and phytocenotic abundance of natural dominants and subdominants, a decrease in layering, changes in the ratio of life forms towards the prevalence of ephemera.

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GEOCHEMISTRY OF BIOMICROELEMENTS IN IRRIGATED SEROZEMS IN THE SOUTH OF FERGANA

Abstract: The article presents the biomicroelements composition of irrigated soil in the serozems zone in the south of Fergana. According to the content of microelements, serozems to the depth of the parent rocks are arranged in the following order: dark>typical>light. In the horizons of serozems according to Clark, the concentration of the studied microelements occupy the following row: B>Mo>Zn>Mn>Cu.

Keywords: serozem, content of biomicroelements, honey, zinc, manganese, molybdenum, boron, migration, geochemical province, concentration, Clark concentration.

Introduction. The prevalence of biomicroelements in one or another systems of nature is the most important characteristic, which reflects their role in the genesis of this system. Comparison of common biomicroelements in soil and soil-forming rocks of the object of study and plants allows us to consider and evaluate the influence of biomicro and macroelements from biogeochemical positions. The interest to biomicroelements is caused by their participation in the most important life process – exchange substances.

Back in the early sixties, A. E. Fersman [1] wrote that human economic activity in its scale and significance had already become comparable with the processes of nature itself.

The studies of V. V. Kovalsky [2], B. A. Yagodin [3], V. I. Panasin [4], G. Yuldashev and M. T. Isagaliev [5] proved the high physiological role of microelements in living organisms and their influence on soil fertility, yield and quality of crops. Their specific influence on the character of the synthesis and function of many biological active substances of plants and animals has been established.

Lack or excess of elements in soil and food, drinking water causes endemic disease of animals and human.

At present, in Uzbekistan a small number of chemical elements are successfully used in practice for regulating metabolic processes in order to improve the quality and increase the productivity of agricultural crops. Their additive to mineral fertilizers can cause certain changes in chemical, biogeochemical regimes of soil and plants.

A large number of works by D. Sattarov [6], A. Shamuratova, D. Sattarov and others [7] are devoted to this issue, where it is stated that the introduction of a small amount of micro fertilizers significantly affects soil fertility and the purposeful formation of agrochemical backgrounds for enable growth and plant development.

Solving these problems is almost impossible without knowing the level of chemical elements in soil and plants, especially those that play a special role in plant life. Currently, a direct link has been established between the content in the environment (in soil and water) of microelements (Mn, Cu, Zn, Mo, B, etc.) and photosynthesis, protein metabolism, growth processes, plant resistance to adverse environmental factors, such as lack of moisture, elevated or lowered temperatures, resistance to disease, etc.

Since microelements play an important role in the fate of living organisms, the latter ones react sensitively both to deficiency and to excess in the environment. Consequently, the study of these trace elements biogeochemical point of view is an urgent problem of irrigated agriculture and soil science.

Object and methods of the research. Trace element analysis of soil and gross and mobile forms of trace elements in soil were determined by the Kruglova and Verigina method,

the object of research is irrigated dark, typical and light serozems formed on loess and loess loams in south Fergana.

Results of the research. Any fluctuation in the content of elements in soil, and sometimes in soil-forming rocks, even in irrigated water, can cause changes in the chemical composition of the plants growing on them. While investigating soil and plants first of all elements such as Cu, Zn, Mn, B, Mo took our interest. As it was mentioned above these elements play an important role in the life of plants, as a certain physiological and biochemical role.

A study of the distribution of copper in soil has shown that dark gray soil are relatively rich in this biomicroelements. The parent rocks of the studied dark, light, typical gray earth contain almost the same amount of copper, where its gross form varies, respectively, in the intervals of 10.3–11.7 mg/kg.

As for the arable horizons of gray soil, here and in other horizons to the depth of the parent rocks according to the copper content, the dark>typical>light serozems are arranged in the following order. But at the same time, copper fluctuation in the serozem profile is 21.2–29.5 mg/kg. A relatively low content of mobile copper occurs in all subtypes of serozem, but the tendency to reduce its content from dark to light serozem persists.

Elementary landscape largely determines the level of content of mobile and gross forms of biomicroelements in soil blocks. The content of copper and molybdenum was very low compared to other trace elements. The content of zinc and boron was relatively close to each other. A high content of manganese was observed both in soil and in soil-forming rocks. But it should be noted that in soil-forming rocks the content of gross manganese is almost 2.5–3 times less than in soil, which is due to the properties of eluvial, rocky soil-forming rocks.

Trace elements Cu, Zn, Mn, Mo, B are vital for cotton, wheat plants and they cannot be replaced by other elements and play a specific biogeochemical role. The need for cotton and other crops of the cotton complex in these trace elements has been proven by Kruglova, Aliyeva [8], Sattarov, Yagodin, and others [6; 3]. In the conditions studied by us, the soil factor contributing to the deficiency in the migration of trace elements can be attributed to carbonate content (6–10%), gypsum in the zone, low humus content and the formation of barriers on the transitional-carbonate-illuvial horizon.

But it should be remembered that the main source of trace elements for crops in the irrigated area is soil. Despite the fact that in agronomic practice, mobile forms of microelements are important, in geochemical studies, their gross forms in the soil play an important role.

Copper accumulation in the upper horizons, a characteristic feature of the distribution of copper in the soil profile. This phenomenon is primarily associated with the results of the influence of various soil-geochemical factors.

Basically, the concentration of copper in the top layer of soil reflects its bioaccumulation at the sorption and humus barrier, as well as modern anthropogenic influence. In the soil of the serozem belt studied by us, the copper content in the soil horizons, with the rare exception of subsurface horizons, where copper is less than 22 mg/kg, is contained within 24.8–29.1 mg/kg, which gives basement to classify the serozems of southern Fergana secured by copper. According to above mentioned, we can conclude that the foothill landscapes according to the classification of Kruglova and Aliyeva belong to the provinces of sufficient copper content in the soil. Irrigated dark, typical, light gray soil on the content of gross copper are geochemical enrichment provinces.

The average zinc content in the surface layers of soil dark and typical gray makes up 121.2–131.3 mg/kg, in light gray soil 73.1 mg/kg, and in arable horizons in soil-forming rocks of gray soil 43.1–48.4 mg/kg. According to this indicator, irrigated dark and typical serozem, where the zinc content is more than 100 mg/kg belong to the group of soil with excessive content.

The soil of the serozem series, that is, the dark serozem contain manganese more than 600–800 mg/kg, it contains up to 900 mg/kg, whereas in the arable horizons of typical and light serozem it contains 685.4–708.3 mg/kg In the underlying horizons, manganese is contained not less than in arable horizons. Even in some horizons it is observed more than in arable depths.

The content of molybdenum in the soil was close to their concentration in parent rocks and varies in the intervals of 2.5–3.1 mg/kg. In the arable horizons it contains 3–3.5 mg/kg, approximately the same pattern is repeated in the subsoil horizons. In this case, the soil of the serozem belt can be attributed to the provision of molybdenum to the normally secured (>1–3 mg/kg).

In the earth's crust and in soil, boron is distributed nonuniformly. It concentrates mainly in the surface soil horizons. Its content in the arable horizons of the studied soil of the serozem series varies in the intervals of 73–97 mg/kg, whereas in the subsoil horizons it contains 75–81 mg/kg. From the data it is clear that there is no deficit in boron, but an excess. The soil of the gray earth belt can be attributed to the geochemical enrichment provinces in terms of boron content.

Below are the rows of Clarke concentrations (CC) and Clarke scattering (Cp) of elements in these soil (table). It can be seen from the above materials that the CC of boron in the arable horizons of the studied soil varies from 6.1–8.1 with a higher concentration corresponding to irrigated dark serozem, which is associated with the genetic characteristics of dark serozem. In the remaining soil of the serozem range, the content takes intermediate situation.

Clark series of trace element concentrations in soil (upper horizon)

Name soil	Gross	Movable
Irrigated dark serozems	$\frac{B}{8.09} > \frac{Mo}{3.2} > \frac{Zn}{1.58} > \frac{Mn}{0.9} > \frac{Cu}{0.63}$	$\frac{Mo}{0.32} > \frac{B}{0.18} > \frac{Cu}{0.07} > \frac{Mn}{0.03} > \frac{Zn}{0.02}$
Irrigated typical serozems	$\frac{B}{6.86} > \frac{Mo}{3.18} > \frac{Zn}{1.46} > \frac{Mn}{0.71} > \frac{Cu}{0.53}$	$\frac{Mo}{0.25} > \frac{B}{0.17} > \frac{Cu}{0.09} > \frac{Mn}{0.05} > \frac{Zn}{0.02}$
Irrigated light serozems	$\frac{B}{6.09} > \frac{Mo}{2.74} > \frac{Zn}{0.88} > \frac{Mn}{0.69} > \frac{Cu}{0.45}$	$\frac{Mo}{0.22} > \frac{Mn}{0.17} > \frac{Cu}{0.04} > \frac{B,Zn}{0.02}$

CC of gross boron in serozems in southern Fergana in the humus horizon varies within 6.09–8.09, that this position is related to a higher content of humus. The size of the boron from top to bottom in the profile and in the verticality of the serozems gradually decreases to 4.83 in the parent rock. As expected, after boron, the second place is occupied by molybdenum CC with a CC of 3.2–2.7. In general, in the arable layers of serozem by CC, the studied elements occupy the following row: boron > molybdenum > zinc > manganese > copper.

Conclusions. Taking into account the gradation of soil on the content of trace elements are available to plants and their content in the soil of serozem, the following can be noted: according to the content: the mobile form of copper, these soil belong to the II-group of normal and secured; zinc in the soil of serozem range, where it contains 0.95–1.94 which belong to the group of poorly secured and secured; mobile manganese serozem poorly endowed, the content of mobile manganese in dark serozems, where it contains 16–36 mg/kg; rolling boron soil are located on the border of increased secured and enriched (0.27–2.1 mg/kg); in molybdenum can be attributed to the group normally and highly secured.

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STUDY ON SOME PARAMETERS OF LIPID METABOLISM IN THE CEREBRAL TISSUES OF RATS WITH THE ROTENONE – INDUCED MODEL OF PARKINSON'S DISEASE

Abstract: The work was initiated to study the role of lipids, lipid peroxidation processes and antioxidant enzymes of the cerebral tissues of rats with the rotenone-induced model of Parkinson's disease. An attempt to find correlations between the behavioral performance of rats and changes in lipid compositions of the brain regions within the various periods of experimentally induced Parkinson's disease was made. Changes in the behavioral performance of the animals were established to take place on the 2nd day after administration of rotenone, to increase peaking on the 4th day, and to decrease on the 9th day. The changes in the behavioral performance of the animals with the neurodegenerative disease in question was found to correlate with changes in lipid composition of their cerebral tissues within the various periods of the experimentally induced neurodegenerative disease.

Keywords: neurodegeneration, Parkinson's disease, behavioral tests, corpus striatum, lipids, phospholipids, cholesterol, lipid peroxidation, antioxidant enzymes.

Introduction. Today, degenerative nerve diseases, also called neurodegenerative diseases, are figuring larger among underlying causes of work decrement and mortality increase. However, regardless of the enormous aggregation of data on the factors underlying the onset of the diseases, understanding of mechanisms accounting for the processes is far from perfect. The extracellular deposition of amyloid-beta protein followed by formation of the senile plaques inducing apoptosis, causing pathological activation of the microglia and initiation of the immune inflammation is suggested as a key aspect [1; 2; 3]. At the moment, the role of sphingomyelin cycle in apoptosis and a neurodegenerative disease's onset is under discussion [4; 5; 6]. Meanwhile, there is no the single viewpoint of the root cause for neurodegenerative diseases ultimately resulting in the death of brain cells. In our opinion, a disorder in lipid metabolism causing secondary changes in

the biochemistry of amyloid-beta protein and tau protein, as well as in reactions of oxidative stress, is a potential cause for the onset of neurodegenerative diseases.

In the view of the aforesaid, the work was initiated to study the role of lipids, lipid peroxidation processes and antioxidant system of the cerebral tissues in the rotenone-induced model of Parkinson's disease.

Materials and methods

The experiment was conducted on the outbred rats weighing 250–300g kept on a standard diet. Prior to administration of rotenone, all rats were subjected to the cognitive tests [7; 8]. For the purposes of experiment, all animals were divided into three groups, to name the group including intact animals (IG), the exposure group (EG) consisting of animals receiving rotenone in the vegetable oil intraperitoneally in the dose of 2.5 mg per kg of animal's weight for 7 days and the control group consisting (CG) of animals intraperitoneally receiving the vegetable oil. The McGraw Stroke Index Scale was used to evaluate the neurological status of the animals; behavioral activity was assessed be means of the open field test on the 2nd, 4th and 9th day after rotenone administration. Materials for biochemical and histological investigation from the striatum were taken on the 12th day after rotenone administration. The Bligh and Dyer method was used for total lipid extraction [9]. Fractionation of lipids was performed by the thin-layer chromatography according to M. Kates [10]. Phospholipid quantification was performed as described elsewhere [11]. The cholesterol was determined as described elsewhere [12]. The total protein was determined with modified Lowry method according to Hartree [13]. Initial levels of the substrates reactive with thiobarbituric acid were determined as described elsewhere [14]. Activity of antioxidant enzymes, such as catalase, superoxide dismutase and glutathione reductase was estimated as describes elsewhere [15; 16; 17]. Cary 60 spectrophotometer (Agilent Technologies, USA) was used to make optical measurements. Student's t-test was used to process the data.

Results and discussion

Prior to Parkinson's disease (PD) modeling, behavioral performance of animals was tested to evaluate main PD symptoms, such as hypokinesia, bradykinesia and oligokinesia, postural instability, unsteadiness of gait, and the accessory ones, to name muscle rigidity and tremor, which are not always present in experimental PD [18]. Total symptom intensity was scored (from 1 to 18), as well [19].

The 7-day administration of rotenone was demonstrated to cause some changes in the behavioral performance of the animals in the open field test (Table 1, Fig. 1).

Table 1.– Behavioral performance of animals in the open field test

Behavioral activity	Groups of animals		
	Intact (n=5)	Control (n=5)	Exposure (n=15)
Latent period (s)	52.3 ± 15.3	44.5 ± 20.3	90.6 ± 25.6
Distance traveled (м)	13.4 ± 7.8	12.5 ± 8.5	4.3 ± 2.1
Line crossings (n)	19.2 ± 2.0	17.3 ± 1.6	4.6 ± 1.1**
Squares transversed (n)	54.5 ± 16.4	52.3 ± 8.3	8.6 ± 4.2**
Groomings (n)	2.5 ± 0.5	2.4 ± 0.3	1.6 ± 0.2
Frequency of head-dipping	25.2 ± 5.4	20.3 ± 6.3	7.4 ± 3.1*

** significance level $p \geq 0.05$*

*** statistically significant differences, significance level $p < 0.05$;*

Confirming the presence of PD symptoms, our findings in the open field test are consistent with the literature data reporting an elongation of the latent period in adaptation of animals to new conditions, and a reduction in the distance traveled in the playpen and as a consequence, the number of the line crossings, of the squares transversed and of the frequency of hear-dipping.

Our findings demonstrated that the main PD symptoms, such as retardation of motion and reduction in its frequency, as well as postural instability and unsteadiness of gait manifested as late as on the 2nd day after rotenone administration. The accessory ones, the rigidity, in particular, appeared on the 4th day; as to the resting tremor, the symptom could be seen in 10% of the animals on the late PD stages.

The dynamics of behavioral performance in the animals early in the course of the rotenone – induced model of Parkinson's disease seems to be a result of changes in lipid compositions of dopamine receptors' (DR) rafts and synaptic compartments with the functional properties strongly determined by the lipid compositions of the nerve cell membranes.

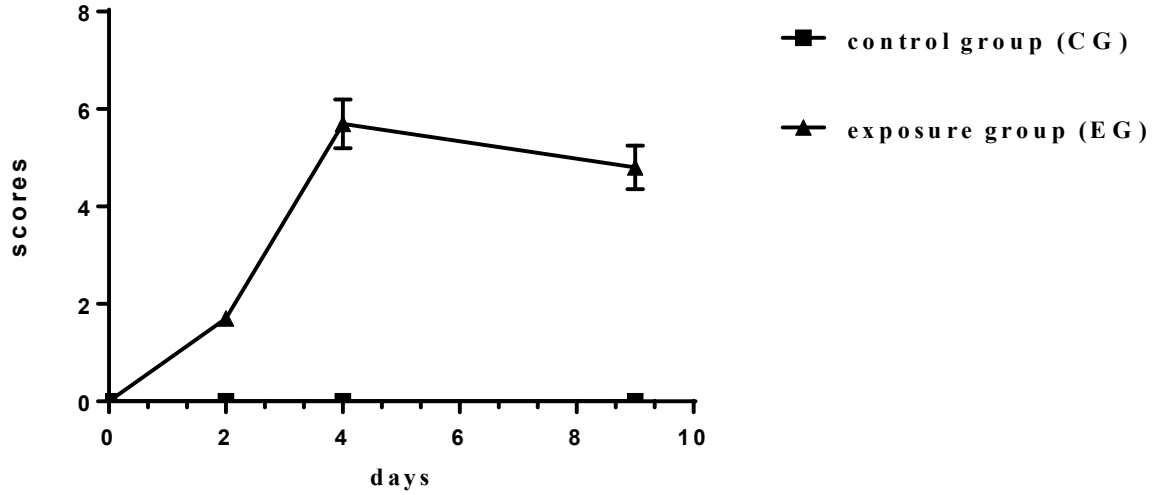

Figure 1. Changes in behavioral activity of rats according to the McGraw Stroke Index Scale on the 2nd, 4th and 9th day after administration of rotenone: *x* axis – scores in the cognitive test, *y* axis – days of experiment

In the view of the above, the lipid composition, lipid peroxidation and antioxidant enzymes' activity in the brain of animals from the control and the exposure group were studied. Table 2 demonstrated changes in lipid composition of the brain tissues of rats with the rotenone – induced model of Parkinson's disease on the 2nd, 4th and 9th day of rotenone administration.

Table 2. – Lipid composition of striatum regions of the rat brain on the 2nd, 4th and 9th day after rotenone administration

Phospholipids and lipids	Control group	Exposure group (n=15)		
	Time after administration	2nd day	4th day	9th day
	μg of rotenone/g of tissue	μg of rotenone/g of tissue	μg of rotenone/g of tissue	μg of rotenone/g of tissue
Lysophospholipids	10.9 ± 0.5	12.5 ± 0.6	16.4 ± 0.3**	13.1 ± 0.4**
SPH	131.2 ± 3.8	120.7 ± 3.3	111.5 ± 3.2**	118.1 ± 3.1**
PC	589.38 ± 28.6	571.6 ± 25.6	554.0 ± 21.3	560.0 ± 20.6
PS	197.4 ± 9.5	177.7 ± 6.5	167.8 ± 5.6**	156.4 ± 5.1**
PI	91.7 ± 4.8	85.3 ± 3.2	78.9 ± 2.5	82.5 ± 3.1
PE	506.6 ± 22.4	491.4 ± 20.3	476.2 ± 15.6	486.3 ± 19.1
Cardiolipin	61.2 ± 3.1	60.0 ± 3.5	55.1 ± 2.5	58.1 ± 2.1
PA	15.4 ± 0.8	16.9 ± 1.0	17.6 ± 1.1	17.2 ± 1.2
Total phospholipids	1604.2 ± 32.6	1536.1 ± 30.3	1477.4 ± 35.2**	1491.8 ± 36.3*
TC (mg/g of tissue)	19.3 ± 0.3	19.8 ± 0.2	21.9 ± 0.1**	21.0 ± 0.3

Abbreviations: ***SPH*** *– sphingomyelin,* ***PC*** *– phosphatidylcholine,* ***PS*** *– phosphatidylserine,* ***PI*** *– phosphatidylinositol,* ***PE*** *– phosphatidylethanolamine,* ***PA*** *– phosphatidic acid,* ***TC*** *– total cholesterol;*

*** statistically significant differences, significance level $p < 0.05$;*

** significance level $p \geq 0.05$*

As our findings demonstrated, on the 2nd day after rotenone administration concentrations of cholesterol, lysophospholipids and phosphatidic acid (PA) tended to increase while those of sphingomyelin (SPH) fractions, phosphatidylserine (PS) and phosphatidylinositol (PI) appeared to decrease. Total phospholipids changed insignificantly. On the 4th day after rotenone administration, the tendency above seemed to preserve, but the range of changes was more significant than of those seen on the 2nd day (Table 2). Thus, cholesterol, lysophospholipids and PA can be seen to increase by 8%, 50%

and 14%, respectively, both SPH and PS decreased by 15%, while PI reduced by 14%. There was 8% reduction in the total phospholipids.

Cholesterol was found to increase by 6% on the 9th day after rotenone administration. As compared to those in the control animals, concentrations of lysophospholipids and PA were increased, while those of SPH, PS and PI appeared to reduce, but their absolute values were lower than those observed on the 4th day after rotenone administration. Less significant changes in lipid composition of the brain tissues could be attributed to lower accessibility of the substrates by phospholipases and LPO.

The role of cholesterol, phospholipids and lipid peroxidation in the functioning of the nerves remains obscure. Some authors demonstrated the crucial role of cholesterol, phospholipids and other components in the neuroplasticity, neurility and apoptosis of the nerve cells (20, 21, 22). According to Isakina (23), concentrations of PI and PE reduced by 30.3 and 8.4%, respectively, in the stimulated nerve as compared with those in the non-stimulated one, and the data could be the evidence for close relationship between lipid components of nerve cell membranes and neurility.

The changes we have found in phospholipids seem to affect the neuroplasticity of the synaptic part and neurility and to be a cause for changes in the behavioral performance of the animals with the rotenone-induced Parkinson's disease. LPO and antioxidant enzymes are known to have a significant effect on the lipid composition of cell membranes. With that in mind, we studied LPO products and activity of some antioxidant enzymes in the brain regions of interest within the various periods of rotenone administration. Changes in LPO parameters and activity of antioxidant enzymes in the regions of interest on the 2nd, 4th and 9th day after administration of rotenone (in %) can be seen in (Fig. 2).

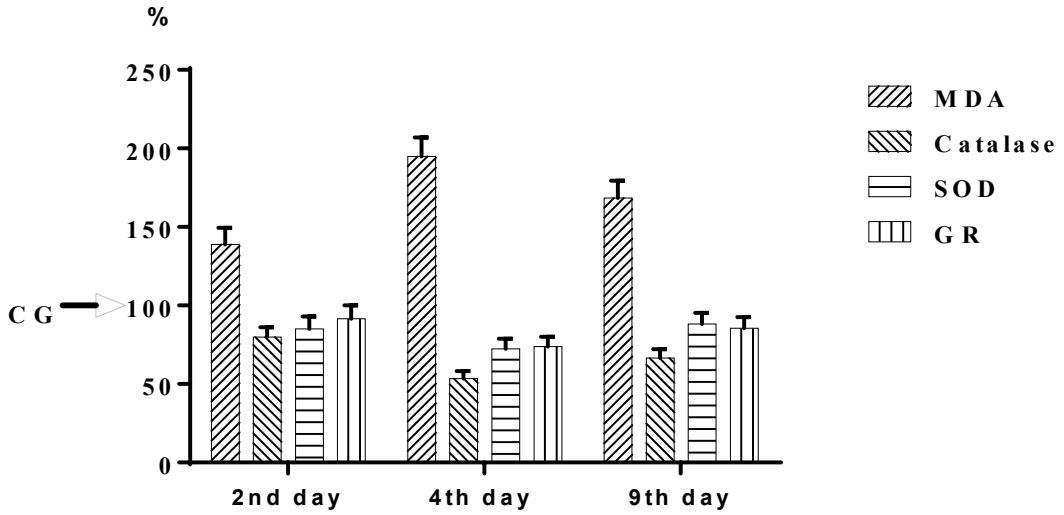

Figure 2. Changes in LPO parameters and activity of antioxidant enzymes in the striatum regions of interest on the 2nd, 4th and 9th day after administration of rotenone (in percentage of control)
MDA – malondialdehyde; SOD – superoxide dismutase; GR – glutathione reductase; CG – control group.

The LPO activation could be seen as late as on the 2nd day after rotenone administration with more significant stimulation on the 4th day and slight reduction on the 9th day. Presumably, this can be explained by lower accessibility of the substrates to LPO. In the context of reduction in total phospholipids upon experimental induction of Parkinson's disease, levels of phospholipids rich with the unsaturated fatty acids seem to reduce too.

According to Isakina (23), upon nerve stimulation LPO products increased, while concentrations of diene conjugates and malondialdehyde are 20.4 and 27.7% higher, respectively, than the control ones. This can be the evidence for the fact that certain levels of LPO products is constantly present in the nerve tissue, and only a concentration threshold crossing results in neurodegenerative diseases.

In accordance with our findings, changes in lipid composition of the brain regions of interest appear as late as on the early stages of experimentally induced PD. Intensification of the changes seems to have a significant effect on the signal reception and transduction by the nerve cells to result in changes of behavioral performance of the animals with experimentally induced PD. The increase in the levels of cholesterol in the cerebral tissues upon the PD model of interest seems to be associated with its unique property to impact and maintain the microviscosity of cell membranes.

Thus, levels of cholesterol and phospholipids, as well as LPO activity and the one of antioxidant system are the most significant factors having an impact on physical properties of cell membranes facilitating optimal conditions for the recep-

tor and synaptic parts of neurons. Changes in the parameters upon experimentally induced model of the disease seem to be a cause for changes in the behavioral activity of the animals.

Conclusions

To sum up, concentrations of cholesterol and phospholipids, as well as activity of the LPO and antioxidant system are the factors producing the most significant effect on physical properties of cell membranes facilitating optimal conditions for the function of receptor and synaptic parts of a neuron. Changes of the parameters generated upon experimentally induced neurodegenerative disease in animals seem to be a cause for changes in their behavioral performance.

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TAXONOMIC ANALYSIS OF ALGAE SPREAD IN ECOSYSTEMS OF THE CITY

(as an example of Andijan city)

Abstract: The analysis of several common algae species on the ecosystem in the city of Andijan. There are 100 types of recreational areas, 116 species in the residential areas, 95 in the industrial area and 76 species in the area of transport.

Keywords: Soil algae, recreation, residential, industry, transport, taxonomic.

The Ferghana valley, the Central Asian pearl, including the beautiful nature of the Andizan Region, is well-known not only for Uzbekistan, but also for the entire population of Central Asia and other countries. One such site is the city of Andijan, which is one of the most important issues in the analysis of the current development of soil algae in the current ecological state, which is spread in various environmental zones such as recreation, residential, industry and transport.

There are recreational objects – amusement parks, small dendroparks in the city. Navoi, Bogi Babur, Children's Park, Nodirabegim and other amusement parks in Andijan are the ideal places for the city's guests.

In the scientific literature [1], urban settlements, anthropogenic landscapes, that is, cultural, administrative, medical, educational institutions, small gardens (green zones) are called settlement zones.

In Andijan there are recreation areas, residential areas, production facilities, companies and major transport routes. The main source polluting the atmospheric air, soil and water reservoirs of the city is the emissions from the production process and smoke from vehicles [3; 5; 7]. We can clearly see the anthropogenic impact on living organisms, including soils, in such ecological areas. Residential, recreational, industrial, and transportation areas of Andijan city were selected and sampled from the points identified in the city map.

Fritsch a John's (1942) "soil culture" and "water culture" methods were used in studying systematic, taxonomic composition of algae in the soil. (Hollerbach, Shtina and others).

100 samples of soil specimens from soil samples taken from recreation areas of Andijan city were identified. They systematically concern 5 sections, 8 classes, 18 orders, 33 families and 46 categories. The taxonomic composition of the algae flora of recreation area soils is shown in the chart below.

Table 1.– The taxonomic composition of the algae flora of recreation area soils

№	Parts	Number of taxons, in percentage											
		classes		orders		families		species		types		Types and kinds of types	
		number	percent	number	percent	number	percent	Number	percent	number	percent	number	percent
1	Cyanophyta	1	12.5	2	11.11	8	24.24	12	26.1	32	32.65	33	33
2	Chlorophyta	4	50.0	9	50.0	16	48.49	19	41.3	40	40.82	40	40
3	Xanthophyta	1	12.5	4	22.22	4	12.12	7	15.22	13	13.27	13	13
4	Euglenophyta	1	12.5	1	5.56	1	3.03	2	4.35	4	4.08	4	4
5	Bacillariophyta	1	12.5	2	11.11	4	12.12	6	13.03	9	9.18	10	10
	Total	8	100	18	100	33	100	46	100	98	100	100	100

According to the parts *Cyanophyta* consists of 33 percent. Consisting of 40 types among algae *Chlorophyta* has made 40 percent. These two parts has made 73 percent with 73 types in the flora of recreational area. *Xanthophyta* has made 13 percent with 13 types, *Bacillariophyta* has made 10 percent with 10 types. The fewest type (4) belongs to the part of *Euglenophyta*. In the respect of biological variety class 50 percent of types belong to the part of *Chlorophyta*. In the number of taxons belonging to the orders *Chlorophyta* consists of 50 percent. 4 orders in the part of *Xanthophyta, Cyanophyta* and *Bacillariophyta* have 2 taxons each concerning the order. According to the orders *Chlorophyta* has the most taxons, but

belongs to the *Euglenophyta* part of the fewest taxons. In the variety according to families of taxons, it has made 48.49 percent with 16 families, and in *Cyanophyta* part it is as twice as few (24.24%). *Xanthophyta* and *Bacillariophyta* have made 12.12 percent each having 4 families. According to the number of species *Chlorophyta* has made the most – 41.3 percent whereas *Cyanophyta* – 26.1 percent, *Xanthophyta* – 15.22 percent. According to the number of types *Chlorophyta* is in the first place making 40.82 percent of all the types and reresentatives of *Cyanophyta* part has taken the second place with 32.65 percent. There is no mutual closeness in the number of taxons belonging to each part.

Dominant types are various and belong to the 3-part: *Lyngbya foveolatum, Microcoleus vaginatus, Phormidium autumnale, Ph. boryanum, Ph. formosum, Nostoc punctiforme, Cylindrospermum lichenoforme* from *Cyanophyta* part were more frequently encountered; *Hantzschia amphyoxys* from *Bacillariophyta* part were more frequently encountered than the others. *Chlamydomonas gloeogama, Bracteacoccus minor, Chlorella vulgaris* from *Chlorophyta* part were frequently encountered in the row of dominants.

The soil samples taken from the further residential areas were studied and totally 116 types of algae were identified in these samples. Taxonomically they belong to 5 parts, 8 classes, 9 orders6, 38 families, 51 species. Number of types corresponding to the same class is equal to 14.5; the same order – 12.9 the same family – 3.05, the same species – 2.27. Among them, *Cyanophyta* part was the most spread and consisted of 42 types, its share made 36.21 percent. *Chlorophyta* part consisted of 31 types, its share was 26.71 percent, *Bacillariophyta* part consisted of 22 types, its share was 18.97 percent, *Xanthophyta* part consisted of 18 types, its share was 15.52 percent, the least spread one was *Euglenophyta* part, which consisted of 3 types, its share was 2.59 percent.

Table 2. – The taxonomic composition of the algae flora of residential area soils

№	Parts	Number of taxons, in percentage											
		Classes		orders		families		species		types		Types and kinds of types	
		number	percent	number	percent	number	percent	number	Percent	number	percent	number	percent
1	Cyanophyta	1	12.5	2	22.22	10	26.32	15	29.42	42	37.17	42	36.21
2	Chlorophyta	4	50.0	3	33.33	15	39.47	20	39.22	30	26.55	31	26.71
3	Xanthophyta	1	12.5	2	22.22	4	10.53	7	13.72	18	15.93	18	15.52
4	Euglenophyta	1	12.5	1	11.11	2	5.26	3	5.88	3	2.65	3	2.59
5	Bacillariophyta	1	12.5	1	11.11	7	18.42	6	11.76	20	17.7	22	18.97
	Total	8	100	9	100	38	100	51	100	113	100	116	100

According to the number of types in their taxonomic composition, *Cyanophyta* and *Chlorophyta* parts covered 2/3 piece, namely, 62.92 percent, *Bacillariophyta* and *Xanthophyta* made 34.49 percent. C*yanophyta* part of the taxons is related to the alkalinity of soil conditions, in particular, the increase in intoxication, resuscitation, and natural conditions of lighting. Taxonomy of the *Chlorophyta* part is associated with the appearance of an ephemeral character with the appearance of anemic states for the organism with a transition to an increase due to the loss of moisture in the development of *Bacillilarophyta* [5–7].

Biodiversity in the soil of industrial enterprises, firms, firms is relatively small compared to other ecological regions studied. 95 types of algae belonging to 7 classes, 16 orders, 34 families, 44 species were identified in this area. All the types' correspondence to the same class made 13.57; to the same order – 5.93; to the same family – 2.79; to the same species – 2.16. *Cyanophyta / Chlorophyta ratio* is 1.42; *Cyanophyta / Bacillariphyta* ratio is 3.38. Biodiversity of taxons belonging to *Xanthophyta* and *Euglenophyta* parts is fewer than those of other parts.

Table 3. – The taxonomic composition of algae in the soils of industrial areas

№	Parts	Number of taxons, in percentage											
		class	%	order	%	family	%	species	%	type	%	Types and kinds of types	%
1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
1	Cyanophyta	1	14.3	2	12.50	9	26.47	13	29.55	43	47.23	44	46.32

1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
2	Chlorophyta	3	42.8	9	56.25	17	50.0	20	45.45	30	33	31	32.63
3	Xanthophyta	1	14.3	2	12.50	3	8.82	3	6.82	4	4.4	4	4.21
4	Euglenophyta	1	14.3	1	6.25	1	2.94	2	4.54	3	3.3	3	3.16
5	Bacillariphyta	1	14.3	2	12.50	4	11.77	6	13.64	11	12.07	13	13.68
	Total	7	100	16	100	34	100	44	100	91	100	95	100

Taxons belonging to *Cyanophyta* part consist of 44 types and have made 46.32 percent. Taxons belonging to *Chlorophyta* part consist of 31 types and have made 33 percent. Taxons belonging to *Bacillariophyta* are few, they consist of 13 types and have made 14 percent. 4 and 3 types were recorded from *Xanthophyta* and *Euglenophyta* part.

According to the number 3 parts were the most among taxons identified in the soils of industrial areas: species types of *Phormidium autumnale, Ph. favosum, Microcoleus vaginatus, Lyngbya foveolarum* were frequently encountered in *Cyanophyta* part*; Hantzshia amphyoxys, Navicula atomus, N. mutica* were frequently encountered in *Bacillariophyta* part*;* species types of *Chlamydomonas* were frequently encountered in *Chlorophyta* part, cocoid structure types such as *Chlorococcum humicola, Chlorella vulgaris* were frequently encountered.

"Uzbekistan", "Bobur", "Navoi" and "Istiqlol" are the avenues with the heaviest traffic in the city of Andijan. 76 species were identified in 32 soil samples taken from 0.5, 1.0 m beside the asphalted areas of these streets. In terms of taxonomy, they belong to 6 parts, 9 classes, 19 orders, 30 families, 40 species. The resulting data are presented in the table below.

Table 4.– The taxonomic composition of algae in the soils of heavy traffic motorways

№	Part	Таксонлар сони, фоизи											
		class	%	order	%	family	%	species	%	type	%	Types and kinds of types	%
1	Cyanophyta	1	11.11	2	10.53	8	26.67	10	25.0	31	41.89	31	40.79
2	Chlorophyta	4	44.45	10	52.63	13	43.33	17	42.5	26	35.14	27	35.52
3	Xanthophyta	1	11.11	3	15.79	3	10.0	4	10.0	4	5.41	4	5.26
4	Euglenophyta	1	11.11	1	5.26	1	3.33	2	5.0	3	4.05	3	3.95
5	Bacillariophyta	1	11.11	2	10.53	4	13.34	6	15.0	9	12.16	10	13.16
6	Pyrophyta	1	11.11	1	5.26	1	3.33	1	2.5	1	1.35	1	1.32
	Total	9	100	19	100	30	100	40	100	74	100	76	100

On the heay traffic motorways whose taxonomic composition was studied: *Cyanophyta* made 40.79 percent 31 types, *Chlorophyta* made 35.52 percent having 27 types; *Bacil1ariophyta* made 13.16 10 types, and *Xanthophyta, Pyrophyta, Euglenophyta* made 10.53 percent having totally 8 types. The number of the types belonging to the same class was 8.4; to the same order – 4.0; to the same family – 2.53; to the same species – 1.9.

As in the industrial area, there are 58 species of Cyanophyta and Chlorophyta in these systems, with 76.31% of the total algae in the transport area. There are few biodiversity varieties in the remaining 5 species. This situation is characterized by a number of factors and specific features of the algae of these branches.

The taxons belonging to the *Xanthophyta* sector, which are "sensitive" to soil contamination, were less recorded in the samples. Although taxons of the *Xanthophyta* part, which are considered to be the base of the soil, are more common, their biological diversity is often not significantly significant.

The following taxons from the *Cyanophyta, Chlorophyta, Bacillariophyta* parts were more frequent according to algae samples: *Phormidium autumnale, Ph. boryanum, Microcoleus vaginatus, Oscillatoria brevis, O. Formosa, Chlorococcum humicola, Chlorella vulgaris, Stichococcus minor, S. Choolatii, Navicula radiosa, Hanthschia amphyoxys, Nitzschia palea.*

The following taxa were always found in each sample: *Phormidium autumnale, Ph. boryanum, Microcoleus vaginatus, Oscillatoria brevis, O. formosa, Synechococcus aeruginosus, Stigonema minor. Euglena terricala, Characiopsis minama, Navicula minuscula, Amphora veneta, Hautzschia amphyoxys. Chlamydomonas humicola, Chlorella vulgaris, Trochisia aspera.*

Algae types belonging to 100 samples of soil specimens taken from the recreational areas of Andijan city were identified. Systematically, they belong 5 parts, 8 classes, 18 orders,

33 families and 46 species, and ranked second among biodiversity species among analyzed ecological areas.

Soil algae of total 116 species of algae have been identified in the samples taken from the soil of residential areas. Taxonomically, they belong to 5 parts, 8 classes, 9 orders, 38 families, 51 species and ranked first among biodiversity species.

The further algae identified in the samples taken from industrical ecological area consist of 95 types. Systematically, they belong to 5 parts, 6 classes, 16 orders, 34 families, 44 species and ranked third among biodiversity species.

76 types were identified in the samples, ranked last among biodiversity species, taken from the transport area. Taxonmically, they belong to 6 parts, 9 classes, 19 orders, 30 families, 40 species.

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EFFECT OF METHANOGENESIS-BASED ORGANIC FERTILIZER ON THE WHEAT RHIZOSPHERIC MICROSCOPIC FLORA

Abstract: Low doses of the methanogenesis-based organic fertilizer derived from the farm chicken's manure turned out to stimulate growth of various physiological groups of microorganisms in the wheat rhizospheric soil. Of note, as compared with the treatment of the soil with the combined organic-inorganic fertilizer, treatment with low doses of the organic fertilizer resulted in increase of the microorganisms above. The majority of the spore-forming bacteria in the wheat rhizospheric soil were established to exist as the vegetative cells.

Keywords: farm chicken's manure, microorganisms, organic fertilizer, wheat.

Introduction

Any country's food, economic and national security at large, to a great extent, depends on its farmlands' conditions and fertility [1]. Inorganic and organic fertilizers are essentially different in their effect on a soil's carbon mineralizing activity. Mobilizing hard mineralizable components of the soil organic matters, an inorganic fertilizer failed to stimulate the soil's mineralization. In contrast, the organic fertilizers increased actual carbon mineralizing activity of gray forest soil. Provided with an active organic matter, the soils treated with a mixed organic-inorganic system took an intermediate position [2]. The soil's microbiological activity is the key factor for growth of a root system, which in its turn produces significant effect on the accumulation of microorganisms in the soil. Today, the issue of an effect produced by an organic fertilizer based upon chicken manure's fermentation on microbial flora of a crop's root systems remains explored insufficiently.

The work was initiated to study dynamics of a growth of rhizospheric microorganisms of the wheat under the effect of various doses of the organic fertilizer, obtained by anaerobic fermentation of the farm chicken's manure, and the inorganic fertilizer in a sierozemic soil in a laboratory setting.

Materials and methods

Previously, we presented mineral and organic compositions of the dehydrated farm chicken manure's based organic fertilizer obtained by means of anaerobic fermentation at 55 °C with subsequent dehydration. Laboratory experiments demonstrated that low doses of the organic fertilizer (0.2 ton/hectare or 0.5 ton/hectare) stimulated growth and progress of the wheat blades and rhizosphere [3].

The dynamics of the wheat rhizospehric microorganisms was observed in pots containing 1 kg of a sierozemic soil (fourthly) taken from a pilot section of Institute of Microbiology, Uzbek Academy of Sciences. Below are various doses of the fertilizers in sequence, to name, sample 1 (a control without any fertilizer), sample 2 with the organic fertilizer's (OF) dose of 0.2 ton/hectare, sample 3 with the OF dose of 0.5 ton/hectare, sample 4 with the OF dose of 1 ton/hectare, sample 5 with the OF dose of 0.2 ton/hectare +nitrogen + phosphorus+ +potassium (30% NPP mix), sample 6 with the OF dose of 0.5 ton/hectare + 30% NPP mix, sample 7 with the OF dose of 1 ton/hectare+30% NPP mix, and sample 8 with the dose of 20 ton/hectare of the dehydrated cattle's manure.

To determine total numbers of ammonifying bacteria in the rhizospheric soil of the wheat, meat-and-peptone agar was used; spore ammonifiers were studied in a medium consisting of equal parts of meat-and peptone agar and wort agar. To measure amounts of actinomyces, starch-and-ammonia agar was used. The numbers of microfungi were studied in Czapek's medium [4; 5].

Results

Our study on the total numbers of ammonifying bacteria in the wheat rhizospheric soil demonstrated that in 20 days after treatment with low doses of organic fertilizers, such as 0.2, 0.5 and 1 ton/hectare (samples 2, 3 and 4, respectively) total numbers of bacteria as compared to the control were respectively 2.2, 2.31 and 2.1 times higher (Table 1). Simultaneous treatment with organic and inorganic fertilizers (0.2 ton/hectare of OF + 30%NPP, 0.5 ton/hectare of OF + 30%NPP and 1 ton/hectare of OF+30%NPP) (samples, 5, 6 and 7, respectively) resulted in higher growth of the ammonifying bacteria in the wheat rhizopsheric soil in 20 days.

As compared to the control, amounts of microorganisms in samples 5, 6 and 7 in meat-and-peptone agar were 3.3, 4.4 and 3.4 times higher to be 7.3×10^6, 9.6×10^6 and $7.9 \times \times 10^6$ cells/g, respectively. In 40 days bacterial activity turned out to intensify after treatment with 0.2 and 0.5 ton/hectare of organic fertilizer (samples 2 and 3) to be 6.9×10^6 and $7.4 \times \times 10^6$ cells/g, respectively. The combined treatment with the organic and inorganic fertilizers in 40 days resulted in a decline of total amounts of ammonifying bacteria in the wheat rhizospheric soil, as compared with both control and experimental samples treated with 0.2, 0.5 and 1 ton/hectare of the organic fertilizer. Minimum ammonifying bacteria (1.1×10^6 cells/g) were found in the soil treated with 1 ton/hectare of the organic fertilizer +30%NPP in 40 days.

Our study demonstrated that spore-forming forms of ammonifying bacteria accounted for 40% in the wheat rhizospheric soil within 40 days of the experiment (Table 1). Low doses of the organic fertilizers, such as 0.2 and 0.5 ton/hectare (samples 2 and 3, respectively), and the combined treatment with the organic and inorganic fertilizers turned out to stimulate both growth of the nonspore-forming bacteria and development of vegetative cells of spore-forming ones. The ratio of total numbers of ammonifying bacteria and their endospores upon treatment of the soil with the OF doses of 0.2 and 0.5 ton/hectare (samples 2 and 3, respectively) was established to be the minimum one, as compared to other doses. The treatment of the soil with the OF low doses (0.2 and 0.5 ton/hectare) appeared to stimulate growth of nonspore-forming ammonifying bacteria; the majority of spore-forming bacteria in the wheat rhizospheric soil is thought to exist as the vegetative cells. The dehydrated cattle's manure in the dose of 20 ton/hectare served as the second control (sample 8). Our study demonstrated that, as compared with the first control, in 20 days after treatment, total numbers of ammonifying bacteria increased by 4.4 times. However, in 40 days total numbers of ammonifying bacteria in samples 8 and 2 was 7.2×10^6 cells/g. In 40 days, the ratio of total numbers of bacteria and their endospores in samples 8 and 2 was 27% demonstrating prevalence of spore-forming bacteria in sample 8. While in sample 2 the bulk of ammonifying bacteria turned out to be nonspore-forming; the majority of the spore-forming bacteria existed as the vegetative cells (the ratio of total numbers of bacteria and their endospores was 2.08%). Our study demonstrated that low doses of the organic fertilizer contribute to growth both of spore-forming heterotrophic bacteria and their nonspore-forming forms.

The increase in actinomyces in the wheat rhizospheric soil was established to parallel a decline in microscopic fungi.

Conclusion

Thus, low doses of the methanogenesis-based organic fertilizer derived from the farm chicken's manure turned out to stimulate growth of various physiological groups of microorganisms in the wheat rhizospheric soil. Of note, as compared with the treatment of the soil with the combined organic-inorganic fertilizer, treatment with low doses of the organic fertilizer resulted in increase of the microorganisms above. The majority of the spore-forming bacteria in the wheat rhizospheric soil were established to exist as the vegetative cells.

Table 1.– Dynamics of ammonifying bacteria in the wheat rhizospheric soil

No.	Composition	Total number of bacteria, mln/ha			Number of endospores, mln/ha			Total number of bacteria/ endospores ratio,%		
		Initial	In 20 days	In 40 days	Initial	In 20 days	In 40 days	Initial	In 20 days	In 40 days
1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*
1	Control	2.10±0.08	2.2±0.05	3.0±0.15	0.76±0.03	0.83±0.03	1.20±0.06	36.2±0.21	37.7±0.21	40.0±0.20
2	0.2 ton/ha OF	2.10±0.08	4.9±0.12	7.2±0.24	0.76±0.03	0.21±0.01	0.15±0.007	36.2±0.21	4.2±0.21	2.08±0.1
3	0.5 ton/ha OF	2.10±0.08	5.1±0.23	6.9±0.21	0.76±0.03	0.20±0.01	0.21±0.01	36.2±0.23	3.9±0.10	3.04±0.15
4	1 ton/ha OF	2.10±0.08	4.7±0.14	3.9±0.17	0.76±0.03	0.23±0.01	0.14±0.004	36.2±0.24	4.8±0.21	3.6±0.17
5	0.2 ton/ha OF +30% NPP	2.10±0.08	7.3±0.25	1.3±0.04	0.76±0.03	0.34±0.01	0.08±0.003	36.2±0.21	4.6±0.22	4.0±0.2
6	0.5 ton/ha OF +30% NPP	2.10±0.08	9.6±0.25	1.5±0.05	0.76±0.03	0.47±0.02	0.07±0.002	36.2±0.25	4.8±0.23	4.6±0.21

1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*
7	1 ton/ha OF +30% NPP	2.10±0.08	7.9±0.20	1.1±0.02	0.76±0.03	0.41±0.02	0.68±0.03	36.2±0.23	5.1±0.21	6.18±0.21
8	Dehydrated cattle's manure 20 ton/ha	2.10±0.08	9.7±0.21	7.2±0.24	0.76±0.03	0.29±0.01	0.20±0.01	36.2±0.22	29.0±0.25	27.0±0.22

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SELECTION OF NUTRIENT MEDIA FOR THE CULTIVATION OF BACTERIAL STRAINS OF BACILLUS THURINGIENSIS AGAINST CATERPILLARS OF GYPSY MOTH (LYMANTRIA DISPAR)

Abstract: *B. thuringiensis* (*Bt*) is widely used against gypsy moth. However, due to the high cost of nutrient media required for the cultivation of this bacterium, large-scale production of biopreparation based on them is expensive. In this study, we tried to develop a cost-effective media based on local and available raw materials. The results of the study showed that bacterial strains grown on potato medium, after 7 days of incubation with larvae of L. dispar, showed an average statistical insecticide activity of 49.5%, and after 14 days of 81.63%. Insecticide activity of B. thuringiensis bacterial strains grown on the medium based on the wastes from the production of alcohol – the bard, after 7 days of exposure was 48.71%, after 14 days – 87.53%. The cell quantity and the insecticidal activity of B. thuringiensis bacterial strains grown on a nutrient medium based on skimmed milk powder was higher than the above-mentioned nutrient media. So, the Bt 26 strain, grown on a medium based on dry milk, showed the highest growth titer – $5.7 \cdot 10^8$ CFU / ml. The average insecticidal activity of bacterial strains grown on skimmed milk powder after 7 days was 59.55%, after 14 days it reached 93.3%. Based on the data obtained, it can be concluded that nutrient media based on powdered milk and bards are cheap, effective and available in the production of preparations based on bacteria B. thuringiensis.

Keywords: Gypsy moth, *Bacillus thuringiensis*, insecticidal activity, δ-endotoxin, nutrient media.

Introduction

One of the most common groups of pests in the forests of Uzbekistan are the needle and leaf eating insects, which forms foci of mass reproduction. Lepidoptera and hymenoptera, which eat the needles and leaves, characterized by large fluctuations in the number and are able to periodically reproduce in large-scale over large areas. The most harmful of them is the gypsy moth [1; 2].

Currently, worldwide work is underway to develop highly effective methods of controlling pests based on *B. thuringiensis* strains of insecticidal bacteria. For the production of bioinsecticidal preparations based on B. thuringiensis strains, waste of local industries can be used, based on the fact that they contain nutrients for normal growth and development of bacteria [3; 4].

The purpose of this research is to study the insecticidal activity of local strains of insecticidal bacteria *B. thuringiensis,* grown on various nutrient media based on cheap local raw materials.

Materials and Methods

Object of study: local strains of bacteria *B. thuringiensis Bt*1, *Bt*18fo, *Bt*26, *Bt*54, *Bt*81, *Bt*82, *Bt*91 and *Bt*94 [4] and the larvae of the gypsy moth 2–3 years old (L. dispar) [5; 6].

The composition of nutrient media (%):

1. Standard medium (PB): Pepton-1.0; glucose is 0.6; NaCl-0.5; K2HP04–0.05; MgS04–0.02, (pH-7.0);

2. Medium on the basis the wastes from the production of alcohol – the bard: –25.0, NaCl-0.5; pH 7.0–7.2;

3. Medium based on potato extract: extract – 20, glucose – 0.5; NaCl-0.25; pH 6.8–7.0;

4. Medium based on skimmed milk powder – 1.0, sucrose-0.5; NaCl-0.5; K2HP04–0.05; MgS04–0.02; (pH-7.0).

The cultures were grown on a rocking chair at 150 rpm, at a temperature of 29–3 °C.

The insecticidal activity of local strains of *B.thuringiensis* was determined using the method of V. Guliy et al. [7]. Apple leaves pretreated with 70% ethanol were used as feed for the caterpillars. 15 g of apple leaves were placed in a glass jar and mixed with 2 ml of bacterial suspension with a titer of $2x10^8$ spores and crystal / ml, mixed thoroughly, later 30 test insect caterpillars, previously fasted for 16–20 hours, were placed.

Results and discussion

One of the determining factors of bacterial growth in nutrient media is the presence of carbon and nitrogen (C / N). We have used various nutrient media that affects the toxin formation in local strains of bacteria *B. thuringiensis.*

Undoubtedly, standard environment based on peptone is universal for the cultivation of most microorganisms. As it is known, the composition of peptone has a large number of amino acids positively affecting the growth and development, as well as contributing to the production of crytoxins. In accordance with Figure 1 (a), the *Bt*82, *Bt*91 and *Bt*94 bacterial strains have high insecticidal activity (100%) against to L.dispar caterpillars within 14 days of exposure. It should be noted that the bacteria *Bt*54, *Bt*81, *Bt*82, *Bt*91 and *Bt*94 are specific to *L. dispar*, as they were isolated from dead insects. At the same time, strains *Bt*54 and *Bt*81 showed the lowest activity, 76.6% and 93.3%, respectively. The *Bt*1, *Bt*18fo and *Bt*26 strains isolated from other dead insects (*G.mellonella*) showed both high (Bt1–96.6%) and moderate (*Bt*18fo and *Bt*26–73.3% and 86.6%, respectively) insecticidal activity. The average insecticidal activity of bacterial strains of *B. thuringiensis* within 7 days is 58.3%, and after 14 days – 90.8% (Table 1). The environment based on peptone is expensive for the cultivation of bacteria *B. thuringiensis* on a production scale. Based on the aforementioned facts, search was made for nutrient media based on cheap, affordable waste of local industries.

Table 1.– The statistical average insecticidal activity of *B. thuringiensis* strains on different nutrient media

Nutrient media	**Statistical average insecticidal activity of bacteria grown on different nutrient media,%**		**Statistical average insecticidal activity of each strain of *B. thuringiensis* bacteria after 14 days of exposure,%**								
	7 days	**14 days**	***Bt*1**	***Bt*18fo**	***Bt*26**	***Bt*54**	***Bt*81**	***Bt*82**	***Bt*91**	***Bt*94**	**control**
potato extract	49.5±4.23*	81.63±3.38									
bard	48.71±4.25	87.53±2.18	89.95 ± 1.22	76.62 ±3.43	86.62 ±2.11	81.6 ±2.03	87.47 ±4.36	92.47 ±4.13	97.47 ±3.35	97.5 ±4.88	0
skimmed milk powder	59.55±3.19	93.3±2.23									
peptone	58.3±1.10	90.8±2.33									

*Note: *– significant differences to control group (P < 0.05), n = 3;*

The medium based on potato extract is one of the cheapest and the most full-fledged nutrient media for growing bacteria of the group *B. thuringiensis* [8]. As it is known, the potato tuber contains: protein – 2.0%, hydrocarbons – 18.0%, fats – 0.1%, crude fiber – 0.7%, ash – 1.%, water – 76.3% and other [9]. Cultivation on the potato medium for 2 days gives good and abundant growth of the strains of the bacteria *B. thuringiensis*. The formation of the growth of bacteria is different from crops grown on other nutrient media. Approximately after 32 hours of cultivation on potato medium, the formation of spores and crystals begins and then by 55 hours of cultivation, 95% sporulation is observed. Such "precocity" is probably associated with an insufficient amount of nitrogenous substances in the composition of the potato environment compared with carbohydrates. According to the results of experimental data, it has been established that bacterial strains of *B. thuringiensis*, grown on potato medium, have varying degrees of insecticidal activity with respect to caterpillars of the gypsy moth (*Limantria dispar L.*). In accordance with figure 1b, the insecticidal activity of the studied cultures ranges from 70.0% (*Bth*26) to 93.3% (*Bth*91). Among the bacteria tested, strain *Bt* 91 shows the highest insecticidal activity (93.3%) within 14 days of observation. The average statistical data of the insecticidal activity of bacterial strains grown on potato medium for 7 days is 51%, and for 14 days – 81.6% (table 1). Thus, the cultivation of bacteria B. thuringiensis on potato medium does not reduce the insecticidal activity, moreover, when cultivated on this medium, the cycle of sporulation is shortened, which gives an economic benefit in the production of a biological product.

Next, we carried out exploratory studies to study the nutritional value of bards. Analysis of the chemical composition of the bards (the final waste of alcohol production) showed the presence of 2.4% of complete protein, 2.0–3.5% of non-fermentable carbohydrates, 1.2–2.3% of nitrogenous substances. The total content of ammonium nitrogen is 52.3 mg /l, nitrates –

0.30 mg/l, nitrites – 0.30 mg/l [10]. In addition, the bard also contains different amino acids. Earlier, we used this medium to optimize the production of β-exotoxin by bacterial strains of B. thuringiensis [11]. As shown from the results of experimental data, the studied bacteria *B. thuringiensis* also gives good growth on a solid medium and gives abundant biomass in a liquid nutrient medium. Sporulation is observed after 40 hours of cultivation. And after 65 hours of cultivation, 95% spore and crystal formation were noted. Bacterial strains *Bt*91 (96.6%) and *Bt*94 (100%) have the highest insecticidal activity in bacteria B. thuringiensis bacteria grown on a medium bard showed the highest insecticidal activity (Fig. 1 (c). The average statistical data of *B. thuringiensis* bacteria within 7 days of cultivation is 48.71%, and at 14 days it is 87.53% (Table 1). It should be noted that the insecticidal activity of strain *Bt*94 in relation to caterpillars of gypsy moth grown on a medium containing bard significantly higher than on potato extract. On the basis of the obtained results on the study of insecticidal activity in bacteria *B.thuringiensis* grown on the medium with bard, it can be concluded that this medium satisfies the nutritional needs of the crops and ensures full growth and development.

Next, the strains of *B. thuringiensis* were cultured in a nutrient medium based on skimmed milk powder. Analysis of the chemical composition showed that skimmed milk powder contains mainly: 35% proteins, milk sugars – 52%, fats – 1% and 6% – mineral substances [12]. It is noted that sporulation in *B. thuringiensis* strains in skimmed dry milk is observed from 44 hours of cultivation, the formation of spores and crystals is completed by 70 hours of cultivation (95%). The conducted studies show that the studied cultures show different insecticidal activity when cultivated on different nutrient media. Consequently, the *Bt* 91 and *Bt* 94 bacteria strains grown on a medium containing dried milk show the highest entomopathogenic activity of 100.0% during the 14 days of cultivation (fig. d). The strains of *Bt*1, *Bt*18fo, and *Bt*26 bacteria that are not specific to *Lymantria dispar* grown in a medium based on milk powder show high insecticidal activity compared to other nutrient media tested. The average statistical data of entomopathogenic activity of all tested strains within 7 days of incubation is 59.55%, then by 14 days of exposure this indicator reaches 93.3% (Table 1). It should be noted that the strains under cultivation in a nutrient medium based on skimmed milk powder is the insecticidal activity higher compared to a nutrient medium based on potato extract and bard. Because, in the composition of skimmed milk powder there are more nitrogen-containing substances, which probably enhances the synthesis of δ-endotoxin in the cultivation process.

Further, we determined the growth and development of bacteria of B. thuringiensis strains on different nutrient media (Table 2).

Table 2. – The titer of bacterial strains grown on different nutrients after 72 hours of cultivation

Strains of bacteria B. thuringiensis							
*Bt*1	*Bt*18ϕo	*Bt*26	*Bt*54	*Bt*81	*Bt*82	*Bt*91	*Bt*94
amount of bacterial strains grown on 1% peptone medium							
$4.8 \cdot 10^8$	$3.6 \cdot 10^8$	$5.4 \cdot 10^8$	$2.7 \cdot 10^8$	$3.1 \cdot 10^8$	$3.8 \cdot 10^8$	$4.3 \cdot 10^8$	$5.1 \cdot 10^8$
amount of bacterial strains grown on 20% potato broth							
$2.7 \cdot 10^8$	$1.1 \cdot 10^8$	$3.5 \cdot 10^8$	$1.1 \cdot 10^8$	$2.95 \cdot 10^8$	$3.1 \cdot 10^8$	$2.9 \cdot 10^8$	$3.3 \cdot 10^8$
amount of bacterial strains grown on 25% bard							
$3.4 \cdot 10^8$	$3.2 \cdot 10^8$	$4.1 \cdot 10^8$	$2.1 \cdot 10^8$	$2.8 \cdot 10^8$	$3.7 \cdot 10^8$	$3.6 \cdot 10^8$	$4.0 \cdot 10^8$
amount of bacterial strains grown on 1% skimmed milk powder							
$4.5 \cdot 10^8$	$3.9 \cdot 10^8$	$5.7 \cdot 10^8$	$2.4 \cdot 10^8$	$2.6 \cdot 10^8$	$4.3 \cdot 10^8$	$3.9 \cdot 10^8$	$4.9 \cdot 10^8$
The average statistical amount of B. thuringiensis bacterial strains after 72 hours of growth							
$3.85 \cdot 10^8$	$2.95 \cdot 10^8$	$4.67 \cdot 10^8$	$2.07 \cdot 10^8$	$2.86 \cdot 10^8$	$3.72 \cdot 10^8$	$3.67 \cdot 10^8$	$4.32 \cdot 10^8$

In accordance with (table 2), the *Bt*1, *Bt*26, and *Bt*94 strains have an average amount of $3.85 \cdot 10^8$, $4.67 \cdot 10^8$, and $4.32 \cdot 10^8$, respectively. It should be noted that the *Bt*26 strain shows the greatest growth and development when cultured on a medium based on skimmed milk powder ($5.7 \cdot 10^8$) compared with other studied media. The strains *Bt*91 and *Bt*94 specific to *L. dispar* show both high quantity and the high insecticidal activity.

Thus, according to the results of the conducted research, significant differences in the nutritional value of the studied components of the media, affecting both the growth and development of cultures and their insecticidal activity, have been identified. Therefore, from the point of view of economic efficiency and insecticidal activity of bacteria, the studied nutrient media based on dried milk and bards are cheap and affordable, which makes it possible to recommend them as potential sources for cultivating bacteria of the Bt group on an industrial scale.

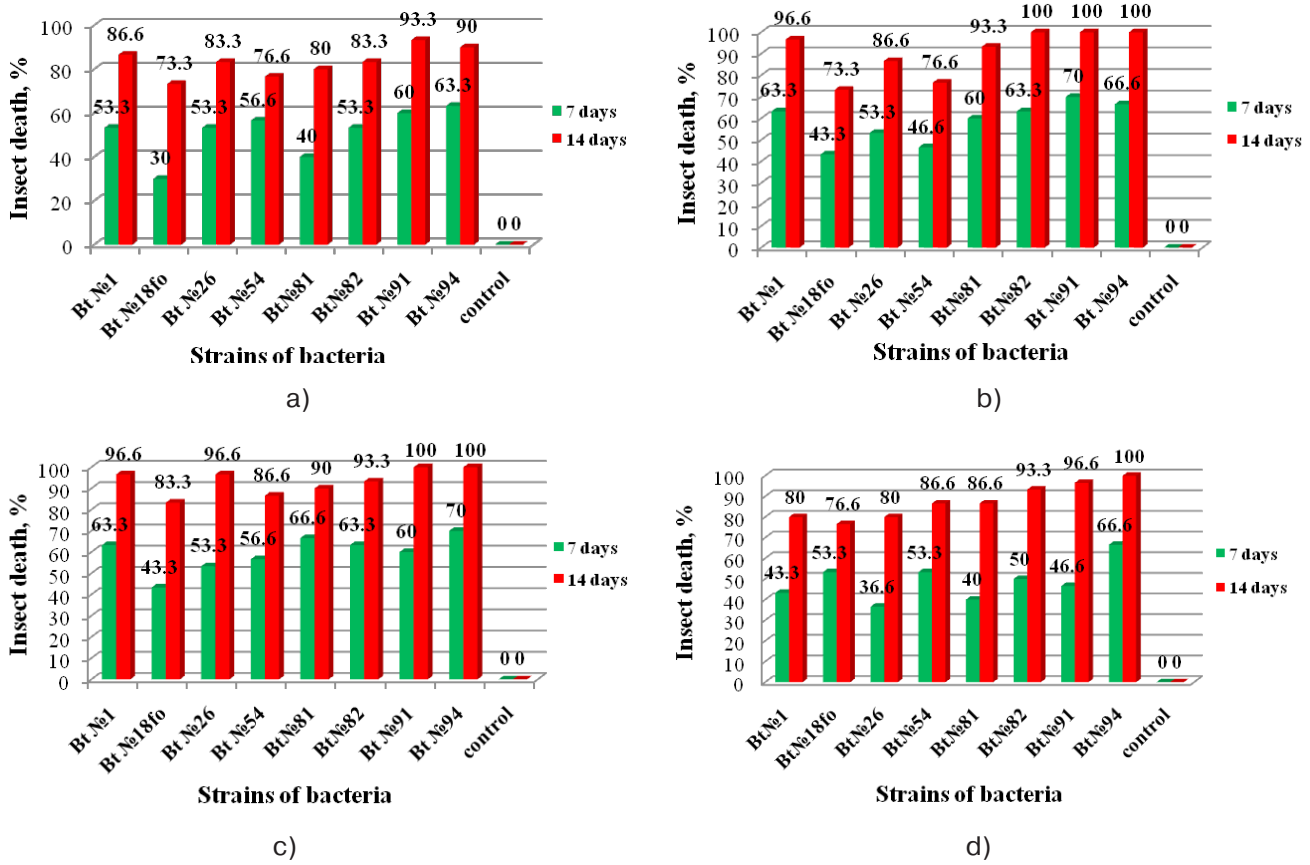

Figure 1. The insecticidal activity of B. thuringiensis bacteria grown on: a) standard peptone; b) potato extract; c) the bard; d) skimmed milk powder

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Section 2. Medical science

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ANTITOXIC EFFECTS OF TWO NEW N-BENZOYL DERIVATIVES OF CYTISINE IN ACUTE AND CHRONIC ALCOHOL INTOXICATION

Abstract: Antitoxic effects of new N-benzoyl derivatives of cytisine in acute and chronic ethanol intoxication have been investigated. It has been established that the test substances have a pronounced antitoxic effect in acute alcohol intoxication and improve animal orientation and exploratory behaviour in chronic alcohol intoxication.

Keywords: Cytisine derivatives, toxicity, antitoxic activity, anesthesia, acute intoxication, chronic intoxication, orientation and exploratory behaviour.

Nicotinic acetylcholine receptors (nAChR) are known to attract the interest of numerous researchers, since the cholinergic system occupies one of the key positions in the development of neurodegenerative brain diseases, including Alzheimer's disease, Parkinson senile dementia, as well as alcoholism, drug addiction, etc. They activate higher integrative activity of brain, restore impaired mnestic and mental functions, reduce neurological deficit and increase the body's resistance to various extreme factors [1–4]. Severe cholinergic dysfunction, density and plasticity of cholinergic receptors decreasing were observed in various types of amnesia [5–9]. Currently, nAChR are considered as an interesting target for the development of new drugs for the treatment of central nervous system dysfunctions [8–9].

Cytisine has a high affinity for many nAChR subtypes, but low penetration through the blood-brain barrier due to low lipophilicity [6–9]. The targeted research to create new products based on N-benzoyl cytisine derivatives carry out in the Institute of Chemistry of Plant Substances of the Academy of Sciences of the Republic of Uzbekistan [10–12]. The purpose of this study is the evaluation of neuroprotective and antitoxic effects of new N-benzoyl derivatives of cytisine: N-benzoylcytizine hydrochloride and N-hydroxyethylcytizine hydrochloride in acute and chronic alcohol toxicity.

Materials and methods of investigation. The effect of studied drugs on acute alcohol intoxication was investigated on white mice males weighing 18–20 grams. The animals were injected intraperitoneally with 24% aqueous ethanol solution at a dose of 4.8 g/kg. The time of onset and termination of alcohol anesthesia ("lateral position") was recorded. The studied substances were administered at doses of 0.1–0.5–1.0–5.0 mg/kg subcutaneously in 30 minutes before ethanol injection. Each dose was tested on 10 mice. Pentyleneterazole and caffeine were used as a reference drugs.

Chronic intoxication was caused by daily intragastric administration of a 15% ethanol solution at a dose of 4 g/kg using an atraumatic metal probe for 30 days. Ethanol introduction was stopped from 31th day and experimental therapy with the studied drugs was carried out for 7 days at doses of 0.1–0.5–1.0–5.0 mg/kg subcutaneously followed by testing for orien-

tation and exploratory behaviour of mice in the "open field". The locomotor activity was evaluated by the number of crossed squares, the research activity by the number of peeking into the hole, the orientation — by the number of stands on hind legs. Each dose of the substance was tested on 10 animals. The control group of mice under the same experimental conditions was administered sterile distilled water instead the investigated substance. Piracetam was used subcutaneously as an ethalon drug at a dose of 400 mg/kg. The study of acute toxicity was performed on mice with subcutaneous method of application.

Results and discussion

It was established that intraperitoneal administration of 24% ethanol solution at a dose of 4.8 g/kg causes anesthesia (lateral position) in 100% of experimental and control animals. In the control group, the average duration of anesthesia was 119.2 minutes. Preliminary use of N-benzoylcytisine hydrochloride and N-hydroxyethylcytisine hydrochloride had a pronounced analeptic effect. N-benzoylcytisine hydrochloride at doses of 0.1–0.5–1.0–5.0 mg/kg shortened the duration of anesthesia compared with the control group of animals by 19.5%, 40.3%, 43.4%, and 34.4%, respectively. Under the same experimental conditions, N-hydroxyethylcytisine hydrochloride reduced the lateral position of mice compared to the control group of animals by 27, 7, 30, 36.1, and 28.4%, respectively. Both cytisine N-benzoyl derivatives were not inferior to pentyleneterazole and caffeine in comparison with the ethalon drugs, and even exceeded its effect at doses of 0.5 and 1.0 mg/kg (Table 1).

Table 1. – Effects of cytisine N — benzoyl derivatives on acute alcohol intoxication (n=10)

No.	Animal group	Dose, mg/kg s/c	Duration,		Effectiveness, %
			minutes	%	
1	Ethanol 4.8 g/kg i/p	–	119.2±5.3	100%	–
2	Pentylenetetrazole	10	87.6±7.4	73.4%	–26.6%*
3	Caffeine	10	79.4±7.6	66.6%	–33.4%*
4	N-benzoylcytisine hydrochloride	0.1	96.0±8.0	80.5%	–19.5%
		0.5	71.2±6.8	69.3%	–40.3%*
		1.0	67.5±5.9	56.6%	–43.4%*
		5.0	78.2±6.3	65.6%	–34.4%*
5	N-hydroxyethylcytisine hydrochloride	0.1	86.2±7.8	72.3%	–27.7%*
		0.5	83.5±6.5	70.0%	–30.0%*
		1.0	76.2±6.8	63.9%	–36.1%*
		5.0	85.4±5.6	71.6%	–28.4%*

*Note: * P<0.05.*

The study of orientation and exploratory behaviour in "open field" in chronic alcohol intoxication for 30 days showed that prolonged use of ethanol leads to a significant suppression of locomotor activity and an exploratory behaviour compared to control animals. So, in animals receiving only ethanol, locomotor activity (the number of crossed squares was 4.6 ± 1.0, the control was 11.8 ± 1.2), orientation (the number of racks on hind legs was 1.8 ± 0.2, control — 5.6 ± 0.6) and research activity (the number of peering into the holes is 5.2 ± 0.6, the control is 13.7 ± 1.3) reduced. The use of N-benzoylcytisine and N-hydroxyetylcytisine hydrochlorides at a dose of 0.1 mg/kg increased the number of horizontal movements to 6.4 ± 0.8 and 6.1 ± 1.0, the number of vertical stands to 3.2 ± 0.6 and 2.9 ± 0.5, and the number of holes inspection up to 8.4 ± 0.5 and 7.9 ± 0.7, respectively. Increasing the dose of substances to 0.5 mg/kg and 1.0 mg/kg significantly increases the locomotor and research activity in the "open field" to almost the control values. With further increase of the dose to 5.0 mg/kg leads to decreasing of the abovementioned values (Table 2).

Table 2. – Effects of investigated substances in the "open field" in chronic alcohol intoxication (n=10)

No.	Animal groups	Doses, mg/kg	Horizontal movies	Vertical stands	Holes inspection
1	*2*	*3*	*4*	*5*	*6*
1	Control (distilled water)		11.8±1.2	5.6±0.6	13.7±1.3
2	Ethanol	4000	4.6±0.5	1.8±0.4	5.2±0.6

1	*2*	*3*	*4*	*5*	*6*
3	N-benzoylcytisine hydrochloride	0.1 0.5 1.0 5.0	6.4±0.8 10.9±0.8 10.0±1.2 8.4±0.9	3.2±0.6 5.0±0.8 5.3±0.4 3.8±0.3	8.4±1.1 12.9±1.3 13.6±0.9 7.4±0.6
4	N-hydroxyethylcytisine hydrochloride	0.1 0.5 1.0 5.0	6.1±1.0 9.8±1.2 12.1±0.9 7.4±0.8	2.9±0.5 4.6±0.6 5.2±0.8 3.8±0.4	7.9±0.7 10.2±0.8 12.8±1.2 8.1±1.0
5	Piracetam	400	8.8±1.2	4.0±0.6	9.6±1.4

The average lethal dose (LD_{50}) of N-benzoylcytisine hydrochloride and N-hydroxyethylcytisine hydrochloride at subcutaneous administration were found to be 81 (70 ± 93.1) mg/kg and 435 (381 ± 495) mg/kg, respectively.

Conclusions:

1. N-benzoyl derivatives of cytisine exhibit pronounced anti-narcotic action in acute alcohol intoxication.

2. New N-benzoyl cytisine derivatives have increase the locomotor activity, orientation and exploratory behaviour of animals in the "open field" after long-term alcohol intoxication.

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CAUSES OF LETHAL OUTCOMES IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ACCORDING TO A RETROSPECTIVE ANALYSIS

Abstract: The article provides an analysis of the causes of death in patients with chronic obstructive pulmonary diseases (COPD) according to a retrospective analysis of autopsy protocols. As a result, the authors concluded that diseases of the circulatory system of thrombogenic etiology are the main cause of death in patients with COPD.

Keywords: cause, death, chronic obstructive lung disease.

Chronic obstructive pulmonary disease (COPD), as the most common nosology in the COPD group, has a stable tendency to increase in prevalence and according to who studies, by 2020 will occupy the 5th place in morbidity and 3rd place in the structure of mortality among all diseases [1]. In this connection, one of the main problems of modern medicine is timely treatment, improving the quality of life and reducing mortality among this group of patients.

Given the high degree of COPD comorbidity and coronary heart disease(CHD), the risk of death from cardiovascular accidents in patients with COPD is very high [2]. Given that in the modern world there is a growing number of factors of cardiovascular risk, such as Smoking, overweight, hypodynamia and hypercholesterolemia, as well as the factor that systemic inflammation, as one of the main pathogenetic mechanisms of COPD is a stimulant of hypercoagulation States, we can conclude about the increasing role of cardiovascular disasters in the development of deaths in patients with COPD.

The aim of the study was to study the significance of cardiovascular accidents on the background of thrombosis in the development of deaths in patients with COPD in hospital.

Materials and methods: Retrospective analysis of 281 autopsy protocols of pathologic-anatomical Department of GKB № 1 of Tashkent city clinical hospital and Republican specialized scientific-practical center of Phthisiology and pulmonology of the Ministry of health of Uzbekistan.

Results and discussion: a Retrospective analysis of 281 autopsy findings showed that in 70.0% (197 cases) the cause of death was diagnosed, reflecting the state of hemostasiological disorders, including AMI 74.6% (147 patients), AMI by ischemic type 22.8% (45 patients), PE and Schmidt syndrome by 1% (2 patients), thrombosis of mesenteric vessels (0.5%).

Considering the frequency of thrombogenic disasters as the cause of death, in correlation with final clinical diagnoses for the autopsy noted that diseases of the circulatory system account for 64.9 per cent (128 cases), diseases of the respiratory organs of 21.3% (42 cases), diseases of the genitourinary system is 0.5% (1 case) and neoplasms of 0.5% (1 case).

In 83% of cases (145 cases) thrombogenic catastrophes as a cause of death were registered at the age of 60 years, in 57.7% – at the age of 40–60 years and in 14.3% – up to 40 years. It was noted that the incidence of thrombogenic catastrophes is 1.4 times higher at the age of 40–60 years and 5.8 times higher compared to the age of 40 years. Considering the relationship of age with the development of thrombogenic catastrophes from the structure of the final clinical diagnosis, respiratory diseases occupy the second rank place, yielding to diseases of the circulatory system.

Thrombogenic catastrophes as a cause of death were recorded in 66.0% of men (88 out of 134 men) and 73.9%(108 out of 147 women). Considering the relationship of sex with the development of thrombogenic catastrophes from the structure of the final clinical diagnosis, respiratory diseases occupy the second rank place, yielding to diseases of the circulatory system and do not have a significant difference in the frequency among men and women.

Retrospective analysis of 281autopsiynyh conclusions showed that lifetime diagnosis of chronic obstructive pulmonary disease (COPD), as reflected in the structure of the final diagnosis was only 13.9% (39 cases), and autopsy pathomorphological diagnosis allowed to determine the signs of COPD in 37.0% (104 of 281 autopsies).

Morphological signs of COPD were determined according to the classification of chuchalina (2004) and included: defeat of

bronchial tree in the form of hyperemia and swelling of the bronchial mucosa, strengthening its longitudinal folding, detection in the lumen of small bronchi mucous plugs in 91.3% of cases; signs of emphysema of the lungs of varying severity of 33.7% and signs of diffuse peribronchial pneumosclerosis in 32.7% of autopsies.

Evaluation of the frequency of pathomorphological signs of COPD as a factor of comorbidity, in accordance with the final clinical diagnosis showed that in 63.5% of diseases of the circulatory system there is this factor of comorbidity and its presence was found only in 1.9% of cases of digestive system disease.

Retrospective analysis of 104 autopsy findings with pathomorphological verification of COPD showed that in 93.3% (97 cases) the cause of death was diagnosed, reflecting the state of hemostasiological disorders (thrombosis), including AMI 77.3% (75 cases), AMI by ischemic type 22.7% (45 cases).

In the analysis of causes of death according to the final clinical diagnosis-chronic obstructive pulmonary disease – in 94.9% of cases (37 of 39 cases) the cause is hemostasiological disorders, including AMI in 81.1% (30 of 37 cases) and AMI in 18.9% (7 of 37 cases).

Summary

1. COPD remains a diagnosis-underestimated by clinicians, which creates the risk of incorrect assessment of the patient's condition, without taking into account the aggravating effect of comorbid pathology.

2. In the literature, there is a lot of data on the main causes of death of patients with COPD, such as respiratory failure, lung cancer, pulmonary embolism, but because of the high comorbidity of COPD with cardiovascular disease, and the mechanism of mutual burden of these nosologies, according to our study to date, the main causes of death of patients with COPD are cardiovascular accidents caused by thrombosis. Thus, hemostasiological disorders are the leading causes of death among patients with COPD and comorbid conditions with it – diseases of the circulatory system.

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NATURAL NEUROTROPIC AUTOANTIBODIES IN CHRONIC ALCOHOL INTOXICATION

Abstract: Changes in the content of auto-at to antigens from the nervous tissue are likely to indicate pathogenetic changes in the functioning of the immune system and be used as predictors of damage to the nervous system during alcohol intoxication.

Keywords: Neurotropic autoantibodies, psychoactive substances, alcohol intoxication.

The widespread distribution and use of drugs is a significant socio-economic and medical problem. According to WHO, more than 3% of the inhabitants of our planet are addicted to psychoactive substances, including narcotic substances [4]. It is obvious that alcohol addiction is mediated by its effect on the brain. Ethanol and the product of its biotransformation acetaldehyde have a pronounced neurotropic effect. The effect of ethanol on the brain is associated with its ability to penetrate the membrane and alter the physical properties of the lipid components of the membranes, the content and functions of neurotransmitters in the brain, as well as at different stages of nerve impulse transmission [7]. As a consequence, acute ethanol intoxication is characterized by mental, autonomic, neurological disorders and metabolic acidosis.

Recently, laboratory diagnostics, including the definition of neurospecific proteins (NSB), biologically active molecules that are specific for nervous tissue and perform functions characteristic of the nervous system, have attracted more and more attention. Over the past 30 years, more than 60 different brain NSBs have been characterized. They can be classified according to the localization-structural principle (neuronal, glial; membrane-associated and cytoplasmic, etc.), according to their functional role, and they also distinguish the subgroup of NSBs present in normal conditions and in pathologies [2]. Determining the level of NSB contributes to early diagnosis, because significant changes in their concentration often occur earlier than the damage that can be detected by instrumental examination methods. In addition, they allow an assessment of the prognosis of the course and outcome of the disease, and monitoring of the treatment of patients. Numerous studies have shown their increase in schizophrenia, traumatic brain injury, acute and chronic disorders of cerebral circulation, epilepsy, Alzheimer's disease, multiple sclerosis, etc. [5; 8]. In the literature, there are conflicting single messages on the content of NSB in the serum during alcohol intoxication.

Objective: to determine the concentration of natural neurotropic autoantibodies in the serum of rats during chronic alcohol intoxication.

Material and methods. The experiments were conducted on 48 Wistar male rats weighing 130–150 g. Simulation of chronic alcohol intoxication in rats was performed according to Liber C. S., DeCarli L. M. Animals of the experimental group received ad libitum liquid diet, 36% of the energy value of which was provided by ethanol. In the control isocaloric diet, ethanol was replaced by the carbohydrate component of the diet. Control animals were injected with saline intraperitoneally at a dose of 0.3 ml/100 g. The duration of the experiment was 4 weeks. Studies were conducted on the 7th, 14th, 21st and 28th day from the beginning of the experiment.

The content of neurotropic auto-AT, directed to proteins: neurofilament protein-200 (NF-200), glial fibrillary acidic protein (GFAP), S-100, the main myelin protein (MBP), voltage-dependent Ca channel (VGCC) in serum was determined with the help of ELI-N-Testa IIC "Immunculus", Moscow. Isolation of protein-antigens was performed according to the method of A. B. Poletaeva et al. [7]. Data on serum immunoresistance of the analyzed samples, obtained in absolute units of optical density, were converted into conventional units (UE) [6]. Digital material processed by the method of variation statistics. To study the relationship between the parameters studied, a correlation analysis was performed in the program Statistica 6.0.

Results and discussion. It is known that the clinical manifestations of alcohol intoxication are characterized mainly by disorders in the nervous system [10]. At the same time, an important role in the pathogenesis of many diseases is played by autoimmune mechanisms. The results of the determination of neurotrophic auto-AT in the serum of rats under the conditions of modeling chronic alcohol intoxication are shown

in Table 1. As follows from the data presented in the table, the chronic effects of ethanol during the 1st week revealed differences in the levels of auto-AT to different nerve tissue proteins relative to intact rats. So, if the content of auto-AT in the serum to GFAP, S-100 and VGCC significantly increased by 43.8; 31.4 and 47.2%, then NF-200 and MBP had only a tendency to increase. As the length of the introduction of ethanol lengthened, the content of auto-AT to NSB in the serum of experimental animals gradually increased significantly. The greatest changes were revealed by the final date of the introduction of the toxicant, which was manifested by a significant increase in their content: to NF-200, GFAP, S-100 MBP and VGCC significantly increased by 130.9; 182.8; 152.2; 54.2 and 121.7% relative to the values of intact rats. As can be seen from the above data, the content of auto-AT to NBC progressively increases as alcohol dependence worsens, this is more pronounced for NB-200 such as NF-200, GFAP, S-100 and VGCC and a lesser degree for MBP.

As can be seen from the above data, the content of auto-AT to NBC progressively increases as alcohol dependence worsens, this is more pronounced for NB-200 such as NF-200, GFAP, S-100 and VGCC and a lesser degree for MBP.

Table 1. – The content of neurotropic autoantibodies in the serum of rats with chronic ethanol poisoning, M ± m

Groups and study dates	NF-200	GFAP	S-100	MBP	VGCC
Intact	5.272 ± 0.373	3.878 ± 0.288	5.208 ± 0.892	14.836 ± 0.695	2.448 ± 0.232
2nd week	8.673 ± 0.703	7.852 ± 0.387	9.434 ± 0.506	18.692 ± 0.491	4.558 ± 0.307
3rd week	11.122 ± 0.352	10.544 ± 0.495	12.708 ± 0.35	22.582 ± 0.44	5.816 ± 0.155
4th week	14.762 ± 0.653	15.769 ± 0.663	17.262 ± 0.552	25.196 ± 0.637	7.993 ± 0.506

*Note: * – the differences between the indices of the intact and experimental groups are significant, P < 0.05.*

To date, the effects of ethanol have been established for GABA-, glutamate, including NMDA receptors, 5-HT3-serotonin and nicotine cholinergic receptors, as well as for voltage-dependent calcium channels and rectifying potassium channels directed inward [1]. However, as shown by our research, the list of neurospecific proteins modified by alcohol is not limited to this list. The studies revealed a more pronounced intensity of autoimmune reactions during alcohol intoxication, as evidenced by a significant increase in the concentration of auto-antibodies to NF-200, S-100, GFAP, MBP, VGCC.

It should be noted that the NF-200 specific axon protein and upward abnormal levels of auto-AT to NF-200 may indicate with high probability that degenerative changes in axons, including their myelin sheaths (demyelination). Our results are consistent with other authors, who also observed an increase in auto-AT to NF-200 in diseases that are accompanied by neurodegenerative processes (schizophrenia, neurosyphilis, epilepsy) [1]. Protein S-100 is a Ca-dependent regulator of many functions (regulation of apoptosis, regulation of neurogenesis, trophic factor of serotonergic neurons). Depending on the concentration, S-100 proteins have a trophic or toxic effect on neurons and glial cells. They act as mediators in the interaction of glia and neurons and, in general, as one of the nodal molecular components of complex intracellular systems that provide functional homeostasis of brain cells, the appearance of auto-AT to S-100 protein is a sign of changes in the CNS associated with emotional disorders, as well as reflects destructive changes in nervous tissue [6]. In this regard, the increase in the serum concentration of auto-AT to the S-100 protein revealed by us confirms and convincingly indicates the progression of changes in the nervous system. An increased level of auto-AT to S-100 protein indicates changes in the structures of the central nervous system, which register emotional status, transduction of signals that control the activity of energy metabolism enzymes in brain cells, calcium homeostasis, cell cycle, cytoskeleton functions, cell proliferation and differentiation, their mobility, secretory processes, the structural organization of biomembranes. It is important to note that S-100 protein is the most specific protein in the brain tissue and the constancy of its concentration ensures the normal functioning of all brain systems. An increase in its level occurs when the glial cells of the brain are damaged and the BBB permeability increases. And also, an increase in aAT to GFAP, MBP, VGCC indicates the aggravation of changes in the brain during alcohol intoxication. An increase in auto-AT to the B-dependent Ca-channel is characteristic of cerebellar ataxia, amyotrophic lateral sclerosis, etc. An increase in the content of auto-AT to GFAP will be associated with dystrophic processes in astrocytes. In addition, this increase may indicate a violation of the barrier function of the BBB. Upward deviations in the content of auto-AT to MBP and NF-200 may, with high probability, indicate degenerative changes in axons, including their myelin sheaths (demyelination). The highest serum concentrations of GFAP were found in neurolepsy. purulent meningitis, febrile schizophrenia, encephalitis, Alzheimer's disease, multiple sclerosis, strokes, open head injury and other critical conditions associated with impaired blood-brain barrier. In addition, the mechanism of the damaging effect of ethanol is the activation of free radical processes. With alcohol intoxication, there is an increase in free radical processes and an increase in the formation of MDA. These processes are activated by increasing

the duration of the introduction of the toxin. The enhancement of free-radical processes leads to an increase in BBB permeability and the formation of auto-at to NSB and neurotransmitters.

Thus, the results of the performed studies show the dependence of the severity of autoimmune reactions of the majority of the studied neutropic autoantibodies on the chronic effects of alcohol intoxication. At the same time, chronic effects of ethanol are accompanied by changes in opioidergic, adenosinergic, GABAB-ergic, glycinergic and other systems, as well as signal transduction processes (secondary and tertiary messengers). The processes of membrane destruction in brain tissue during alcohol intoxication can be viewed from the standpoint of autoimmune disorders. Changes in the content of auto-at to antigens from the nervous tissue are likely to indicate pathogenetic changes in the functioning of the immune system and be used as predictors of damage to the nervous system during alcohol intoxication. Therefore, alcohol intoxication is accompanied by damage and death of neurons, astrocytes, oligodendrocytes and microglia. Ethanol, acetaldehyde and its adducts are the trigger of these violations. A unfolded chain of interrelated pathological processes arises – the release of NSB, which entails the loss of tolerance of the immune system to the antigen of the brain and the development of autoimmune reactions.

Conclusion:

1. The dependence of the severity of autoimmune reactions to NF-200, GFAP, S-100 MBP and VGCC proteins on the duration of intoxication with ethanol was established.

2. The results indicate that alcohol intoxication is accompanied by damage and death of neurons, astrocytes, oligodendrocytes and microglia.

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CONGENITAL RISK FACTORS IN UZBEK POPULATION WITH NONSPECIFIC AORTOARTERIITIS

Abstract: The distribution of HLA antigens in patients with aortoarteriitis in the Uzbek population (UP) was studied. 42 patients with nonspecific aortoarteriitis (NAA) were examined, the control group consisted of 100 healthy donors of Uzbek nationality. The results of the studies demonstrate that the most frequently identified antigens are HLA-B13, B40 and DR2. These antigens play an important role in predisposition to NAA. The more rarely identified antigens are: HLA-A10 and B35 playing the role of protectors in predisposition to NAA. HLA-B40 antigen has the highest relative risk (RR = 6.7). Combinations of these antigens in the individuals' phenotype increase the risk of NAA. The most frequently demonstrated haplotypes are: HLA-A11/B40, B40/DR2, A3/B13.

Keywords: nonspecific aortoarteriitis, HLA antigens, Uzbek population, phenotype, risk, haplotypes.

The recent decades saw the rise of the incidence of NAA in different countries of the world including CIS countries. In the 30s–50s NAA was classified with a casuistic disease but today it ranks second in frequency of involvement of aortic arch branches, yielding only to atherosclerosis [4].

The etiology and, in many respects, the pathogenesis of this disease have not been specified until now and thus remain the point at issue.

The majority of the research workers think that NAA is an autoimmune disease marked by primary involvement of the intima and media of the aorta and main vessels [5]. On account of the key role the immune mechanisms play in the pathogenesis of NAA it should be assumed that certain allelic genes of the HLA system are implicated in it. As established, the HLA system controls the immune system of man. However, in the literature there are only single controversial communications about the relationship between some HLA-antigens and NAA [1; 6].

The purpose of the present study was to examine distribution of HLA-antigens in the UP presenting with NAA.

Materials and methods. The present work is based on an analysis of the data on 42 UP aged 15 to 36 years (medium age 22.3 years) who were examined at the Department of Angiology of Bukhara regional Multidisciplinary Medical Center. There were 18 men and 24 women. All the patients were diagnosed to have chronic NAA. 26 patients had a continuously recurrent and 16 a latent disease pattern.

The diagnosis was established on the basis of the disease history, objective examination, physical and instrumental studies (volumetric sphygmography, rheoencephalography, Doppler ultrasound, contrast aortography). All the patients were found to have aortic arch syndrome. In 15 patients, it was associated with vasorenal hypertension, and in 4 patients with vasorenal hypertension and aortic bifurcation syndrome. Class I and II HLA-typing was performed using the 2-step microlymphocytotoxic test with a panel of typing sera provided by the Saint-Petersburg Research Institute of Hematology and Blood Transfusion, Ministry of Public Health and Medical Industry of the RF. On analysis account was taken of 12 locus A HLA-antigens: A1, A2, A3, A9, A10, A11, Awl9, A25, A28, A32, Aw33, Aw34; 16 locus B antigens: B5, B7, B12, B13, B14, B15, B16, B17, B18, Bw22, B27, B35, B40, B50, B51, B60; 4 locus C antigens: Cwl, Cw2, Cw3, Cw4; 14 locus DR antigens: DR1, DR2, DR3, DR4, DR7, DRw8, DR9, DRwlO, DRwll, DR12, DRwl3, Drwl4, DRwl5, DRwl6; 5 locus DQ antigens: DQw2, DQw3, DQw4, DQw7.

Distribution of HLA-antigens in the patients' population was studied as compared to distribution of the same antigens in the healthy Uzbeks (n-100) living in the Bukhara region. The reliability of the frequency of HLA-antigens distribution

in the groups under comparison was computed with the aid of the χ^2 criterion (criterion of correspondence). The association force was expressed via the relative risk (RR), the value indicates how many times more often or more seldom the individuals with the given HLA phenotype may develop the disease as compared to those lacking this phenotype. The RR was calculated according to the formula Woolf:

$$RR = \frac{a \cdot b}{d \cdot c},$$

where a, b, c, d are values of the four-pole table: a – the number of patients with the given antigen, b – the number of patients lacking this antigen, c – the number of healthy individuals with the given antigen, d – the number of individuals without this antigen.

Results and discussion. Studies have shown that in the Uzbek population there were antigens of the HLA-F locus in the compared groups, such antigens as Al, A2, A3, A9, A28, A32. HLA=B5, B7, B8, B12, B50 are among specificities of the HLA-B locus, Cw2, Cw4 among those of C locus, DR1, DR3, DR4, DR7, DRw8, DR9, DRwlO, DRwl 1, DRwl3, DRwl4 among those of DR locus, and DQ2, DQ4, DQw7 among those of locus DQ. However, together with uniform distribution of HLA-antigens in the group of NAA patients, the frequency of which noticeably exceeds that identified in the controls. These are All (25% versus 13.7% in the controls), B13 (55% and 19.6%), B40 (30 and 5.9%). Among class II HLA antigens, these are DR2 (45% versus 21.1% in controls, DRwl 6 (7.5 and 1.1%).

Meanwhile the statistically significant difference in the frequency of HLA-antigen identification in NAA patients and healthy individuals was established for antigens such as B13 ($\chi^2 = 4.08$; $p < 0.05$; RR = 3.54); B40 ($\chi^2 = 5.35$; $p < 0.05$; RR = = 6.7); DR2 ($\chi^2 = 7.0$; $p < 0.05$; RR = 3.8). As seen from the data obtained, the highest relative risk is discovered in Uzbeks having HLA = ^{r}B40 phenotype; on combination in the HLA-phenotype of the above-indicated antigens (B13, B40, DR2), the RR appreciably rises, increasing the disease risk in its carriers. It follows from the data presented that HLA=B13, B40and DR2 antigens may be regarded as unfavourable antigens determining predisposition to NAA in the Uzbek population. As compared to the healthy population, the frequency of identification of certain antigens in NAA patients was, on the contrary, considerably lowered. These are HLA = A10 (50% versus 21.6% in the control) and B35 (5 and 23.5%) antigens.

Therefore, these antigens determine the resistance to NAA in the UP and can be classified with protective genetic factors of NAA.

Analysis of the antigenic combinations has demonstrated that HLA-phenotypes, namely B13 = B40; A2 = A3 and haplotypes: A1/B7; A1/B13; A2/B13; A11 /B40; B40/DR2 occurring at an increased rate in the patients are most significant for NAA occurrence in the UP. As seen from, six HLA haplotypes were identified most frequently in patients with NAA. Of these, 3 were found to be of statistical power. The highest reliability was marked for B40/DR2 haplotype ($\chi^2 = 6.05$; $p < 0.01$), then there follow A11/B40 haplotype ($\chi^2 = 5.07$; $p < 0.01$) and A3/B13 haplotype ($\chi^2 = 3.89$; $p < 0.05$).

The data obtained allow the conclusion to be drawn that predisposition to NAA in the UP is associated precisely with these HLA haplotypes. The positive importance of the gene linkage nonequilibrium was established for all these haplotypes. For instance, as far as HLA = A3/B13 haplotype is concerned, the observed frequency was 2.3 times higher than theoretically expected and that for HLA-B40/DR2 haplotype was 2.1 times higher. The greatest difference between the observed and theoretically expected frequency was noted for HL A = A11 haplotype, constituting 4.9. The data presented evidence the significance of these haplotypes for predisposition to NAA in the UP. We are thus confident that NAA is marked by the genetic factors of predisposition to NAA associated with the HLA system.

The HLA markers identified point to the polygenous nature of the hereditary factors of predisposition to NAA. The genetic markers of predisposition to NAA in the Uzbek population are HLA = B13, B40and DR2 antigens.

Khraishi M. M. et al. [6] who studied class I and II HLA-antigens in europeoids in the USA failed to reveal any significant difference in the frequency of their identification in NAA patients and healthy subjects. At the same time they discovered a statistically significant decrease in the frequency of DR1 antigen which may indicate its protective role in the pathogenesis of NAA.

The other research workers [7] identified in Japanese patients with NAA an association with HLA = Bw51, Bw52 related to a group of HLA = B5 antigen crossovers.

Our findings evidence the presence of HLA- associated genetic predisposition to NAA in the UP. HLA-B40, B13 and DR2 antigens appeared markers of predisposition to NAA. The relations discovered indicate the polygenous nature of the hereditary factors of predisposition to NAA in the Uzbek population. It should be noted that the data on the relationship between HLA-DR2 and NAA in the UP coincide with those obtained by Japanese authors. Mechanisms of the impairment of the genetic control of immune response are likely to underlie predisposition to NAA in Uzbeks with DR2 antigen. This is confirmed by the deficiency of T lymphocytes and subpopulation of T-suppressors in the patients with NAA [8; 9] Of note, the identified associations (HLA = B40, B13, DR2) in the Uzbek population with NAA were established for the first time. Nevertheless the association with HLA = B13

antigen was determined previously in the Uzbek population presenting with infectious allergic bronchial asthma and pollenosis whereas the association with HL A = B40 antigen was recognized in patients suffering from atopic bronchial asthma. This points to the presence of the common pathogenetic mechanisms underlying these diseases.

It has been demonstrated recently [2; 3; 8] that in Uzbeks, the presence of HLA = B13 antigen is associated with a high level of mitogen-induced proliferative activity whereas the presence of HLA-B40 antigen with the reduced spontaneous level of lymphocyte proliferation. Therefore, the presence of these antigens in individuals and alterations in lymphocyte immune responsiveness may also be initially unfavourable factors that form the basis for the development of the autoimmune process associated with NAA.

Thus, the data presented indicate that investigation of the HLA-antigenic composition of the tissues is a research priority and is badly needed organization of the goal-oriented examination of the population. Determination of the HLA phenotype permits identification of the subjects predisposed to NAA by screening a group of subjects at high risk for the disease, thereby enabling early prophylaxis of the pathology to be carried out. Our investigations make a definite contribution to the understanding of the mechanisms of the relationship between the HLA system and predisposition to autoimmune diseases in the UP.

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ASSOCIATION ANALYSIS OF THREE MDR1 (ABCB1) GENE VARIANTS (C1236T, G2677T AND C3435T) AND THEIR GENOTYPES OF THE RHEUMATOID ARTHRITIS PATIENTS

Abstract: Genetic studies of the polymorphism genotypes of the MDR1 gene in 76 patients with rheumatoid arthritis showed certain dependencies on the stability of the basic therapy. The triple genotype CT-GT-CT (C1236T-G2677T / A-C3435T) was found to be common among patients with drug resistance. From this it follows that the genotypes of polymorphisms of the MDR1 gene may have a certain effect on the course of RA.

Keywords: rheumatoid arthritis, MDR1 (ABCB1), RA, genotype, polymorphism.

Rheumatoid arthritis (RA) is the most common inflammatory rheumatic disease, characterized by a progressive course with the formation of deformities and severe functional disorders of the musculoskeletal system, damage to internal organs, which leads to disability and reduced life expectancy of patients [8, 93–97]. Over the past decade, major changes have occurred in the management of RA patients, which have significantly improved the results of treatment and made it possible to set the main goal – achieving clinical remission (recommendations of EULAR, 2013). Targeted progress is associated not only with the use of basic disease-modifying anti-rheumatic drugs, but also with specially developed innovative genetically engineered biological preparations (GIBP). However, despite the entire arsenal of modern drugs in the treatment of this disease, in 25–30% of cases, "complete clinical remission" or "low disease activity" is not achieved due to refractoriness to treatment [5, 1484–1487]. This is due to the fact that currently RA is considered as a complex disease, the development of which is influenced by both genetic factors and environmental factors [2, 13–15; 3, 56–58]. It is well known that the response to the effects of chemical factors, including the response to medication, is individual and depends on lifestyle, age, gender, ethnicity, health, nutrition, interactions of the drugs used, individual metabolic characteristics. According to some estimates [4, 59–60], from 50 to 90% of adverse pharmacological responses is determined by the genetic characteristics of individuals. The study of individual genetic differences underlying the variability of the body's response to a particular drug is of paramount importance for the optimization of pharmacotherapy. It follows from this that it is necessary to search for new approaches in the treatment of RA, i.e. the expansion of pharmacogenetic research, in particular the study of the relationship of the genotype with the clinically significant effect of the drug and the perverse reaction to the drug, as well as the study of the relationship of the genotype with the drug metabolism. Therefore, in recent years, most attention is paid to the metabolic characteristics of metatrexate in the liver under the predominant influence of transport proteins, in particular, the P-glycoprotein (P-gp) group of proteins, which is encoded by the MDR1 gene (multi drug resistancegene 1) [4, 59–60; 7, 933–936]. The product of the MDR1 gene is P-gp, acting as a transmembrane pump, and affects the action of many drugs [5], in particular metortrexate. According to [1, 427–433], the activity of this protein primarily depends on the polymorphism of the gene encoding its structure. Therefore, genetic studies aimed at studying the characteristics of the protein transport system (MDR1) involved in the metabolism of basic drugs allow us to solve

problems regarding the prediction of the clinical course of RA, as well as the issues of selecting effective doses of basic therapy to achieve the main goal of "clinical remission" of the disease.

Materials and methods of the research. The study involved 76 patients with RA of uzbek nationality, of which women accounted for 73 people, and men – 3 patients, aged 48.9 ± 15.9 years, with disease duration 7.5 ± 3.1 years. RA was diagnosed according to the criteria of the American College of Rheumatology (ACR). 75.6% of patients had high and 24.4% moderate RA activity (DAS28).

Genotyping of ABCB1 gene. Venous blood of 3 mL was drawn from patients during their visit to the the Rheumatology Department and stored in EDTA tubes. Genomic DNA was extracted from blood samples using an "RIBO-prep" reagents (AmpliSens, Russia). Genotyping A reagent kit was used to determine the MDR1 C3435T, C1236T, T3435C polymorphism. (SINTOL, Russia).

The PCR of G2677A, polymorphism was performed in a total volume of 25 mkl, using 100 ng of genomic DNA with 20 pmol primers each, 0.2mM of each dNTP, 1 × buffer, 2 mM of $MgCl_2$ and 1 U *Taq* DNA polymerase The MDR1 C3435T, C1236T, T3435C genes polymorphism was determined using the polymerase chain reaction assay. The cycling conditions performed in 7500 Fast Real time PCR system (Applied Biosystems, USA).

The results were subjected to static processing using the computer program EXCEL and STATISTICA 6.0., With the calculation of the arithmetic mean and deviation errors (M ± m). The significance of differences was calculated using the Wilcoxon method.

Results. In the present study, 76 patients with RA were evaluated for the presence of C1236T, G2677T and C3435T polymorphisms of the ABCB1 gene. As shown by the results of genetic analysis in patients with RA, normal and mutant homozygotes as well as heterozygotes were detected for all selected polymorphisms (Table 1). In our results, the normal homozygous polymorphism of the three isoforms of the MDR1 gene SS genotype was found in the C3435T isoform in 31.5%, in the G2677T isoform in 27.6% of patients with RA. It is noteworthy that in RA patients with a carrier of normal C1236T homozygotes, the genotype did not occur at all. In turn, mutant homozygotes were found in all isoforms of this gene, but there was no significant difference between them in the frequency of occurrence ($p > 0.05$). Thus, TT genotype was found in C3435T isoform in 29%, in G2677T isoform in 27.6%, and in patients with C1236T isoform in 27.6%.

Especially significant was the presence of heterozygotes (CT genotype), which had a high occurrence rate of 39.5% with the C3435T isoform, with the G2677T isoform at 44.8% and the C1236T isoform at 72.4%.

Table 1. – Allele and genotype frequencies of RA patients

MDR1 gene	Patients (n=76)	%
C1236T		
CC	0	0
CT	55	72.4
TT	21	27.6
Allele		
C	55	36.1
T	97	63.9
G2677T		
GG	22	28.9
GT	31	40.7
TT	23	30.2
Allele		
C	75	49.4
T	77	50.6
T3435C		
CC	24	31.5
CT	30	39.5
TT	22	29.0
Allele		
C	78	51.3
T	74	48.7

The allelic frequency showed that the C allele was found in the T3435C isoform in 51.3%, in the G2677T isoform in 50% and in the C1236T isoform in 36.1% of patients. In the analysis of allelic forms, the T allele was found in the T3435C isoform in 48.7%, in the G2677T isoform in 50% and in the C1236T isoform in 63.9% of patients.

Table 2. – Comparative analysis of combined genotypes of RA patients

Triple genotypes	Patients n=76	%	Double genotypes	Patients n=76	%
T3435C-G2677T- C1236T			**T3435C-G2677T**		
CC-GG-CC	0	0	CC-GG	0	0
CC-GG-CT	0	0	CC-GT	4	5.2
CC-GG-TT	0	0	CC-TT	20	26.31
CC-GT-CC	0	0	CT-GG	4	5.2
CC-GT-CT	4	5.26	CT-GT	23	30.2
CC-GT-TT	0	0	CT-TT	3	3.94
CC-TT-CC	0	0	TT-GG	18	23.68
CC-TT-CT	1	1.31	TT-GT	4	5.26
CC-TT-TT	19	25.0	TT-TT	**0**	**0**
CT-GG-CC	0	0	**T3435C-C1236T**		
CT-GG-CT	3	3.94	CC-CC	0	0
CT-GG-TT	0	0	CC-CT	7	9.21
CT-GT-CC	0	0	CC-TT	17	22.3
CT-GT-CT	20	26.32	CT-CC	0	0
CT-GT-TT	4	5.26	CT-CT	27	35.5
CT-TT-CC	0	0	CT-TT	3	3.9
CT-TT-CT	2	2.63	TT-CC	0	0
CT-TT-TT	1	1.31	TT-CT	21	27.6
TT-GG-CC	0	0	TT-TT	1	1.3
TT-GG-CT	17	22.3	**G2677T-C1236T**		
TT-GG-TT	1	1.31	GG-CC	0	0
TT-GT-CC	0	0	GG-CT	21	27.63
TT-GT-CT	4	5.26	GG-TT	1	1.3
TT-GT-TT	0	0	GT-CC	0	0
TT-TT-CC	0	0	GT-CT	28	36.8
TT-TT-CT	0	0	GT-TT	3	3.9
TT-TT-TT	0	0	TT-CC	0	0
			TT-CT	4	5.2
			TT-TT	19	25

When we analyzing the triple genotyping from 27 combinations of genotypes in our study, 16 did not occur at all, and the most frequently occurring genotype was CT-GT-CT, which was found in 26.32% of cases. Besides, two more genotypes were encountered more often than others: CC-TT-TT-22.36% and TT-GG-CT-21.1% (table number 2). The remaining 8 genotypes were found in an insignificant number (CC-TT-CT, CT-TT-TT, TT-GG-TT,– 1.31% genotypes, CT-GG-CT-3.94%, CT-GT-TT –5.26%, CT-TT-CT-2.63%, TT-GT-CT-6.57%. When analyzing double genotyping, CT genotype dominance was revealed (T3435C / G2677T-30.2%; T3435C / C1236T – 35.5%; G2677T / C1236T-40.7%)

Our results suggest that the CT genotype might be a susceptibility factor for the disease phenotype. In our further studies, based on the triple genotype, we plan to formulate a phenotypic characterization for RA patients.

Discussion. As mentioned above, drug resistance is one of the important factors affecting the effectiveness of RA therapy. Individualization of pharmacotherapy, which is engaged in pharmacogenetics, consists of identifying polymorphic markers associated with changes in the body's

response to drugs, developing methods for genotyping patients, and introducing this approach into practical medicine. Recently, there has been an increase in the number of reports that some cell membrane transporters may influence the distribution of drug compounds. P-gp encoded by the gene MDR1 is a transport protein that plays a key role in the removal of a number of drugs from the cell [9, 496–503]. Some researchers suggest [5, 1484–1489] that there is an association of MDR1 gene polymorphisms with the efficacy and safety of many drugs. Currently, many polymorphic markers in the MDR1 gene have been studied, but three of them, C1236T, G2677T / A, and C3435T, are preferred to study associations. The rest, as a rule, occur with a low frequency, which does not explain the widespread disturbances in the functioning of P-gp. The C3435T and C1236T polymorphisms are believed to lead to a decrease in the expression of the MDR1 gene, and the "apparent" influence of the polymorphic marker G2677T/A is attributed to the linkage effect [10]. Therefore, in our work, we investigated the relationship between the three isoforms of the gene MDR1 (ABCB1) in RA. According to the literature [6], MDR-1 was one of the MDR genes, and its polymorphism was correlated with the activity of P-gp. Indeed, according to the literature [9, 496–503], the likelihood of clinical remission of RA after therapy with methotrexate and glucocorticosteroids in patients with the carrier of the 3435TT mutant genotype is higher than in patients with the 3435CC and 3435CT genotypes. This causes a discussion, since it follows from this that mutant genes have a double effect on the metabolism of drugs. Firstly, as a gene that has been altered against the background of environmental factors, it can have an inadequate effect on the body on the one hand [12, 546–554] and, secondly, a positive one, like suppression of disease activity and its response to therapy [7, 933–937]. Therefore, the results of our studies indicate the need for further clarification of the role of the influence of mutant homozygotes on the metabolism of metatrexate in patients with RA of Uzbek nationality, since the frequency of occurrence was high in all MDR-1 isoforms.

According to the literature, there is no doubt that during the carriage [11, 1041–1049], the genotype MDR13435 CT has a bad response ($p = 0.01$) to methotrexate, and with the CC-genotype, the positive response is opposite ($p = 0.01$). Therefore, recently, an attempt has been made to develop a prediction or predictive model containing genetic and clinical indicators for identifying patients with drug resistance to methotrexate.

Of particular interest is the study on the identification of frequencies of polymorphic variants of MDR1 genes, because according to the results of our studies, the triple genotype CT-GT-CT (C1236T-G2677T / A-C3435T) was common among patients with drug resistance. Literature data on the role in the combination of the above ternary genotypes on the metabolism of metatrexate in RA are absent. Therefore, further research is needed to understand the relationship between polymorphisms of the ABCB1 gene and the perception of PA treatment.

Conclusions: Genetic studies of the polymorphism genotypes of the MDR1 gene in RA patients showed certain dependencies on the stability of the basic therapy. The triple genotype CT-GT-CT (C1236T-G2677T / A-C3435T) was found to be common among patients with drug resistance. From this it follows that the genotypes of polymorphisms of the MDR1 gene may have a certain effect on the course of RA. The obtained data can be used in studies devoted to the study of the functional manifestations of polymorphic variants of MDR1, in the study of individual pharmacokinetics of various drugs, as well as in population-genetic studies. The data on the distribution frequencies of the studied alleles can serve as material for comparing the results in population studies by other authors.

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PSYCHOTROPIC ACTIVITY OF N-(3-OXY-4-METHOXY-6-BROMOBENZOYL) AND N-(3-BROMO-4-METHOXYBENZOYL) CYTISINE HYDROCHLORIDE

Abstract: Psychotropic activity of new N-benzyl cytisine derivatives in open field conditions, their antihypoxant activity on a model of normobaric hypoxia with hypercapnia, anti-narcotic (ethaminal sodium, alcohol) and anticonvulsant activity (pentylenetetrazole) have been studied. It was established that the investigated substances have a psychostimulating effect, increase locomotor activity, exploratory behavior, the resistance of brain to hypoxia, and have antinarcotic and weak anticonvulsant action.

Keywords: cytisine derivatives, nootropic activity, antihypoxant activity, locomotor activity, convulsions, narcosis, exploratory behavior.

Introduction and research methods: Nowadays, one of the priorities of psychopharmacology is the search for effective and safe drugs for the pharmacological correction of neuropsychiatric disorders that, according to a multicenter study, were diagnosed in 50–75% of the world's population [1–4].

Nootropic drugs are widely used in the complex therapy of neurological dysfunctions. They are used to treat various disorders of cognitive, mental functions, including mnestic, arising from hypoxia, intoxication, acute and chronic alcoholism, cranial brain injuries, with various degenerative brain lesions, Alzheimer's disease, to enhance creative activity, especially in the elderly and senile age, recovery of mental retardation of children, as well as increasing the body's resistance to extreme conditions [5–8].

In this regard, the search for promising new nootropic drugs is conducted among representatives of various classes of chemical compounds, including among substances of plant origin [9–11]. Cytisine derivatives are promising substances in this area [12–16].

The purpose of this work is to study the psychotropic activity of new N-benzyl derivatives of cytisine: N-(3-hydroxy-4-methoxy-6-bromobenzoyl) cytisine hydrochloride and N-(3-bromo-4-methoxybenzoyl) cytisine hydrochloride.

The analyzed substances were administered subcutaneously at doses of 0.1, 0.5, 1, and 5 mg/kg. Each dose was tested on 10 mice males weighing 18–22 grams. A control group of mice under the same experimental conditions were injected with sterile isotonic NaCl solution.

The effect of the studied compound and the etalon drug (piracetam) on the exploratory behavior was performed in open field 40 × 40 cm area, drawn on 10 × 10 cm squares with 16 round holes of diameter 4 cm. The behavior of the experimental mice was observed in 30 minutes after the preliminary subcutaneous administration of the preparations. During 2 minutes a number of horizontal displacements by the number of crossed squares, the number of stepping on the hind legs and a number of surveyed holes have been registered. The average values of group

parameters, standard deviations and confidence intervals were calculated.

Antihypoxant activity was studied using a model of normobaric hypoxia with hypercapnia. Animals were placed by pairs in hermetically sealed cans of 500 cm^3. The survival time of mice under hypoxia was recorded, and the percentage increase in survival time was calculated relative to the control group. Each dose was tested on 10 animals. Experiments were performed compared with the drug piracetam.

Analeptic effect of the substances was assessed by their antagonism to sodium ethaminal and ethanol intraperitoneally at doses of 50 mg/kg and 4.8 g/kg, accordingly, in 30 minutes after the subcutaneous injection of the studied substances. The duration of lateral position was recorded. The effectiveness of the investigated substances was compared with pentylenetetrazole and caffeine.

Convulsions were caused by subcutaneous administration of pentylenetetrazole at a dose of 80 mg/kg. The studied substances were injected subcutaneously in 30 minutes before pentylenetetrazole. Tremor, the duration of convulsions and time of animal death were detected.

The acute toxicity was studied at subcutaneous injection of substances. The data were processed by Student and Litchfield-Wilcoxon methods.

Results and discussion: the new N-benzyl derivatives of cytisine N- (3-hydroxy-4-methoxy-6-bromobenzoyl) and N-(3-bromo-4-methoxybenzoyl) cytisine hydrochloride showed high psychotropic activity.

The tested N-benzyl cytisine derivatives significantly increased locomotor activity and exploratory behavior of experimental mice in the open field depending on the administered dose. The introduction of N- (3-hydroxy-4-methoxy-6-bromobenzoyl) cytisine and N- (3-bromo-4-methoxybenzoyl) cytisine at a dose of 0.1–0.5–1.0 mg/kg increased locomotor activity by 60.4–104.6% and 13.9–134.8%, respectively; the number of vertical stands depending on the administered dose was 38.8–122.2% and 11.1–111.1%, and the number of surveyed holes was 39.2–87.5% and 48.9–85.7%, respectively. At a dose of 5 mg/kg the number of horizontal movies, vertical stands and examined holes decreased (Table 1). These effects are attributed to many known nootropic drugs.

Table 1.– Effects of N-benzoyl derivatives of cytisine on locomotor activity of mice (n=10)

No.	Investigated substances	Dose, mg/kg s.c.	Number of horizontal movies	Number of vertical stands	Number of examined holes
1	Control (isotonic NaCl solution)	0.2	8.6 ± 0.8	3.6 ± 0.3	11.2 ± 0.9
2	Piracetam	400	13.8 ± 0.6*	4.6 ± 0.4	16.4 ± 0.7*
3	N-(3-oxy-4-methoxy-6-bromobenzoyl) cytisine	0.1	14.2 ± 1.0*	5 ± 1.1	15.6 ± 1.3
		0.5	17 ± 1.5*	6.8 ± 0.5*	17.4 ± 1.7*
		1.0	17.6 ± 1.4*	8 ± 0.7*	21 ± 1.9*
		5.0	18.8 ± 1.2*	6.2 ± 0.4*	18.4 ± 1.6*
4	N-(3-bromo-4-methoxybenzoyl) cytisine hydrochloride	0.1	7.4 ± 0.7	3.2 ± 0.3	12.2 ± 0.9
		0.5	20.2 ± 1.8*	7.4 ± 0.5*	13.5 ± 1.5
		1.0	17.8 ± 1.5*	7.6 ± 0.6*	20.8 ± 2.0*
		5.0	13 ± 1.0*	5.8 ± 0.4*	14.6 ± 1.3

*Note: * P < 0.05*

The study of N-(3-hydroxy-4-methoxy-6-bromobenzoyl) cytisine and N-(3-bromo-4-methoxybenzoyl) cytisine antihypoxant activity on the model of normobaric hypoxia with hypercapnia showed a distinct protective effect, increasing the survival time in comparison with the control group of animals (Table 2). N-(3-hydroxy-4-methoxy-6-bromobenzoyl) cytisine increased the survival time of experimental mice in comparison with the control group at doses of 0.1 and 0.5 mg/kg by 24.4 and 22.4%, respectively, and exceeded piracetam.

Table 2.– Mice survival time in normobaric hypoxia with hypercapnia (n=10)

No.	Investigated substances	Dose, mg/kg s.c.	Survival time, min.	Increase of reserve time,%
1	*2*	*3*	*4*	*5*
1	0.9% NaCl solution (control)	0.2	24.5 ± 3.3	–
2	Piracetam	400	27.2 ± 2.9	11%

1	*2*	*3*	*4*	*5*
3	N-(3-oxy-4-methoxy-6-bromo-benzoyl) cytisine	0.1	30.5 ± 2.1	24.4%*
		0.5	30 ± 2.3	22.4%*
		1.0	27.2 ± 1.9	11%
		5.0	29 ± 1.5	19.8%*
4	N-(3-bromo-4-methoxybenzo-yl) cytisine hydrochloride	0.1	27.5 ± 2.3	12.2%
		0.5	25.6 ± 2.7	4.4%
		1.0	27.5 ± 2.9	12.2%
		5.0	26.7 ± 2.5	8.9%

*Note: * P < 0.05*

The investigated substances showed marked antagonism to the somnolent effect of sodium ethaminal and alcohol intoxication (Tables 3.4). Being preliminary injected before pentylenetetrazole introduction, they increased the latent period and duration of convulsions (Table 5). The investigated substances at a dose of 1 mg/kg decreased animal death on this model.

Table 3. – Antagonistic effect of investigated substances to ethaminal sodium somnolentent effect (n=10)

No.	**Investigated substances**	**Dose, mg/kg**	**Somnolent effect duration**		**Effectiveness, %**
			min	**%**	
1	Ethaminal sodium i.p. (control)	50	92.6 ± 8.8	100%	–%
2	Pentylenetetrazole s.c.	10	64.7 ± 6.5	69.8%	–30.2%*
3	Caffeine s.c.	10	68.4 ± 5.9	73.8%	–26.2%*
4	N-(3-oxy-4-methoxy-6-bromo-benzoyl) cytisine hydrochloride s.c.	0.1	76.5 ± 6.8	82.6%	–17.4%
		0.5	74.2 ± 5.9	80.1%	–19.9%
		1.0	63.5 ± 6.1	68.5%	–31.5%*
		5.0	52.8 ± 5.2	57%	–43%*
5	N-(3-bromo-4-methoxybenzo-yl) cytisine hydrochloride s.c.	0.1	55.2 ± 5.6	59.6%	–40.4%*
		0.5	61.4 ± 6.3	66.3%	–33.7%*
		1.0	46.3 ± 5.0	50%	–50%*
		5.0	64.2 ± 5.9	69.3%	–30.7%*

*Note: * P < 0.05*

Table 4. – Antagonistic effect of investigated substances to alcohol intoxication (n=10)

No.	**Investigated substances**	**Dose, mg/kg**	**Somnolent effect duration**		**Effectiveness, %**
			min	**%**	
1	Ethanol i.p. (control)	4.8	107.5 ± 8.9	100%	–%
2	Pentylenetetrazole s.c.	10	75 ± 7.5	69.7%	–30.3%*
3	Caffeine s.c.	10	71.4 ± 6.2	66.4%	–33.6%*
4	N-(3-oxy-4-methoxy-6-bromo-benzoyl) cytisine hydrochloride s.c.	0.1	77.5 ± 7.9	72%	–28%
		0.5	74.6 ± 8.0	69.3%	–30.7%*
		1.0	62.8 ± 6.5	58.4%	–41.6%*
		5.0	54.2 ± 4.7	50.4%	–49.6%*
5	N-(3-bromo-4-methoxybenzo-yl) cytisine hydrochloride s.c.	0.1	79.2 ± 7.9	73.6%	–26.4%*
		0.5	74.8 ± 6.1	69.5%	–30.5%*
		1.0	66.2 ± 6.4	61.5%	–38.5%*
		5.0	64.5 ± 5.8	60%	–40%*

*Note: * P < 0.05*

Table 5.– Effects of investigated substances on pentylenetetrazole convulsion parameters and animal survival (n=10)

No.	Investigated substances	Dose, mg/kg s.c.	Starting of convulsions, min	Duration of convulsions, min	Mice survival	
					died	survived
1	Pentylenetetrazole (control)	80	5.2 ± 0.6	15.8 ± 2.1	10	0
2	Pyracetam	400	6.4 ± 0.8	19.4 ± 1.9	9	1
4	N-(3-oxy-4-methoxy-6-bromobenzoyl) cytisine hydrochloride	0.1	6.2 ± 0.7	15.2 ± 1.9	10	0
		0.5	5 ± 0.6	19.7 ± 1.8	9	1
		1.0	6 ± 0.8	18.6 ± 2.0	9	1
		5.0	7.6 ± 0.5	23.6 ± 1.5	10	0
5	N-(3-bromo-4-methoxybenzoyl) cytisine hydrochloride	0.1	4.8 ± 0.4	18.8 ± 1.9	10	0
		0.5	7 ± 0.6	16.6 ± 2.2	10	0
		1.0	7.8 ± 0.5	20.5 ± 1.5	9	1
		5.0	5.6 ± 0.6	17 ± 1.9	10	0

The acute toxicity of N-(3-hydroxy-4-methoxy-6-bromobenzoyl) cytisine and N- (3-bromo-4-methoxybenzoyl) cytisine in s.c. introduction was 1275 (1118 ± 1453) mg/kg and 820 (713 ± 943) mg/kg, respectively.

Conclusion: Thus, it has been established that N-(3-hydroxy-4-methoxy-6-bromobenzoyl) cytisine and N-(3-bromo-4-methoxybenzoyl) cytisine hydrochloride increase research behavior of animals and show antihypoxant and antitoxic activity. These substances are of great interest in searching for new psychotropic drugs among cytisine derivatives.

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METABOLIC ACTIVITY OF LUNGS IN THE DEVELOPMENT OF AN EXPERIMENTAL MODEL OF SURGICAL SEPSIS

Abstract: Analyzing the results obtained, it can be noted that on the first day of the reproduction of EMHS in the lung, the passage of blood through this organ was accompanied by a marked decrease in albumin and α-2 globulins. Against this background, the proportion of coarse proteins, gamma globulins, which play an important role in the immune responses of the body, increased. Apparently, this phenomenon is due to the increased synthesis of this fraction of blood in the lung tissue in this pathology. In the process of development of EMHS, a significant decrease in the total protein content in serum is observed, which may be due to a decrease in the synthesis of albumin in the liver.

Keywords: experimental model of surgical sepsis, protein fractions, albumin, globulins, mixed venous blood, arterial blood, venous-arterial difference.

The tendency to an increase in the incidence of sepsis in combination with the continuing high mortality contributes to the emergence of more and more new research in this area [1; 2].

Studies of the organ exchange of protein fractions in the lungs in sepsis are few. Meanwhile, there are enough prerequisites for close attention to these compounds [4; 5].

The **aim** of our work was to study the nature of the organ metabolism of protein fractions directly in the lungs during the development of an experimental model of surgical sepsis (EMHS).

Material and research methods. In the experiment, 47 outbred rabbits of both sexes weighing 1500–2500 g were used on the usual laboratory diet of the vivarium of the Tashkent Medical Academy, which meets the requirements of the sanitary epidemiological service.

All animals were divided in to 2 groups:

– control – 12 intact rabbits (without modeling the pathological process);

– the main – 35 rabbits with EMHS.

EMC, with its characteristic phase stages, was modeled according to the original method developed by us – "A method of modeling surgical sepsis with the systemic inflammatory response syndrome of the body" by introducing autoclave suspension into the soft tissues against the background of a preliminary change in the organism's reactivity by analogy with the nature of the pathological process that occurs in clinical practice.

The content of protein fractions in blood samples obtained at the entrance to the lungs in mixed venous blood (CRS) and at the exit of the lungs, in arterial blood (AA) in intact animals (control) and on the 1st, 3rd, 7th, 14th day of the development of EMC.

The protein fractions of blood – albumin, α-1, α-2, β, and γ-globulins (%) were separated by electrophoresis on agarose films.

Results obtained and their discussion. The study of protein fractions revealed an ambiguous relationship of metabolic lung function to albumin and to the total level of globulins. In the control series of experiments, the level of albumin in the CRS was 56.8 ± 1.42%, whereas at the exit from the lungs in AK, its level decreased to 52.4 ± 1.23%($p < 0.05$). VAR, amounting to "–" 4.4 ± ± 0.02%, indicated the utilization of this substrate by the lungs. Unlike albumin, the total amount of globulins increased in the blood sample at the exit of the lung. VAR of the total level of globulins in the control series of experiments was positive and amounted to "+" 2.03 ± ± 0.05%. It should be noted that such changes were noted in all 12 animals studied in this series (Table 1).

Table 1.– The nature of changes in the content of albumin and globulins (%) in various blood samples in the dynamics of the development of EMHS

Blood Tests	Series of experience				
	Control	Dynamics of EMHS			
		1 day	3 day	7 day	14 day
Albumins (%)					
ICV	56.8 ± 1.42	49.1 ± 1.54*	48.2 ± 1.39*	43.3 ± 1.21*	38.1 ± 1.13*
AK	52.4 ± 1.23	44.9 ± 1.12	43.4 ± 1.11*	37.4 ± 1.11*	32.0 ± 1.1*
Total hemoglobin level (%)					
ICV	40.4 ± 1.23	50.7 ± 1.48	51.71 ± 1.98*	56.3 ± 1.12*	61.1 ± 1.13*
AK	42.43 ± 0.98	54.41 ± 1.23	54.5 ± 0.87	56.79 ± 1.11	56.46 ± 0.93*

** P < 0.05 reliable with respect to the control series of experiments*

On the first day of the development of EMHS, the level of albumin decreased as compared with the control series of experiments both in ICV (by 7.7%) and in AK (by 7.5%), respectively. The BAR at that time, which amounted to "–" 4.2 ± ± 0.07%, did not have significant differences compared with the control series of experiments. In this period of development of EMHS, the total level of globulins increased both in ICV (by 10.3%) and in AK (by almost 12%, respectively). BAR at this time increased compared with the control series of experiments in a significant value, reaching the level of "+" 3.71 ± 0.08% ($p < 0.05$).

Unlike albumin, VAR of the total level of globulins did not change unequivocally. In particular, on the 1st day of the development of EMHS, the level of BAP increased from "+" 2.03 ± ± 0.05% in the control series of experiments to "+" 3.71 ± 0.08% during the study period ($p < 0.05$). At the same time, the 3rd day of the development of the pathological process was characterized by a decrease in VAR compared with the previous experiment period to "+" 2.79 ± 0.07%, however, it was higher than the control values. Subsequently, VAR, in terms of the total level of globulins, progressively decreased, and on the 14th day of the development of the pathological process, VAR changed from a "plus" value in favor of a "minus" one, reaching to the level "–" 4.64 ± 0.03% ($p < 0.05$). This circumstance testified to the predominance of catabolic processes over anabolic in the lungs with respect to the substrate under study. On the other hand, a comparative approach to the study of the content of the main fractions of the total protein in various blood samples indicated a high specificity of the metabolic activity of the lungs in relation to globulins, which determined the need for a detailed study of the fractions of globulins.

The study of globulin fractions in ICS showed the most significant changes with respect to α1 – and to α2-globulins (Table 2). Their level in ICS progressively increased with the development of AMHS. At the same time, on the 14th day of the disease, the level of the above fractions in the ICS increased by 1.9–2.0 times compared with the control series, whereas the level of α1 – and α2 –globulins was 1.5 and 1.2 times, respectively ($p < 0.05$).

Among all the studied globulin fractions, α1 – globulins distinguished themselves by relative instability. Their level in SVK increased by the 1st day of the development of the pathological process 1.4 times, and over the next 3–7th day it relatively stabilized. In the next 14 days of observation, the level of this fraction of globulins in the ICS increased again to 14.9 ± 1.2% and reached its maximum value for the entire study period. Regarding α1-globulins, it is necessary to note a gradual increase in its level in ICS, which by the 14th day of development of AMHS had a significant value ($p < 0.05$) in relation to its level in the control series of experiments.

The study of the distribution of globulin fractions in AK showed the following: a progressive type of increase in its level compared with the control series of experiments was noted in relation to the α1 – and α2-globulins. Moreover, in the case of α-globulin, the level of its concentration in AA increased from the control series on the 14th day of the disease by 1.6 times, then the level of α 2-globulins increased by the 14th day of the pathological process by 1.8 times, that is, more significantly compared with the control series of experiments.

Regarding the change in the concentrations of α1 – and α-globulins in AK at the exit from the lungs, it can be noted that their dynamics were wave-like. In particular, the relative increase in the level of α1-globulins in arterial blood on the 1–3rd day of the development of EMHS in the subsequent observation period decreased and was below the control values.

Table 2. – The nature of changes in the content of globulin fractions (%) in various blood samples in the dynamics of the development of AMHS

Globulin Fractions (%)	Series Of Experience				
	Control	Dynamics of EMHS			
		1 day	3 day	7 day	14 day
ICV					
α_1	5.3 ± 1.1	6.0 ± 1.9	7.8 ± 1.1*	8.5 ± 1.9*	10.1 ± 2.1*
α_2	7.2 ± 1.8	11.1 ± 2.8	11.11 ± 2.3*	13.9 ± 2.3*	14.5 ± 1.9*
β	10.2 ± 1.5	14.6 ± 2.2*	13.4 ± 2.7	13.9 ± 2.9*	14.9 ± 1.2*
γ	17.7 ± 1.9	19.0 ± 2.3	19.4 ± 2.2*	20.0 ± 2.8*	21.6 ± 1.2*
AK					
α_1	7.65 ± 1.19	8.21 ± 1.81	8.2 ± 1.13	6.41 ± 1.12	7.82 ± 0.92
α_2	7.42 ± 1.44	11.42 ± 1.78	11.23 ± 1.2	13.25 ± 1.4*	13.21 ± 2.11*
β	12.21 ± 1.93	18.2 ± 1.23*	18.1 ± 2.11*	15.6 ± 1.37*	11.0 ± 1.92
γ	15.15 ± 2.31	16.58 ± 2.34	16.97 ± 1.8*	21.53 ± 2.3*	24.43 ± 1.32*

** P < 0.05 reliable with respect to the control series of experiments*

Similar metabolic activity of the lungs was also shown in relation to α2-globulins. However, in this case, the leveling of VAR occurred against the background of an increase in its physiological parameters on the 1st day of the development of EMHS. At the same time, the modified BAR on the 14th day of the development of AMHS was 5.9 times higher compared with the control series of experiments, whereas in the case of α1-globulins only 1.1 times.

The metabolic activity of the lungs in relation to the глоб-globulins was characterized by a progressive increase in VAR at the 1–3 day of development of AMHS by 1.8 and 2.3 times, respectively. In the subsequent periods of experiments, VAR for this indicator decreased sharply, retaining its "positive" value. This tendency led to a leveling of the relationship of the metabolic activity of the lungs to the α –globulins, decreasing to "–" 3.9 ± 0.1%, that is, by the 14th day of the development of the pathological process, the lungs begin to actively utilize the α –globulins, apparently, for own synthetic needs.

This conclusion we made was not casual, since with respect to the metabolic activity of the lungs to α -globulins it changed in the opposite sense. With relative stability and nature of VAR in this indicator on the 1–3rd day of development of AMHS in the subsequent periods, we found a tendency for VAR in the relation of the metabolic activity of the lungs to this indicator. She acquired a "plus" value and gradually increased. That is, the lungs in this case synthesized α -globulins, increasing their level in AK at the exit of the lungs.

An assessment of the dynamics of the albumin / globulin ratio showed that with the development of AMHS, there was a progressive decrease in its CRS and at the entrance to the organ, and in the AK at the exit of the lungs.

On the 3rd day of the development of EMHS, the level of this index in the ICS slightly increased (from 3.4 ± 0.1 units to 3.6 ± 0.2 units), whereas in AK it did not actually change, decreasing insignificantly from 2 5 ± 0.8 units up to 2.4 ± 0.9 units Against the background of the relative stabilization of the level of this coefficient in AA, on the 7th day of the development of AMHS, there was a significant decrease in the CRS at the entrance to the lungs. That is, against the background of a progressive decrease in this coefficient at the entrance to the lungs, the metabolic activity of the lungs maintained its level within the previous period of the experiments.

Subsequently, on the 14th day of the development of the pathological process, the albumin / α – globulin ratio decreased in the CRS, leading to an increase in its level in AK at the exit of the lungs.

In contrast to the changes in the coefficients described above, an analysis of changes in the albumin / α – globulin curve correlation revealed ambiguity with respect to AK at the exit from the lungs. The progressive reduction of this coefficient in the SVK at the entrance to the lungs was accompanied by ambiguous changes in its arithmetic value in the AK at the exit from this organ. An intensive decrease in the level of this coefficient in AK was accompanied by a decrease in its VAR. At the same time, starting from the 7th day of the development of AMHS, we identified the leveling by the lungs of this coefficient. The lungs led to a progressive decrease in the level of albumin / α – globulin coefficient in AK due to an increase in the proportion of – globulins against the background of a decrease in albumin. When the level of fluctuations of this coefficient in the VBC in the range of 2.2 ± 0.1 units on the 7th day of the disease up to 1.8 ± 0.07 units. on the 14th day of the pathological process, its level in AK decreased to 1.7 ± ± 0.07 units. on the 7th day, and up to 1.3 ± 0.03 units. on the 14th day of the development of EMHS. This, in turn, indicated that the hypermetabolic processes occurring in the lung tissue

during these periods of development of the AMHS were a consequence of the progression of the purulent-septic process, whereas changes in the ICS were a consequence of the generalization of the process of the 7–14th day of the disease.

Analyzing the obtained results, it can be noted that on the first day of reproduction of EMHS in the lung, the passage of blood through this organ was accompanied by a pronounced decrease in albumin and α-2 globulins. Against this background, the proportion of coarse-grained proteins, gamma globulins, which play an important role in the immune responses of the body, increased [5; 6; 10].

Apparently, this phenomenon is due to the increased synthesis of this fraction of blood in the lung tissue in this pathology.

In the process of development of EMHS, a significant decrease in the total protein content in serum is observed, which may be due to a decrease in the synthesis of albumin in the liver, which is also confirmed by literature data [10].

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EFFICACY OF TRAZODONE IN NON-SPECIFIC BACK PAIN: A RANDOMIZED CONTROLLED TRIAL

Abstract: Antidepressants have been prescribed for the treatment of depression and management of chronic low back pain. However, there is no evidence for their efficacy in non-specific low back pain. This study aimed to examine the efficacy of antidepressant compared with the standard treatments in reducing pain, depression level caused by pain in individuals with non-specific back pain. A randomized controlled trial with 6 weeks follow up of adults with chronic non-specific back pain. Total of 40 patients were recruited, randomized and equally divided into 2 arms: control group and study group. The control group received standard therapy while the study group received an addition of antidepressant trazodone. At 6 weeks, it was found that there was a significant reduction of pain (VAS scale) and a significant decrease in depression(Hamilton rating scale for depression). Hence, this study suggests that Trazodone (Trittico), an antidepressant may be an effective treatment for chronic non-specific back pain.

Keywords: non-specific back pain, depression, lumbalgia, chronic back pain, trazodone, serotonin reuptake inhibitors.

Back pain has contributed to a significant proportion in neurological disorders cases. Among these cases, non-specific low back pain has been reported that it affects people of all ages and is a leading contributor to disease burden worldwide. It is also the second most frequent (after respiratory symptoms) reason for seeking medical attention in developed countries.

Chronic pain is a very costly medical phenomenon. The pain treatments including medical care, employee compensations, and loss of productivity involve more than $100 billion a yearin the United States [1; 5]. Apart from that, depression which leads to loss of productivity, substance abuse and/or suicide has contributedto the society about $43 billion a year. The frequency of depression in the general population ranges from 4% to 8%. When there is chronic pain in individuals, the depression can be 3–4 times higher [3].

Back pain is the most common occurrence among all causes of chronic pain. Non-specific back pain is pain that is not caused by any specific pathology, such as infection, tumor, osteoporosis, ankylosing spondylitis, fracture, inflammation, radicular syndrome and horsetail syndrome. The episodes of non-specific musculoskeletal pain disturb 60–85% of the population during life [2,3].Generally, the painwears off by itself. About 90% of patients will recover within 6 weeks, however, 7–10% of cases that this pain becomes chronic. It has been established that 25–60% of patients may experience reoccurrence of chronic back pain within a year after the initial episode. At the same time, over one year, 3–4% of the population is temporarily disabled, and 1% of people of working age become disabled due to chronic back pain [1].

Depression in combination with chronic pain may be higher as compared to depression with any other chronic illness. Up to 57% of patients with chronic pain were diagnosed with depression.Persistent or chronic pain seems to be reciprocally associated with depression and anxiety disorders as the chronic pain can lead to long lasting emotional disturbances, low mood state such as depression and anxiety [3].

Depression is a virtually universal complication of intractable pain. When pain prevents patients from doing the things that give them satisfaction and purpose in life, depression is unavoidable. Hence, antidepressants have become a routine adjunctive therapy for most forms of chronic pain. The antidepressants may inhibit of amines, norepinephrine and serotonin in the CNS, which consistently leads to an increase in the activity of the anti-nociceptive system, causing an increase in the pain threshold, mood modification, and lastly providing a reduction in pain.

The effectiveness of antidepressants for the treatment of major depression is well documented; however, the analgesic properties of this class of medication are yet to be indicated. It is important for the patient to understand for which of these

applications an antidepressant is being prescribed. Likewise, it is important that the physician understand that antidepressants can treat both pain and depression [4].

The aim of our study was to determine the effectiveness of modern antidepressants in chronic nonspecific back pain as a comprehensive treatment. Hence, Trazodone, a serotonin reuptake inhibitor was chosen as it has evidence in treating chronic pain, but its effectiveness in non-specific back pain has not been sufficiently studied.

Materials and methods. The study was conducted in the outpatient setting in 1st Tashkent city clinical hospital and Medical Center "Neyrohelp", Tashkent. All adults over 18 years with chronic (> 12 weeks) back pain at the time of inspection with concomitant depression were recruited. According to the criteria of the Cochrane spinal group 2005, patients with concomitant specific diseases of the spine, including ankylosing spondylitis, osteoporosis, spondylo-arthropathy, the presence of radicular compression syndrome, or diseases accompanied by destruction, osteoporosis of the vertebra, severe spinal deformity, the presence of a hernia of an intervertebral disk measuring 1.0 cm or more, sequestered hernias, pseudospondilolisthesis above II degree, with signs of myelopathy (according to CT, MRI), infections, tumors, fractures, rheumatoid arthritis, autoimmune processes, rheumatic and other neurological diseases were excluded for this study.

The patients ($N = 40$) were randomly assigned to either standard treatment with NSAIDs, muscle relaxants, vitamin B complex for 10 days (control group) or standard treatment with addition of Trazodone (Trittico) (study group). The dose of Trazodone (Trittico) was prescribed on a taper-up scale with 50 mg once daily for 7 days followed by 100 mg once daily for 14 days and continue with 150mg once daily for 21 days in order to minimize the side effects.

The primary outcome parameters were mean VAS score for pain assessment and the mean of the Hamilton scale for the depression severity at the end of each week throughout the 6 weeks of treatment.

Both group of patients were comparable as they were matched for age, sex, and clinical indicators. The average age in the recruited patients were 57.2 ± 1.3 years.

Results and discussions. According to the pain score using VAS scale, there was a decrease in both groups at first week. However, the VAS score increased gradually in control group while the score continued to decrease in study group. At 6th week, the VAS score in study group (2.9) showed halved of the score presented in control group (6.05) (*Figure 1*). Besides, all patients in the study group reported there was an improvement in quality of life throughout the study period.

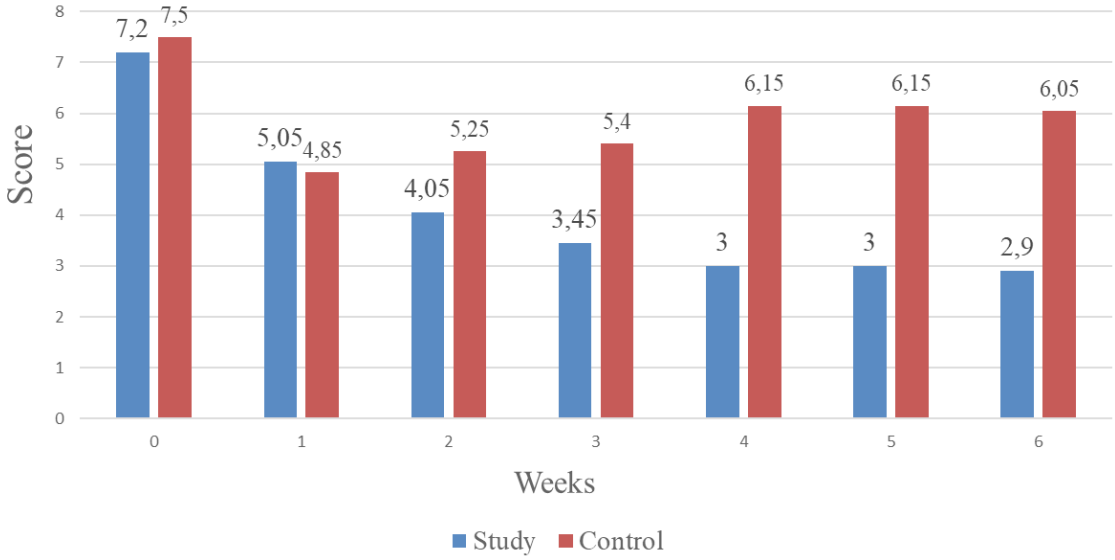

Figure 1. Pain score (VAS scale)

The assessment of depression using Hamilton scale showed a significant improvement in the mental state in patients of the main group (Figure 2). In patients in the control group, improvement was only observed at the beginning of the examination while receiving standard therapy.

In study group, 45% of the patients ($n = 9$) experienced some side effects including nausea, headache, weekness, and drowsiness within first 2 weeks of treatment. 5 patients with drew from the study in between period while the other 4 patients continued the treatment as they have noted the disappearance or significant reduction of the symptomsafter second week of treatment.

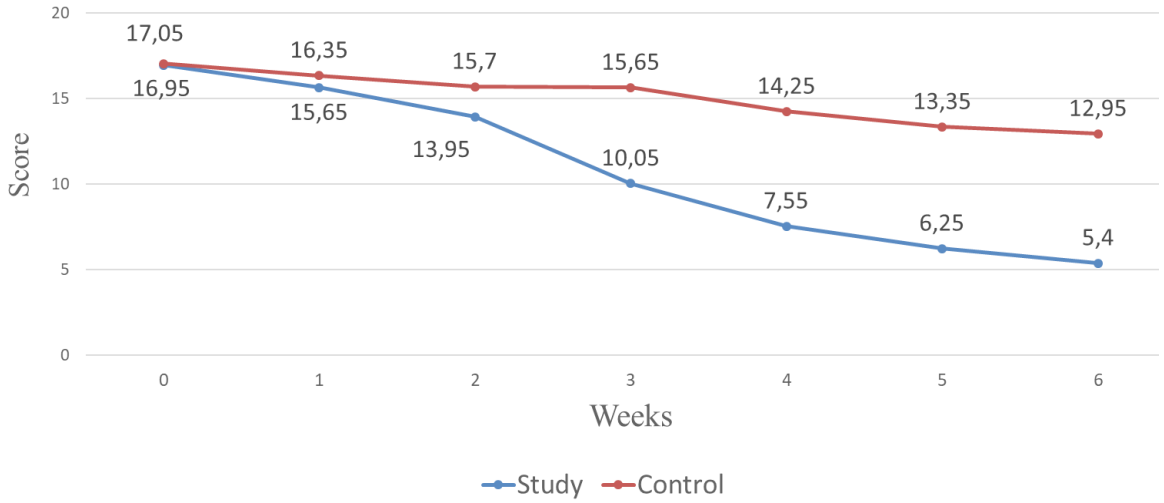

Figure 2. Depression score (Hamilton scale)

Conclusion:

This study showed a reasonable and expedient use of antidepressants as a complex treatment of chronic nonspecific back painas it reduces the pain and the depression symptoms, providing a long-lasting effect. Hence, this study suggests the use of trazodone in treating nonspecific back pain, in the presence of chronic depression and the absence of intolerance in the patient.

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DIAGNOSTIC SIGNIFICANCE OF ENDOTHELIN-1 AND L-FABP IN PATIENTS WITH CERVICAL CANCER

Abstract: In this article, the diagnostic significance of endothelin-1 and L-FABP in diagnostic of cervical cancer (CC)has been studied. To realize the goal, venous blood of 53 patients with CC and 25 patients with cervical leukoplagia (CL) was examined. The results of the study showed that in patients with cervical cancer, the level of endothelin-1 and L-FABP were higher by 38.5%, vs to control and by 14.6%, compared with the results of patients with CL. To clarify the significance of endothelin-1 and L-FABP in the development of CC, we studied the content of some tumor markers (CA125, PEA, CA 19–9, AFP and β-CG) and their correlation. There were statistically significant increases in CA125, PEA, CA 19–9, AFP and β-CG in CC patients, compared with the data of patients with CL.

Keywords: cervical cancer, leukoplagia, endothelin-1, L-FABP and oncomarkers.

Cervical cancer (CC) is one of the most common form of neoplasm among the women malignancies. Each year, 371.000 of new cases of cervical cancer are registered in the world and 190.000 of women die each year [6; 7; 13]. Early detection and treatment of precancerous diseases of the cervix can completely prevent the cancer. The use of new instrumental diagnostic methods is not always available and sometimes there are some difficulties for clarifying the diagnosis [1]. Diseaserelated mortality increases because of the lack of a reliable screening technique for early CC detection. Therefore, the development of highly informative methods for the detection of tumors of the ovaries and cervix, as well as early diagnosis of recurrence of the disease is one of the most important tasks of oncogynecology.

In recent years investigation of tumor markers´ (CA 125, CEA, CA 19–9, AFP and β-CG) level in blood serum takes a great place in CC diagnostic [4].

Tumor markers are important indicators of CC clinical presentation. Due to its high sensitivity and specificity, CA125 has a clearly defined and confirmed role in the monitoring of cervical carcinoma. It rises in approximately 50% of malignant diseases of female reproductive organs and in 75–90% of patients with advanced disease. False positive results have been noted in some disorders, both malignant and benign, which to some extent reduce the specificity and sensitivity of the marker. Therefore, the screening of CC includesCA125, CEA, CA 19–9, AFP and beta CG [3; 4].

Recently, much attention has been paid to the role of biochemical markers in the pathogenesis of CC. Endothelin-1 and L-FABP belong to the number of biological active peptides, which play an important role in carcinogenesis. Endothelin-1 is a polypeptide of 21 amino acid residues, has vasoconstrictor and mitogenic activity. Endothelin-1 is the one of the most significant regulators of the vascular endothelium function besides, by controlling mitogenesis, cell survival, angiogenesis, bone remodeling, stimulation of tumor-permeating immune cells, epithelial-mesenchymal changes play an important role in tumor development and metastasis [8; 9; 17]. L-FABP is a member of the fatty acid binding group that is involved in intracellular transfer of biologically active fatty acids and is involved in intracellular signaling pathways, cell growth and differentiation. In addition, by preventing the increase in the concentrations of intracellular fatty acids, protect cells from their cytotoxic effects. Using a series of studies on the effects of chemical carcinogens

on rat liver, the participation of L-FABP in cell growth and differentiation was determined. A significant increase in L-FABP was observed in normal as well as carcinogen-induced hepatocytes. In addition to acting as a fatty acid receptor, L-FABP is the target protein for several genotoxic carcinogens. The binding of these carcinogens to L-FABP promotes mitogenesis and tumor development [5; 11; 14].

The aim of this work was a comparative study of the diagnostic significance of endothelin-1 and L-FABP in blood plasma in patients with CC and cervical leukoplagia (CL).

Material and methods. The content of endothelin-1, L-FABP and some oncomarkers (CA125, PEA, CA 19–9, AFP and β-CG) was studied in patients with cervical cancer who were on treatment at the oncological clinic of the Azerbaijan Medical University. The main group consisted of 53 patients with cervical cancer (mean age – 50.3 ± 1.3 years). The comparison group included 25 women with CL (mean age 42.4 ± ± 2.4 years). The control group consisted of 12 practically healthy women (mean age – 36.9 ± 2.9 years).

In 7(28.0%) patients a simple form of CL was detected, in 13(52.0%) – proliferative, and in 5(20.0%) – atypical. Among the patients with cervical cancer, 2(3.8%) had a squamous cell cornifiredtype, 43(81.11%) had a squamous cell noncornifired type, 6(11.9%) had an adenocarcinoma, and 2(3.8%) had another types.

The concentration of endothelin 1, L-FABP, CA125, PEA, CA 19–9, AFP and β-CG was determined in blood serum in the study groups using Vector Best immunoassay test systems (Russia), on the STAT FAX immunoassay analyzer. These indicators were determined at the time of admission to the hospital before the start of surgical treatment.

The results were represented as M ± m, where M is the arithmetic mean, m is the error of the mean. The reliability of the differences between the groups was assessed using the Mann-Whitney test, for related values or the Student's t-test for unbound values. The difference was considered significant for $p < 0.05$. The correlation analysis was carried out according to the method of Spearman.

Results and discussion:

As can be seen from the obtained results, the content of endothelin-1 and L-FABP in the blood serum increases in both groups of patients (Table 1).

Table 1. – Dispersion analysis of the studied parameters in patients with cervical cancer

Data	Patients group	N	Overage	Stand. deviat.	Stand. error	95% Hgr	95% Lgr	Fiser	p
1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
L-FABP, ng/ml	Squamous cellcornifired	2	2.41	2.96	2.09	0	28.97	5.385	.003
	Squamous cellnoncornifired	43	2.00	1.42	0.22	1.56	2.44		
	Adenocarcinoma	6	3.80	0.17	0.07	3.62	3.97		
	The others	2	5.10	2.55	1.80	0	27.97		
	Total	53	2.34	1.60	0.22	1.89	2.78		
Endothelin, pg/ml,	Squamous cellcornifired	2	9.0	0.1	0.0	8.3	9.6	11.333	.000
	Squamous cellnoncornifired	43	8.5	0.6	0.1	8.3	8.7		
	Adenocarcinoma	6	9.7	0.3	0.1	9.4	10.1		
	The others	2	10.3	0.4	0.3	7.1	13.4		
	Total	53	8.7	0.8	0.1	8.5	9.0		
CEA, pg/ml	Squamous cellcornifired	2	7.30	0.99	0.70	0	16.19	15.631	0.001
	Squamous cellnoncornifired	43	5.36	1.62	0.25	4.86	5.86		
	Adenocarcinoma	6	7.78	1.34	0.55	6.38	9.19		
	The others	2	8.10	0.57	0.40	3.02	13.18		
	Total	53	5.81	1.79	0.25	5.32	6.31		
CA125, ng/m	Squamous cellcornifired	2	36.75	17.32	12.25	0	192.40	4.187	0.010
	Squamous cellnoncornifired	43	34.81	12.02	1.83	31.11	38.51		
	Adenocarcinoma	6	50.30	2.37	0.97	47.81	52.79		

1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
CA125, ng/ml	The others	2	50.70	1.70	1.20	35.45	65.95		
	Total	53	37.24	12.43	1.71	33.81	40.66		
CA19–9, ng/ml	Squamous cellcornifired	2	27.3	11.3	8.0	0	128.9	1.270	0.295
	Squamous cellnoncornifired	43	39.0	11.7	1.8	35.4	42.6		
	Adenocarcinoma	6	35.7	15.0	6.1	19.9	51.5		
	The others	2	49.4	1.7	1.2	34.2	64.6		
	Total	53	38.6	12.1	1.7	35.3	41.9		
AFP, pg/ml	Squamous cellcornifired	2	10.3	4.0	2.9	0	46.5	0.950	0.424
	Squamous cellnoncornifired	43	10.4	2.4	0.4	9.6	11.1		
	Adenocarcinoma	6	11.8	3.2	1.3	8.5	15.1		
	The others	2	12.4	0.2	0.2	10.4	14.3		
	Total	53	10.6	2.5	0.3	9.9	11.3		
β-CG pg/ml	Squamous cellcornifired	2	4.65	0.92	0.65	0	12.91	6.199	0.001
	Squamous cellnoncornifired	43	6.29	1.47	0.22	5.83	6.74		
	Adenocarcinoma	6	8.93	2.61	1.07	6.19	11.67		
	The others	2	7.90	0.71	0.50	1.55	14.25		
	Total	53	6.58	1.83	0.25	6.08	7.09		

In our investigation the level of endothelin-1 and L-FABP in patients with CC increases by 38.5% (8.7 ± 0.1 pg/ml, p < 0.001) or in 5.2 times (2.34 ± 0.22 pg/ml, p < 0.001). İn CL patients it was 20.9% (7.62 ± 0.17 pg/ml, p < 0.05) or in 1.7 times higher than in control cohort (0.76 ± 0.06; p < 0.01). A comparative analysis of the results showed an increase in endothelin-1 and L-FABP level in patients with CC by 14.6% (p < 0.001) or 3.1 times (p < 0.001) compared to those of CL patients. The highest concentration of these markers was observed in the group of patients with cervical adenocarcinoma (9.7 ± 0.1 pg/ml and 3.80 ± 0.07 pg/ml, respectively) and in patients with atypical forms of CL (8.00 ± 0.64 pg/ml and 1.03 ± 0.03 pg/ml, respectively).

Today, endothelin-1 is considered to be a marker of metastasis, angiogenesis and a predictor of the severity of the course of various neoplasms. Since endothelin acts predominantly locally, it is natural to assume that an active synthesis and entry into the bloodstream of the tumor site may be the cause of the progression of angiogenesis and aggravation of the severity of the course. It is known that in tissue damage the endothelin system reacts first, so a sharp increase in endothelin-1 plasma level is considered to be a marker of the activity of the destruction process, including tumor formation. In addition, tumors also contain cells of the immune system that release factors such as endothelin, prostaglandins and tumor necrosis factor alpha (TNF-α) [2; 8; 9; 17].

Increasing the expression of L-FABP leads to the development and progression of the tumor and can also serve as a useful diagnostic marker [5; 10; 14].

In order to study the severity of the oncological process, various cancer markers were determined in all patients. According to the obtained results, the content of CEA increased in CC (5.81 ± 0.25 ng/ml, p < 0.001) and in patients with CL (3.70 ± 0.29 ng/ml; p < 0.01) compare with the control group (CEA – 2.09 ± 0.36 ng/ml). Cervical adenocarcinomas (7.78 ± ± 0.55 ng/ml) and an atypical form of CL (4.98 ± 0.47 ng/ml) showed, the greatest levels of CEA (table 2).

Table 2. – Dispersion analysis of the studied parameters in patients with CL

Data	**Patients group**	**N**	**Overage**	**Stan. deviat**	**Stand. error.**	**95% Hgr**	**95% Lgr**	**Fiser**	**p**
1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
L-FABP, ng/ml	Simple	7	0.43	0.28	0.11	0.17	0.70	17.159	0.000
	Proliferative	13	0.82	0.14	0.04	0.74	0.91		
	Atypical	5	1.03	0.08	0.03	0.94	1.13		
	Total	25	0.76	0.28	0.06	0.64	0.87		

1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*
Endothelin, pg/ml,	Simple	7	7.00	0.44	0.17	6.59	7.41	3.219	0.059
	Proliferative	13	7.82	0.58	0.16	7.47	8.16		
	Atypical	5	8.00	1.43	0.64	6.22	9.78		
	Total	25	7.62	0.85	0.17	7.27	7.97		
CEA, pg/ml	Simple	7	2.66	1.44	0.54	1.33	3.99	5.279	0.013
	Proliferative	13	3.76	1.17	0.32	3.06	4.47		
	Atypical	5	4.98	1.04	0.47	3.69	6.27		
	Total	25	3.70	1.43	0.29	3.11	4.29		
CA125, ng/ml	Simple	7	8.3	1.0	0.4	7.4	9.2	29.381	0.000
	Proliferative	13	15.7	3.9	1.1	13.3	18.0		
	Atypical	5	25.3	5.6	2.5	18.3	32.3		
	Total	25	15.5	6.9	1.4	12.7	18.4		
CA19–9, ng/ml	Simple	7	13.1	6.0	2.3	7.6	18.7	2.616	0.096
	Proliferative	13	19.0	4.7	1.3	16.2	21.9		
	Atypical	5	18.7	7.5	3.4	9.3	28.0		
	Total	25	17.3	6.1	1.2	14.8	19.8		
AFP, pg/ml	Simple	7	5.01	2.16	0.81	3.02	7.01	0.005	0.995
	Proliferative	13	4.95	1.52	0.42	4.04	5.87		
	Atypical	5	5.04	1.80	0.80	2.81	7.27		
	Total	25	4.99	1.69	0.34	4.29	5.68		
β-CG, pg/ml	Simple	7	2.89	1.85	0.70	1.17	4.60	0.860	0.437
	Proliferative	13	2.36	0.27	0.07	2.20	2.52		
	Atypical	5	2.90	0.51	0.23	2.27	3.53		
	Total	25	2.62	1.00	0.20	2.20	3.03		

It is known that the level of CEA correlates with the grade of the cancer. It is shown that low grade tumors produce CEA more actively. According to numerous authors, the marker has prognostic significance, which based on the fact that a high initial level of CEA in the serum indicates a high risk of early relapse [4; 16].

CA 125 is a glycoprotein produced by cells of malignant serous ovarian tumors. It is one of the important tumor markers for monitoring the severity of clinicand effectiveness of the therapy of various types of ovarian cancer (serous, endometrial, clear cell) and CC. CA 125 testing can detect a relapse of the disease 3–4 months before its clinical manifestation [3; 4].

According to our results patients with CC had significantly high level of CA 125. Thus the CA125 concentration in patients with CC was 37.24 ± 1.71 ng/ml($p < 0.001$) and in patients with CL 15.5 ± 1.4 ng/ml($p < 0.01$). As seen from the results, the level of CEA and CA 125 in patients with cervical cancerwas higher by 57.3%($p < 0.001$) and 2.4 times ($p < 0.001$), respectively compared to the results of patients with CL.

The results of the analysis showed that the content of CA 19–9 in patients with cervical cancer was 3.1 times higher than in the control 38.6 ± 1.7 ng/ml ($p < 0.001$) CL patients have about 40% increase of CA19–9 level 17.3 ± 1.2 ($p < 0.05$) with respect to the control values (12.5 ± 1.8 ng/ml). The concentration of CA19–9 was also different in patients with adenocarcinoma of cervix (35.7 ± 6.1 ng/ml) and in patients with atypical form of CL (19.0 ± 1.3 ng/ml).

İn our investigation the AFP content was 3.2 times higher than in control 10.6 ± 0.3 ng/ml($p < 0.001$) and 3.28 ± 0.49 ng/ml respectively as can be seen, the increased amountof AFPwas detected in patients with CL (52.3%) 4.99 ± 0.34 ng/ml ($p < 0.01$). The average concentration of AFP in patients with cervical adenocarcinoma was 11.8 ± 1.3 ng/ml, and in patients with atypical form of CL it was, 5.04 ± 0.80 ng/ml. Consequently we can say that increase of AFP in the blood ofCCpatients indicates the predisposition to the high risk of relapse. It is generally believed that the malignant tumors of liver and ovaries, as well as the cervix produce AFP that enters the bloodstream. Tumor cells of the ovaries and cervix also contain elements of syncytiotrophoblast, therefore they synthesize HG along with AFP [15].

In patients with cervical cancer, the level of β-HCG increased by 3.9 times (6.58 ± 0.25 ng/ml, $p < 0.001$) as compared to the normal. In patients with CL, the concentration

of β-HCG was 2.62 ± 0.20 ng/ml, which is 54.6% higher than in the control group (1.69 ± 0.36 ng/ml, $p < 0.05$). As can be seen from the results, the level of β-HCG in the adenocarcinoma group increased on average by 8.93 ± 1.07 ng/ml, and in atypical forms of CL by 2.90 ± 0.23 ng/ml.

The results of the correlative analysis have revealed a significant increase in the content of CA19–9, AFP and β-CG cancer markers in the blood in patients with cervical cancer in 2.2($p < 0.001$), in 2.1($p < 0.001$) and in 2.5 times($p < 0.001$) respectively in comparison with the data of patients with CL.

Moreover, the direct correlation was found between the level of endothelin-1, L-FABP and other oncomarkers: between the level of endothelin-1 and CEA($r = 0{,}362$; $p < 0.01$), CA125($\rho = 0.330$; $p < 0.05$), L-FABP($\rho = 0.466$; $p < 0.01$), β –HCG($\rho = 0.375$, $p < 0.01$) shows a direct correlation. In addition, a direct correlation was observed between L-FABP and CEA($\rho = 0.295$, $p < 0.05$), β-CG($\rho = 0.295$; $p < 0.05$).

As a conclusion, improvement in early detection of CC can be if add to achieved routine of CC diagnostic investigation of CA125, CEA, CA 19–9, AFP and β-CG.

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THE INFLUENCE GLISIROFITE AND HIS COMPONENTS ON ORGANS IMMUNITY AT SECONDARY IMMUNE DEFICITS

Abstract: It was established, that Glisirofite and components, enter in his composition – extracts of stock-rose and Radix Glycyrrhizae ability on 14–45 per cent ($p < 0.05$) increase number cells in central (thymus, bone mor-row) and peripheral (spleen, lymph node) organs immunity at secondary immune deficits conditions: acute toxic hepatitis, radiation sickness.

Keywords: glisirofit, acute toxic hepatitis, radiation sickness, thymus, bone mor-row, spleen, lymph nodes.

It is known that plants contain various chemicals that have different biological effects and are used in various pathological conditions [4–6], including radiation injuries [8; 9]. The object of research is Glycyrophyte, which consists of stock-rose extract and extract Radix Glycyrrhizae, which contains glycyrrhizic acid (HA) – triterpene glycoside, which is the main bioactive component and exhibits various types of pharmacological activity, including antiviral and antitumor. Earlier it was found that stock-rose has an expectorant effect [1], and HA has anti-asthma [2], anti-ulcer [3], immunemodulatory [10] effects, and is used in the treatment of chronic hepatitis C [7].

The aim of the study is to estimation the effect of Glycyrophite on the organs of immunity in secondary immune deficiencies.

Material and methods

In experiments, outbred mice of 2–3 months age body weight 20–22 g of both sexes were used. To simulate acute toxic hepatitis (ATH), mice for 3 days subcutaneously injected into the thigh area, 0.2 ml of 20% oily solution of the hepatotropic poison – carbon tetrachloride (CCl_4) was injected. After 5 days, the total number of nucleated cells of the spleen (NCS) was counted, as well as in the thymus, bone marrow, mesenteric lymph nodes. The immunomodulating properties of 3 herbal remedies were studied: 1) dry extract of stock-rose; 2) dry extract of Radix Glycyrrhizae (preparation glycyram); 3) Glycyrophyte – a mixture of extracts of stock-roses and Radix Glycyrrhizae in a 1:1 ratio. All herbal remedies were administered at a dose of 75 mg/kg intragastrically for 4 days.

To simulate radiation sickness (RS), mice were irradiated at a dose of 5 Gr. After 5 days, herbal remedies were intragastrically administered to mice for 4 days. Animals were divided into 5 groups. 1) group – control, intact mice; 2) RS; 3) RS + stock-rose extract at a dose of 100 mg/kg; 4) RS + glycyram at a dose of 100 mg/kg; 5) RS + Glycyrophyte at a dose of 100 mg/kg.

Results and discussion

First step was to study the effect of herbal remedies on the total number of cells in the central and peripheral organs of immunity in ATH (Table 1). In the control group, an average of $38.3 \pm 1.7 \times 10^6$ thymocytes is recorded in the thymus. When ATH under the influence of CCl_4, the total number of thymic cells decreases 1.80 times and is $21.3 \pm 0.9 \times 10^6$. It has been established that under the influence of all three studied herbal remedies there is a significant increase in the total number of cells in the thymus of animals with ATH, and the stimulating activity of the agents did not differ from each other. Under the influence of the stock-rose extract, the number of thymocytes increases by 1.26 times, Radix Glycyrrhizae extract – by 1.30 times, Glycyrophyte – by 1.35 times.

Studies of the effect of herbal remedies on the proliferation of cells in the bone marrow of ATH mice gave the following results. In the control group, the bone marrow contains an average of $12.1 \pm 0.4 \times 10^6$ cells. When ATH the number of cells decreases by 1.59 times. In mice with ATH, receiving stock-rose extract and licorice root extract, the number of bone marrow cells significantly increased by 1.24 times and 1.14 times, respectively. A mixture of these extracts has a greater stimulating activity than its original components. Thus, the number of bone marrow cells is $10.1 \pm 0.2 \times 10^6$, which is 1.33 times higher than in the immune deficient group. In its activity, Glycyrophyte significantly exceeds the activity of licorice root extract, but does not differ in activity from stock-rose extract.

Table 1 shows the data on the calculation of the number of NCS when administering the studied agents to mice with ATH. In the control group, this indicator is equal to 169.7 ± ± 7.2 × 10^6.

Table 1.– Effect herbal remedies on number cells in organs immunity at mice with acute toxic hepatitis (ATH) (M±m)

Central organs					
Group	**Dose, mg/kg**	**Thymus' cells × 10^6**	**IR**	**Bone marrow cells × 10^6**	**IR**
1. control (n=7)	–	38.3 ± 1.7	–	12.1 ± 0.4	–
2. ATH (n=7)	–	21.3 ± 0.9[a]	–1.80	7.6 ± 0.3[a]	–1.59
3. ATH + extract of stock-rose (n=7)	75.0	26.8 ± 1.2[ab]	+1.26	9.4 ± 0.3[ab]	+1.24
4. ATH + extract Radix Glycyrrhizae (n=7)	75.0	27.7 ± 1.2[ab]	+1.30	8.7 ± 0.3[ab]	+1.14
5. ATH + Glisirofite (n=7)	75.0	28.7 ± 1.2[ab]	+1.35	10.1 ± 0.2[ab]	+1.33
Peripheral organs					
Group	**Dose. mg/kg**	**Number of NCS × 10^6**	**IR**	**Lymph nodes cells × 10^6**	**IR**
1. control (n=7)	–	169.7 ± 7.2	–	20.3 ± 0.5	–
2. ATH (n=7)	–	105.8 ± 4.5[a]	–1.60	11.9 ± 0.3[a]	1.71
3. ATH + extracts of stock-rose (n=7)	75.0	121.7 ± 5.2[ab]	+1.15	15.1 ± 0.3[ab]	+1.27
4. ATH + Radix Glycyrrhizae (n=7)	75.0	127.0 ± 5.4[ab]	+1.20	14.4 ± 0.4[ab]	+1.21
5. ATH + Glisirofite (n=7)	75.0	132.3 ± 5.6[ab]	+1.25	16.2 ± 0.3[ab]	+1.36

Note: here and in the tables N2, NCS – nucleated cells of the spleen; IR – the index of the ratio: (–) – in relation to 1 gr., (+) – in relation to 2 gr., a – authentically to 1 gr., b – authentically to 2g., c – authentically to 3gr., d – authentically to 3gr

In all groups treated with herbal remedies, a significant increase in the total number of spleen cells was observed. With the introduction of the stock-rose extract, the number of NCS is increased by 1.15 times, Radix Glycyrrhizae extract – by 1.20 times, Glycyrophyte – by 1.25 times. In their stimulating activity, all three herbal remedies do not differ from each other. The results obtained indicate the ability of the studied samples to increase the immunological reactivity of the organism and the total number of cells in the spleens of mice with ATH.

The stimulating effect of herbal remedies was also found for the mesenteric lymph nodes (Table 1). In the control group, the number of cells in the lymph nodes is 20.3 ± 0.5 × 10^6, while with ATH their number decreases by 1.71 times. With the introduction of herbal remedies to animals with liver pathology, an increase in the number in the lymph nodes is observed. And by the strength of the activity, they do not differ from each other. So, under the influence of stock-rose, the number of cells in lymph nodes increases 1.27 times, Radix Glycyrchizae – 1.21 time and Glycyrophyte – 1.36 times.

Based on the obtained results, it can be concluded that the studied herbal remedies have the ability to exert a stimulating effect on the central and peripheral organs of the immune system in mice with ATH.

After radiation exposure, negative changes occur in the organs of immunity (Table 2). Thus, the number of cells in the thymus decreases by 3.15 times, and the bone marrow – by 2.92 times. Under the influence of stock-rose extract, the level of cells in the organs of immunity of irradiated mice increases: in the thymus – 1.25 times, in the bone marrow – 1.21 times. Similar results were obtained with the administration of glycyram to irradiated animals: the number of cells in the thymus increased 1.21 times, in the bone marrow – 1.18 times. More pronounced stimulating activity was found in Glycyrophyte: the number of cells in the thymus increased 1.45 times, in the bone marrow – 1.29 times. As in previous studies, Glycyrophyte in its immune-stimulating activity significantly exceeds that in extracts of stock-rose and glycyram.

Similar data were obtained in peripheral organs of immunity in mice with RS. As can be seen from table 2, the number of NCS in irradiated animals decreases by 4.12 times compared with the control. In groups of mice treated with stock-rose extract and glycyram, the number of NCS increased 1.19 and 1.24, respectively. Under the influence of Glycyrophite, the number of NCS increases 1.42 times. In its activity, Glycyrophyte significantly exceeds that of stock-rose and glycyram extract. Based on the data obtained, it can be concluded that Glycyrophyte and its components are able to a certain extent increase the total number of cells in the spleens of irradiated mice.

Table 2.– Effect herbal remedies on number cells in organs immunity at mice with radiation sickness (RS) (M±m)

Central organs					
Group	**Dose, mg/kg**	**Thymus' cells × 10^6**	**IR**	**Bone marrow cells г**	**IR**
1. control (n=8)	–	44.4 ± 1.1	–	11.1 ± 0.3	–
2. RS (n=8)	–	14.1 ± 0.4[a]	–3.15	3.8 ± 0.1[a]	–2.92
3. RS + extracts of stock-rose (n=8)	100.0	17.6 ± 0.5[ab]	+1.25	4.6 ± 0.1[ab]	+1.21
4. RS + glisiram (n=8)	100.0	17.0 ± 0.5[ab]	+1.21	4.5 ± 0.1[ab]	+1.18
5. RS + Glisirofite (n=8)	100.0	20. 4± 0.6[abcd]	+1.45	4.9 ± 0.1[abd]	+1.29
Peripheral organs					
Group	**Dose, mg /kg**	**Number of NCS × 10^6**	**IR**	**Lymph nodes cells г**	**IR**
1. control (n=8)	–	150.4 ± 4.1	–	26.5 ± 0.7	–
2. RS (n=8)	–	36.5 ± 1.0[a]	–4.12	9.5 ± 0.3[a]	–2.80
3. RS + extracts of stock-rose (n=8)	100.0	43.4 ± 1.2[ab]	+1.19	12.1 ± 0.3[ab]	+1.27
4. RS + glisiram (n=8)	100.0	45.2 ± 1.2[ab]	+1.24	11.7 ± 0.3[ab]	+1.23
5. RS + Glisirofite (n=8)	100.0	51.8 ± 1.4[abcd]	+1.42	12.9 ± 0.3[abd]	+1.36

After irradiation, the number of cells in the lymph nodes decreases 2.80 times. All the studied herbal remedies significantly increase the number of cells in the lymph nodes: stock-rose extract by 1.27 times, glycyram – by 1.23 times, Glycyrophyte – by 1.36 times.

Thus, Glycyrophyte and its source components can increase the number of cells in the central (thymus, bone marrow) and peripheral (spleen, lymph nodes) organs of immunity in secondary immunodeficiency states (acute toxic hepatitis, radiation sickness).

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PARTICULAR DEMOGRAPHIC DATA AND INDICATORS OF MORBIDITY OF THE POPULATION OF THE REPUBLIC OF UZBEKISTAN OVER THE LAST FIVE YEARS (2012–2016)

Abstract: The official data analysis showed a positive dynamics of population growth which has increased by 6% in 2016 comparing to the figures in 2012. Along with the growth of the total population, the number of the population of the regions of the republic has also increased with the growth rate of 7.7%.

According to the retrospective analysis of the general morbidity of the population of the Republic of Uzbekistan, the total incidence in the period 2012–2016 increased by 7.7%over the last 5-year period. Respiratory diseases, blood and hematopoietic organs, digestive system, circulatory system and the endocrine system diseases were recognized as the leading pathology among the population and accounted for 68% of all the 19 classes of diseases.

Keywords: Number of population, retrospective analysis, general and primary morbidity.

Population health, being the most important economic and social potential of the country, is determined by the complex impact of socioeconomic and biological factors and is estimated by a number of indicators, such as demographic indicators, physical development, morbidity, and disability.

Ensuring the quality of life of the population is the issue of especial importance for Uzbekistan as for the state with accelerated development of the economy. The ongoing state reforms have a positive impact on the development of social infrastructure in the regions of the republic [1; 4; 5].Along with the social and economic development of the regions, the dynamic development of the primary health care unit, the availability of medical care at rural medical posts, regional medical associations and regional centers of medical diagnostics, one of the main tasks of which is providing timely and qualitative diagnostics, are of particular importance for the regions of the republic. Improvement of the medical care in rural areas is becoming increasingly urgent and acute issue in the country. Analysis of the morbidity of the population will allow identifying shortcomings and needs to improve the health system and develop socio-hygienic, therapeutic and preventive measures aimed at improving the health of the population.

The purpose of the study was to analyze the dynamics of the population morbidity of the Republic of Uzbekistan for the period of 2012–2016 in order to optimize further the hygienic basis for the provision of targeted diagnostic assistance to the population of the regions of the republic.

Material and methods There was conducted an observational (descriptive) research. Statistical data of state and sectoral health reporting, as well as materials of the State Statistics Committee of the Republic of Uzbekistan for the time period of 2012–2016 [3; 5] were used in the paper. The morbidity is analyzed for 100 thousand of the population in terms of "registered total" and "newly diagnosed" indicators. Calculations and graphical analysis of the data were carried out using the Microsoft Excel program.

Results and discussion According to the State Statistics Committee of the Republic of Uzbekistan, the average annual population of the republic has been growing. Hereby, in 2016 the total population was 31575332 people, which is 1800884 more compared to 2012 figures and the growth rate was 6% (Figure 1).

The process of urbanization and changes in the population distribution of the republic between the village and the city are relevant for Uzbekistan. In accordance with the agrarian orientation of the sectoral structure of the economy, there is a significant predominance of the rural population in the country.

In 2005, 63.9% of the total population was from rural areas. After the organizational and administrative measures to accelerate the urbanization processes, including transformation of a number of rural settlements into urban, there was a reduction in the rural residents share to 48.2%at the beginning of 2008. However, in subsequent years, the share of the urban population was gradually decreasing, mainly due to persistent differences in birth rates between the village and the city, as well as due to migration [1; 2].

Accordingly, in 2016, urban population of the republic has decreased slightly albeit stably, and amounted to 50.56% comparing to 2012 figures(51.34%), the rate of decline was 0.78%.

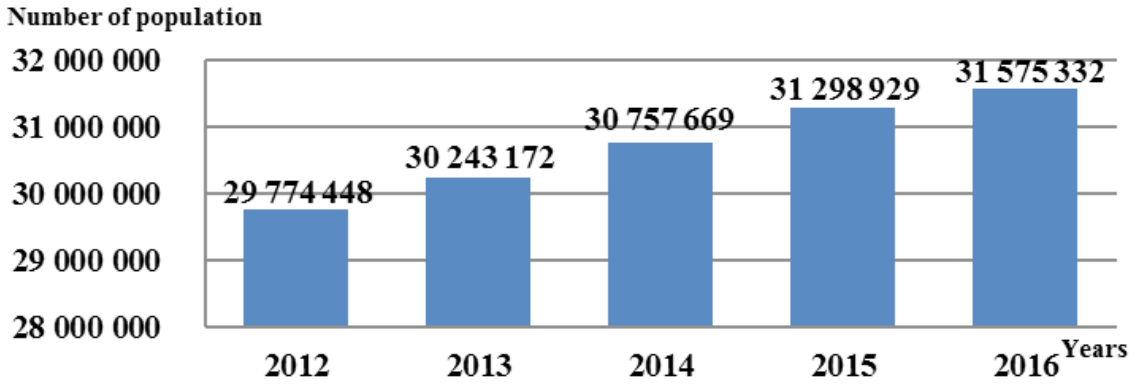

Figure 1. Population dynamics of the Republic of Uzbekistan for the period of 2012–2016

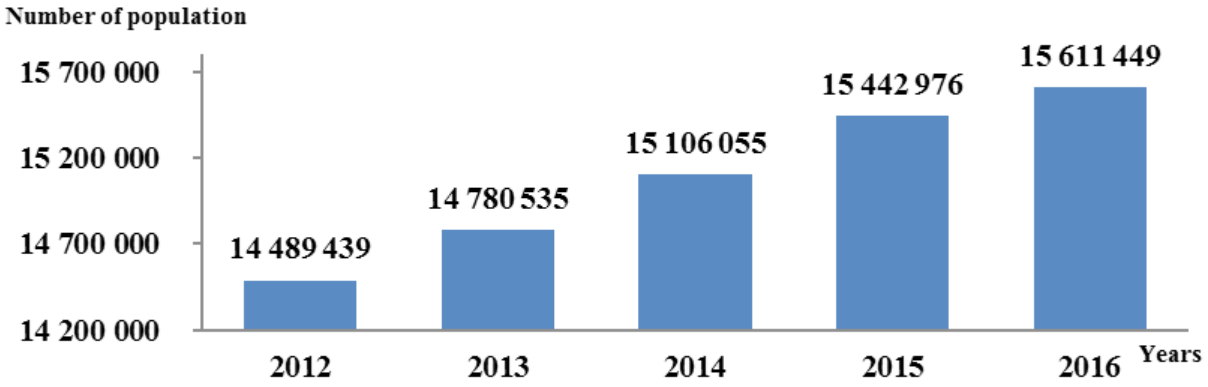

Figure 2. Rural population dynamics of Uzbekistan for the period of 2012–2016

Accordingly, the rural population of the republic is gradually increasing and in 2016 it reached 15611449 people, which is 1122010 more than in 2012 (growth rate 7.7%) (Figure 2).

By conducting the analysis of the morbidity dynamics of the population of Uzbekistan over the last 5-year period, it was revealed that the overall incidence is characterized by the gradual growth, and in 2016 it reached 87,228.1 cases per 100.000population, which is 7.7% higher compared to the 2012 index (Figure 4).

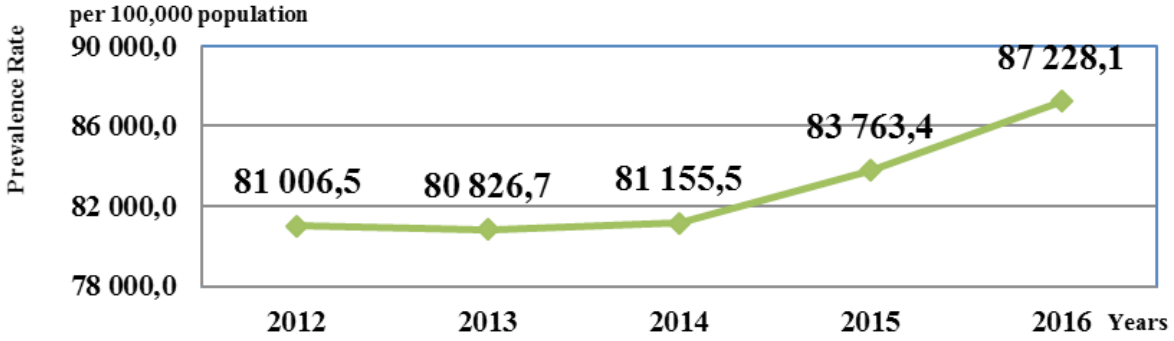

Figure 4. Overall morbidity dynamics of the population of Uzbekistan for 5-year period (2012–2016) per 100,000 population

Based on the results of ranking of the population's general morbidity indicators by disease classes, it was found that the diseases of the respiratory system were the most common, and the average value was 19073.94 cases per 100,000 population or 23% in the total morbidity structure. The growth rate was 23.43% in 2016 relative to 2012. The share of primary morbidity caused by respiratory diseases is on average 81.4%.

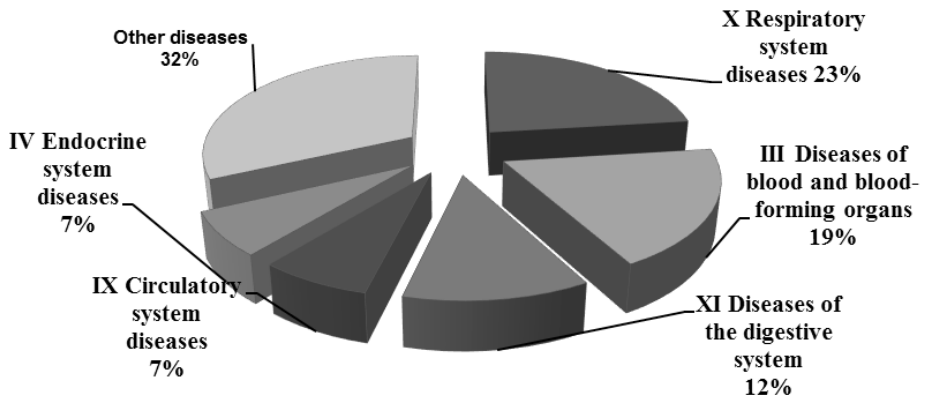

Figure 5. Structure of the overall morbidity of the population (average for 2012–2016)

Diseases of the blood and blood-forming organs, average value of which is 15692.05 cases per 100.000population, are the second most common diseasesin the structure of the general morbidity. At the same time there is a constant decrease in the morbidity rate by years, and the rate of decline amounted to –22.7% by 2016. The share of the blood and blood-forming organsdiseases accounts for 19% in the structure of populationgeneral morbidity, and was formed mainly due to anemia (98%). The number of primary incidence cases of blood diseases and hematopoietic organs is 6365.33 per 100.000 people and is amounted to 40.6% in total morbidity structure.

The incidence of diseases of the digestive system averaged 9817.74 per 100.000 population and has increased by 20.25% over the last 5 years, thereby ranking third in the structure of the overall morbidity; the share of primary morbidity is 64.5%. The main nosologies that form this group of diseases are gastritis and duodenitis (11.9%), diseases of the gallbladder and biliary tract (4.7%), peptic ulcer of stomach and duodenum (3.6%).

Diseases of the circulatory system rank forth in overall morbidity structure of the population and are determined by diseases characterized by high blood pressure and coronary heart disease (40.3% and 18% respectively). Growth rate (22.14%) of the circulatory systemdiseases is characterized by the greatest dynamic incremental changes. The average value for five years was 5935.62 per 100,000 people with a primary morbidity share of 34.2%.

IV class (diseases of the endocrine system, eating disorders, metabolic disorders), with an even and consistent patternover the last five years, is the last on the list of the most common diseases. The growth rate has a tendency to increase (by 3.4%), but remains below the national indicators (7.7%).

Conclusions

1. According to the State Statistics Committee of the Republic of Uzbekistan, the average annual population of the republic has been growing. Hereby, in 2016 the total population was 31575332 people, which is 1800884 more compared to 2012 figures and the growth rate was 6%.

2. Rural population of the republic is gradually increasing and in 2016 it reached 15611449 people, which is 1122010 more than in 2012 (growth rate 7.7%)

3. The general morbidity of the population of Uzbekistan in the period of 2012–2016 increased by 7.7%. The leading pathology among the population is considered to be respiratory diseases (23%), blood and blood-forming organs (19%), digestive organs (11.9%), circulatory system (7.2%) and endocrine system diseases, eating disorders, metabolic disorders substances (7%), which account for 68% of all morbidity cases among 19 classes of diseases.

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USE OF MODERN TECHNOLOGIES IN THE DIAGNOSTICS OF RONCHOPATHY

Abstract: The purpose of this study was to evaluate the results of a polysomnographic study in patients with ronchopathy. We examined 50 patients with ronchopathy who were hospitalized in the ENT department of the 3rd clinic of the Tashkent Medical Academy. All patients underwent an ENT examination, endoscopic examination of the nose and nasopharynx, and polysomnographic study. The study showed that polysomnography is a valuable diagnostic method for patients with ronchopathy, which allows objectifying sleep disorders and timely treatment of ENT diseases for the prevention of obstructive sleep apnea.

Keywords: ronchopathy, endoscopy, sleep disturbance, polysomnography.

Diagnosis and treatment of snoring is a medical and social problem, as evidenced by statistical and epidemiological studies of the spread of snoring and apnea among the population and a large number of publications in both domestic and foreign literature [1; 6; 9; 13; 16].

According to statistics, every fifth person after 30 years of age constantly snores in his sleep. Recent studies have shown that snoring is a precursor and one of the main manifestations of a serious disease – obstructive sleep apnea (OSA) [2; 10; 11; 12]. Under the syndrome of obstructive sleep apnea understand the disease, characterized by the presence of snoring, as a result of periodic subsidence of the upper respiratory tract at the level of the pharynx, cessation of pulmonary ventilation, which is accompanied by a decrease in blood oxygen levels, gross sleep fragmentation and excessive daytime sleepiness [3]. The severity of OSA is determined by the number of episodes of apnea / hypopnea per hour [10]. The disease manifests many symptoms about which the patient often turns to a therapist, cardiologist, neurologist, otorhinolaryngologist, sexologist, psychiatrist, and other specialists, indicating a multi-symptom of the disease and the social aspect of the problem [4; 5].

In Russia over the past 15 years, the problem of snoring and OSA began to pay great attention and isolated it into a separate nosological form – ronchopathy [2]. Ronchopathy is a pathological condition characterized by hyperplastic changes and narrowing of the structures of the upper respiratory tract, soft tissue vibration, the occurrence of an acoustic phenomenon – snoring or snoring [7].

The etiology and pathogenesis of ronchopathy remain not fully understood. It is believed that one of the main causes of snoring is difficulty in nasal breathing [6; 14]. Therefore, most clinicians are convinced that an improvement in nasal breathing can lead to permanent relief from snoring [7; 15]. In contrast to them, a number of researchers argue that the correction of endonasal structures leads to a decrease in the intensity of snoring and the number of episodes of apnea in no more than 20% of cases [6; 7]. There is an opinion that the difficulty of nasal breathing does not have any effect on the occurrence of snoring and OSA [11]. Therefore, the problem of an objective assessment of the respiratory function of the nasal cavity and the determination of the need and extent of endonasal surgery in patients with snoring and OSA takes on a very topical importance.

In recent years, scientific and technological progress has contributed to the emergence and development of new research methods in otorhinolaryngology, including architectonics and the respiratory function of the nasal cavity. Their main advantages are: non-invasive, atraumatic, safe use. Such methods include acoustic rhinometry and anterior active rhinomanometry. These diagnostic methods allow to evaluate the architectonics of the nasal cavity and respiratory function, both in normal conditions and in pathology [13].

However, studies of respiratory function in snoring are few or based on a small number of observations [12]. The question of the extent to which nasal obstruction affects the intensity of snoring and the number of episodes of OSA and the effect of the elimination of nasal obstruction on their course has not been sufficiently studied.

So far, a research methodology has not been developed to evaluate the functional and morphological state of the nasal mucosa in normal, with ronchopathy and obstructive sleep apnea at the examination stage, and thus determined in the choice of rational treatment tactics for this pathology.

One of the important achievements in the field of snoring and OSA was the emergence of polysomnography, a fairly

objective method of assessing the function of breathing during sleep [16].

The variety of existing methods of treatment of ronchopathy indicates a lack of effectiveness of each of them, which leads to the need for further research of this problem.

The development of otorhinolaryngology and insurance medicine dictate the need to objectively substantiate the indications for surgery and evaluate the results of surgical intervention. Objective methods of examination are necessary for understanding the norms and pathologies of the nasal cavity when making a diagnosis and evaluating the outcome of operations. Therefore, the search for objective methods of studying the functional state of the nasal cavity and the standardization of the results of the study of nasal breathing remains an urgent problem of otorhinolaryngology, which determined the purpose of this study.

The purpose of this study was to evaluate the results of a polysomnographic study in patients with ronhopathy.

The material of this study was 50 patients with ronhopathy who were hospitalized in the ENT department of the 3rd clinic of the Tashkent Medical Academy. The age of patients ranged from 18 to 72 years. All patients underwent an ENT examination, endoscopic examination of the nose and nasopharynx, and polysomnographic study. Based on the classification by ronchopathy, patients were divided into 2 groups. The first group consisted of 30 patients who had a mild degree of ronchopathy. The second group consisted of 20 patients with a moderately severe degree of ronchopathy. Patients with severe ronchopathy were not included in the study. All were surveyed. The questionnaire included complaints, anamnestic data and questions based on the diagnostic criteria for the international classification of sleep disorders. The questionnaire reflected the passport part, place of residence, profession, gender, age, height, patient weight and body mass index. If possible, recorded observations of family members who were present at the night snoring of the patient. The control group consisted of 20 healthy volunteers. The research results were statistically processed using Microsoft Excel 2016.

The results of the study. Of the 50 patients, only 16 turned on their own with a complaint of snoring. In 13 of them, the usual snoring was observed for up to 5 years. The remaining 34 patients surveyed filed other complaints, and we received information about snoring as a result of a targeted survey. 32 out of 50 patients had snoring without apnea with a duration of 5–20 years. 3 patients during the survey noted not refreshing and restless sleep, accompanied by dry mouth and headache after waking up. During the working day, they regularly observed drowsiness and low performance.

Examining the ENT organs of patients of the first group showed, that 29% had nasal septum deviation, 25% had vasomotor rhinitis, 13% had polypoid rhinosinusitis, 8% had chronic tonsillitis, and 7% had adenoid vegetation. In the remaining 18% of cases, a mixed pathology of ENT organs was found. Examining the upper respiratory tract of patients of the second group similar data were noted, since 28% had a deviated septum, 20% had vasomotor rhinitis, 15% had polypoid rhinosinusitis, 13% had chronic tonsillitis, 9% had adenoid vegetation. In the remaining 15% of cases, a mixed pathology of ENT organs was found. Inspection data of the upper respiratory tract did not reveal the distinctive features of groups of patients with ronchopathy, which did not affect the results of the polysomnographic study.

To identify the severity of snoring in patients with ronchopathy, a polysomnographic study was conducted. The results of the polysomnographic study are presented in (table 1).

Table 1.– The results of polysomnography in patients with ronhopathy

Indicators	Control group n=20	1 group n=80	2 group n=50
Stage 1 of sleep (S1),%	7.0 ± 0.6	17.5 ± 0.8	14.3 ± 0.7
Stage 2 of sleep (S2),%	30.6	39.8	41.4
Delta-sleep (S3+S4),%	36.5	24.5	22.4
Fast sleep phase (REM- phase),%	23.8	14.8	14.4
Wakefulness in a sleep	1.5	2.1	5.8
Apnea/hypopnea index, episodes/hour	0.3	0.3	0.7
SpO_2,%	98.5	98.2	98.3
HR, beat/minutes	73	74.1	65.6

The results of the study of snoring intensity in patients of group 1 showed that in 35(43.0%) patients 20–40 dB were noted, in 31(38.6%) patients 41–60 dB, in 14(17.4%) patients 61–80 dB The results of the study of snoring intensity in patients of the 2 groups showed that in 10 (20.0%) patients 20–40 dB were noted, in 2 (50.0%) patients 41–60 dB, in 15 (30.0%) patients 61–80 dB In general, in 45(34.6%) patients 20–40 dB were noted, in 56(43.1%) patients 41–60 dB, in 29(22.3%) patients 61–80 dB. It is necessary to take into account the evidence that the high intensity of snoring can affect people around patients, which increases the negative attitude towards patients with ronhopathy.

In patients of both groups, sleep stage 1 (S1) was elongated compared with the control group, which averaged 15.7%. A decrease in the delta of sleep (S3 + S4) (23.2%) and the fast phase of sleep (REM phase) (14.6%) was also noted. In patients with moderately severe ronhopathy, frequent wakefulness during sleep was detected, which averaged 5.8. In these patients, the apnea / hypopnea index was 0.7. It should be noted that in patients with mild ronhopathy this index did not differ from the data of the control group. This fact indicates that patients of the 2 groups are most prone to the development of obstructive sleep apnea. Although patients in both groups have snoring and episodes of apnea / hypopnea, oxygen saturation rates remained within the normal range.

Thus, we can conclude that polysomnography is a valuable diagnostic method for patients with ronhopathy, which makes it possible to objectify sleep disorders and conduct timely treatment of ENT diseases for the prevention of obstructive sleep apnea.

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ANALYSIS OF THE RESULTS OF SURGICAL TREATMENT OF "FRESH" DAMAGE TO THE BILE DUCTS

Abstract: Republican Specialized Center of Surgery and the Clinic of Surgical Diseases of Samarkand State Medical Institute has experience in treating 175 patients with "fresh" iatrogenic of hepatico cholehoh injuries from 2000 to 2017 years. The periods for detecting iatrogenic of bile ducts are divided into those detected intraoperatively (29.1%) or up to 7 days after cholecystectomy (70.9%). Developed algorithms for choosing a method for treating fresh bile ducts damages with an integrated approach to tactical and technical aspects and correction of associated complications reduced the total frequency of postoperative complications from 26.2% to 9.7% and mortality rate from 7.8% to 2.8%.

Keywords: bile ducts, iatrogenic, fresh, injuries, cholangitis, stricture, treatment.

Introduction. According to the World Health Organization, "among various diseases of the biliary system, gallstone disease (GD) is 50–65%. There are more than 1 million in the world, and in our country about 10,000 cholecystectomies per year, while 12.6–47.7% of them are accompanied by interventions on the extrahepatic bile ducts (BD)" [3; 6; 8; 12]. The growth of surgical activity in the treatment of GD led to an increase in the incidence of postoperative complications from 5.6% to 15.9% [1; 9; 14]. Despite the long-established and constantly improving technique of cholecystectomy, the frequency of damage to the bile ducts has no tendency to decrease [2; 4; 7; 13]. The widespread use of endovideosurgical operations in patients with GD and complicated forms of cholelithiasis did not lead to the expected reduction in the incidence of intra-abdominal complications "Compared with traditional cholecystectomy, the introduction of laparoscopic cholecystectomy caused an increase in the frequency of bile duct damage in 2–4 times, and in percentage, 1–3%" [8; 11]. The most complex in the technical execution of surgical interventions aimed at eliminating the consequences of duct injury should be performed only in specialized institutions, but despite some success, unsatisfactory results are observed on average in even the most experienced surgeons in 10% of cases [5; 10]. Such patients need repeated, sometimes repeated reconstructive operations.

Materials and methods. Republican Specialized Center of Surgery named after academician V. Vakhidov and the Clinic of Surgical Diseases of Samarkand State Medical Institute

has experience in treating 175 patients with "fresh" iatrogenic of hepatico cholehoh (HCh) injuries from 2000 to 2017 years. The periods for detecting iatrogenic of BD are divided into those detected intraoperatively (29.1%) or up to 7 days after cholecystectomy (70.9%).

Patients were divided into study groups. The comparison group consisted of 103 (58.8%) patients who, in the period of 2000–2010 years, used standard reconstructive-restorative surgeries for fresh injuries of the main BD. The main group of the study consisted of 72 (41.2%) patients who used the proposed algorithms for choosing the method of surgical treatment of patients with fresh BD injuries in conjunction with the perioperative correction of endogenous intoxication syndrome and prevention of cholangitis in the period from 2011 to 2017 y. In turn the patients were divided by BD iatrogenic revealed during cholecystectomy, i.e. intraoperatively (51 patients) and injuries found in the early postoperative period (124 patients) (table 1).

Table 1.– The distribution of patients in groups for research

Damage type		Comparison group		Core group	
		abs	%	abs	%
Fresh damage to the BD	Intraoperatively	28	27.2%	23	31.9%
	In the early p/o period	75	72.8%	49	68.1%
Total		103	100.0%	72	100.0%

The choice of the method of restoration or reconstructive surgery is affected by the presence of a complication associated with the consequences of damage to the BD. In both groups of the study, the most common pattern of breast cancer in the early postoperative period was in 45 (43.7%) and 30 (41.7%) patients, respectively. The next most common symptom of iatrogenic was bile excretion – in 38 (36.9%) and 28 (38.9%) patients, and in most cases the pattern of damage to the BD was detected intraoperatively.

In a comparative aspect, in the main group, reconstructive surgery was performed mainly in 69(95.8%) patients, whereas in the comparison group, these interventions were performed in 80% of patients (table 2).

Table 2.– Type of final interventions performed at the Republican Specialized Center of Surgery and the Samarkand State Medical Institute clinic

Detection of damage to the BD	Own damage		Damage to other clinics		Total	
	abs	%	abs	%	abs	%
The control group						
External discharge of bile	5	4.9	15	14.6	20	19.4
Recovery	23	22.3	26	25.2	49	47.6
Reconstructive	10	9.7	24	23.3	34	33.0
Total	38	36.9	65	63.1	103	100.0
Core group						
External discharge of bile	1	1.4	2	2.8	3	4.2
Recovery	8	11.1	25	34.7	33	45.8
Reconstructive	7	9.7	29	40.3	36	50.0
Total	16	22.2	56	77.8	72	100.0

Results and discussion. Complicated course of the nearest postoperative period in the comparison group occurred in 27 (26.2%) patients, and in the main group – in 7 (9.7%) patients (table 3).

The table below shows that in the comparison group the number of almost all types of complications in the form of insolvency imposed by anastomoses, hemobilia, cholangitis, multiple organ failure and myocardial infarction prevailed. In the comparison group, in 2 cases, relaparotomy was performed in connection with early postoperative complications and in 8 (7.8%) cases there was a lethal outcome, and in the main group of the study there were no relaparotomy, and the lethal outcome was recorded in 2 (2.8%) sick. In both compared groups, early postoperative complications were more often observed in patients with verified lesions at an early stage after cholecystectomy. The long-term results of surgical treatment of fresh lesions of the gastrointestinal tract were followed up in 92 patients of the comparison group and in 70 patients in the main group.

Table 3.– The frequency of various complications in the early postoperative period

Compli-cation	The control group						Core group					
	i/o		p/o		Total		i/o		p/o		Total	
	abs	%	abs	%	abs	%	abs	%	abs	%	abs	%
The failure of the anastomosis – cholelis	2	7.1	4	5.3	6	5.8	1	4.3	2	4.1	3	4.2
The failure of the anastomosis – biloma	0	0.0	2	2.7	2	1.9	0	0.0	0	0.0	0	0.0
The failure of the anastomosis – peritonitis	0	0.0	1	1.3	1	1.0	0	0.0	0	0.0	0	0.0
Hemobilia	1	3.6	2	2.7	3	2.9	0	0.0	1	2.0	1	1.4
Cholangitis	1	3.6	4	5.3	5	4.9	0	0.0	0	0.0	0	0.0
AHRF	0	0.0	6	8.0	6	5.8	0	0.0	2	4.1	2	2.8
Multiple organ failure	0	0.0	3	4.0	3	2.9	0	0.0	1	2.0	1	1.4
Myocardial infarction, acute cardiovascular failure	0	0.0	1	1.3	1	1.0	0	0.0	0	0.0	0	0.0
All compli-cations	4	14.3	23	30.7	27	26.2	one	4.3	6	12.2	7	9.7
Relapara-tomy	0	0.0	2	2.7	2	1.9	0	0.0	0	0.0	0	0.0
Mortality	0	0.0	8	10.7	8	7.8	0	0.0	2	4.1	2	2.8

The frequency of recurrent cholangitis with the use of algorithms for selecting the method of surgical treatment of patients with fresh ZH injuries in conjunction with perioperative correction of endogenous intoxication syndrome and prevention of cholangitis was noted in 8.6% of cases, while in the comparison group, when performing standard reconstructive-restorative operations, this figure was 20.7%. A comparative analysis of the frequency of development of strictures of superimposed biliodigestive and bilobiliary anastomoses in the compared study groups showed that arresting the pattern of recurrent cholangitis influences the development of strictures of BD. So, the frequency of strictures in the comparison group was 33.7%, while in the main group this indicator was 14.3% of cases.

The overall frequency of complications in the comparison group was 56.3% (58), of which 26.2% (27) developed in the near term and in 30.1% (31) of the observations in the distant period. In the immediate postoperative period, anastomotic failure was noted in 9(8.7%), hemobilia in 3(2.9%) cases. The stricture of the anastomosis without cholangitis in the long term occurred in 12(11.7%) patients. The picture of cholangitis with the subsequent formation of a stricture in this group was noted in 5(4.9%) cases in the near term and in the long term in 19(18.4%) cases, respectively. Other complications associated with the severity of the patients in the comparison group were noted only in the nearest postoperative period in 10(9.7%) cases. Mortality associated with tactical and technical aspects in the group was 4.9%(5 patients). Mortality associated with the severity of the condition was 5.8%(6 patients).

In the main group, the overall incidence of complications was 16.5%(17), while in 6.8%(7) they developed in the immediate, and 9.7%(10) in the late postoperative periods. The frequency of failure of the superimposed anastomosis was 4.2%(3) and was noted in the immediate postoperative period. A stricture of BD without cholangitis was noted in 5.6%(4) cases and was noted in the late postoperative period. The picture of cholangitis with the subsequent formation of a stricture was noted in 8.3%(6) in the separated period after the operation. Other complications associated with the severity of the condition of the patients were in 4.2%(3). All three complications in the main group were noted in the immediate postoperative period. Mortality associated with tactical and technical aspects in the main group and long-term period was 1.4% (1). Mortality associated with the severity of the patients in the immediate postoperative period was 2.8%(2 cases).

Conclusions. Developed algorithms for choosing a method for treating fresh BD damages with an integrated approach to tactical and technical aspects and correction of associated complications reduced the total frequency of postoperative complications from 26.2% (27 patients in the comparison group) to 9.7% (7 patients in the main group) and mortality rate from 7.8% (8 patients) to 2.8% (2 patients). The proposed method allowed us to prevent and arrest attacks of recurrent cholangitis from 20.7% (19 out of 92 patients in the comparison group) to 8.6% (6 out of 70 patients in the main group), thereby reducing the incidence of anastomotic stenosis after reconstructive surgery. about fresh BD damage from 33.7% (31 of 92) to 14.3% (10 of 70). In a comparative aspect, the proposed algorithms for choosing the method of surgical treatment of patients with fresh injuries of the left ventricular, together with perioperative correction of the syndrome of endogenous intoxication and prevention of cholangitis development, allowed to reduce the overall frequency

of postoperative complications in the early and late periods from 56.3%(58 out of 103 patients in the group comparison) to 23.6%(17 of 72 patients in the main group) and mortality from 10.7%(11 patients) to 4.2%(3 patients, respectively).

The proposed comprehensive approach to the treatment of fresh BD injuries reduced the proportion of tactical deficiencies from 26.2% (27 patients in the comparison group) to 9.7%(7 patients in the main group), technical deficiencies from 20.4%(21) to 9.7% (7) and in general, reduce the incidence of complications with these aspects in mind from 46.6% (48) to 19.4% (14), and mortality from 4.9% (5) to 2, 8% (2). This made it possible to obtain good and satisfactory treatment results in 80.6% (58 out of 72), whereas in the comparison group this figure was 49.5% (51 out of 103 patients).

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THE INFLUENCE OF CONTRYKAL ON THE CHANGE OF DIGESTIVE HYDROLASES OF THE STOMACH AND PANCREAS IN SUBACUTE POISONING WITH CARBON TETRACHLORIDE

Abstract: In the article "the effect of contrykal on the change of digestive hydrolases of the stomach and pancreas in subacute carbon tetrachloride poisoning" the data of scientific research conducted on 30 rats in 3 series of 10 rats. In 1 series (control) saline solution was administered for 21 days. In 2 series (experimental) on the model of subacute poisoning, CCl4 was injected for 21 days. 3 series (experienced) in the model of subacute poisoning with CCl4, and in the second group, but further intraperitoneally injected protease inhibitor contrykal daily since 15 days. It was found that under the influence of acute poisoning of CCl4 increases the activity of the pancreas, while reducing the activity of the stomach glands. The use of contrykal on the background of poisoning with CCl4 contributes to the decrease in the activity of the pancreas, with a simultaneous increase in the activity of the gastric glands.

Keywords: contrykal, pancreas, activity of gastric glands.

30 rats in 3 series of 10 rats. In series 1 (control), physiological saline was injected for 21 days. In series 2 (experimental), CCl4 was injected on a model of sub-acute poisoning for 21 days. In series 3 (experimental) on the model of subacute poisoning CCl4, as in the second group, only an additional intraperitoneal injection of the protease inhibitor specific daily began from day 15. It was found that under the influence of subacute poisoning CCl4 increases the activity of the pancreas, with a simultaneous decrease in the activity of the gastric glands. At the same time, the use of contrykal on the background of poisoning with CCl4 contributions to a decrease in the activity of the pancreas, with a simultaneous increase in the activity of the gastric glands.

It was found that in patients diagnosed with viral hepatitis levels of pancreatic enzymes of serum and pancreatic amylase and serum lipase levels increase with the progression of liver disease [4; 10; 16]. It was also determined that in patients with liver cirrhosis, the average rate of free and total acidity, as well as pepsinogen 1 in serum were lower than under normal conditions. While the concentration of serum gastrin and somatostatin in patients with liver cirrhosis was significantly higher. [12; 14; 6].

Works of our laboratory showed physiological metabolism by liver of low-molecular peptides, in particular, CCK-8 [1]. This is confirmed by a number of other researchers [8]. This metabolism can change significantly in liver diseases. It was found that CCK-8 is metabolized to a large extent in healthy individuals and to a lesser extent in patients with liver cirrhosis. Due to this, CCK-8 is not the main form of CCK in plasma in healthy subjects, but significantly increases in patients with liver cirrhosis [9].

The results of the study of the physiological role of cholecystokinin as a regulator of gastrin secretion show that postprandial secretion of gastrin depends on CCK-8 and supports the function of monitoring the feedback of gastrin secretion [15].

It has been shown that CCK-8 produced during food stimulation has an increasing inhibitory effect on the secretion of gastric acid and that this effect is mediated by somatostatin [11].

CCK-8 can play a crucial role in inhibiting the stimulation of gastric acid secretion and controls gastric acid, plasma gastrin and somatostatin secretion [11].

In experiments on dogs in our laboratory found that the joint, intraportal injection of trypsin with short-chain peptides, pentagastrin increases the activity of gastric enzymes, and CCK – 8 pancreas. At this joint, intraportal protease inhibitor contrykal with short-chain peptides pentagastrin reduced fermentability gastro and CCK-8 pancreas [1, 2].

In this regard, we believe that one of the regulatory mechanisms of the ability of the liver to dispose of short-chain peptides and in particular CCK-8 is carried out through the endocrine and through the portal system in the liver pancreatic proteases (trypsin, chymotrypsin) and proteasactive receptors type 2 (PAR-2) liver.

Thus, the use of protease inhibitors can enhance hepatic utilization of short-chain peptides, and in particular CCK-8 in chronic liver diseases of various etiologies, and reduce CCK-8 in the blood. This can help to increase the acidity of gastric juice and significantly accelerate the rate of gastric emptying, which can be effective in atrophic gastritis, in addition to reducing pancreatic amylase, lipase and trypsin in the blood, which can be effective in chronic pancreatitis.

In addition, with joint pancreatitis and hepatitis, there is an increase in proteolytic activity in the blood and a decrease in antiproteolytic activity. On the one hand due to pancreatitis, and on the other hand, the presence of chronic inflammation of the liver, stomach and pancreas causes a violation of the balance in the system of proteolytic and antiproteolytic activity in the direction of increasing proteolytic activity and reducing antiproteolytic activity. Therefore, the use of protease inhibitor can also contribute to anti-inflammatory effects.

These assumptions are supported by studies where it was shown that in rats the use of gabexate-a synthetic low molecular weight protease inhibitor significantly reduced, increased serum transaminase levels and improved liver histology 24 hours after administration of carbon tetrachloride. Tumor necrosis factor α (TNF-α) and interleukin-1β (IL-1β) significantly decreased in rats treated with gabexate compared to rats treated with saline. The use of gabexate also significantly improved survival after a lethal dose of CCl 4 from 0% to 20% [13].

In other studies, it was found that preoperative injection of gabexate significantly improved liver damage compared to other patients (group without gabexate). Postoperative serum transaminase levels decreased markedly due to the marked suppression of IL-6 levels in the blood during liver surgery. This was accompanied by a lower incidence of postoperative complications and a lack of mortality [7].

Purpose of research. On the model of subacute liver poisoning with carbon tetrachloride in rats, to study the effect of protease inhibitor contrykal on changes in the blood of CCK-8, gastrin-17 and digestive hydrolases of the stomach and pancreas, as well as in the composition of gastric mucosal homogenates and pancreas digestive hydrolases, and to justify the mechanisms of these changes.

Material and methods. The experiments were carried out on 30 white laboratory mongrel male rats weighing 180–220 g in 3 series of 10 rats. In 1 series (control) saline solution was injected to male rats orally every other day at the rate of 0.1 ml per 100 g of animal weight for 21 days. In 2 series (experimental) on the model of subacute carbon tetrachloride poisoning. To do this, carbon tetrachloride brand XH (CCl4) was injected orally to male rats every other day, at the rate of 0.1 ml per 100 g of animal weight for 21 days. 3 series (experienced) in the model of subacute poisoning with carbon tetrachloride as in the second group, but further intraperitoneally injected contrykal protease inhibitor (Aprotinin) 25000/kg ATrE daily since 15 days. All rats on the 22nd day after serum decapitation were determined by IFA: pepsinogen-1 (PG1) (JSC "Vector-best", Russia), CCK-8 ("BCM Diagnostics", USA), gastrin-17 (G17) ("Biohit", Finland). Biochemical methods were used to determine amylase pancreatic (JSC "Vector-best", Russia) and lipase pancreatic ("HUMAN", Germany), as well as hepatic samples: alanine transaminase (ALT), aspartate aminotransferase (AST) and total bilirubin. In the composition of pancreatic tissue homogenate, total proteolytic activity (TPA) was determined by spectrophotometric method [5], amylase by photometric method [3] in descending starch color. The total proteolytic activity (TPA) was determined by spectrophotometric method in the composition of gastric mucosal homogenate [5].

The results were processed by the method of variation statistics with the calculation of mean values (M), their errors (m), and the reliability of the difference between the compared Student-Fisher values (t). The results were considered reliable at $P < 0.05$.

Results and discussion. The results of experiments in rats showed that in animals of the experimental group 2 as a result of subacute poisoning with carbon tetrachloride, there was a significant increase in liver samples: ALT, AST, total bilirubin, compared with those of the control group (table).

At the same time, as a result of subacute poisoning with carbon tetrachloride, the degree of change in the hydrolases of the stomach and pancreas in the blood was noted in different directions. Pancreatic amylase and pancreatic lipase significantly increased in relation to the control group. At the same time, pepsinogen-I indices significantly decreased in relation to the control group (table).

Table 1.

Serum markers	Controlled 1st group	Practised 2 nd group	Practised 3 rd group
1	*2*	*3*	*4*
Liver experiments			
ALT (mmol/h*l)	0.56 ± 0.08	1.07 ± 0.1*	0.71 ± 0.08**
AST (mmol/h*l)	1.07 ± 0.13	1.93 ± 0.17*	1.35 ± 0.14**
General billirubine (mkmol/l)	3.9 ± 0.5	9.2 ± 1.2*	6.3 ± 0.4**
Hydrolase of blood			
Pancreatic amylase	63.1 ± 7.9	123.6 ± 13.1*	86.5 ± 9.1**
Pancreatic lipasa	42.6 ± 5.3	94.2 ± 8.6*	69.8 ± 5.7**
Pepsinogen-I (mkg/l)	69.4 ± 8.6	32.5 ± 4.1*	41.3 ± 4.8

1	*2*	*3*	*4*
Peptids			
CCK-8 ng/ml	0.87 ± 0.11	1.63 ± 0.15*	1.17 ± 0.11**
Gastrin-17 pmol/l	7.3 ± 0.92	15.9 ± 1.6*	12.5 ± 1.3
Hydrolase of homogenates			
Amilasa of pancreatic gland ed/100 mg	4892.5 ± 543.7	7362.5 ± 781.9*	6927.4 ± 725.3
TPA of gastric gland ed/100 mg	649.5 ± 59.4	895.3 ± 82.4*	789.5 ± 82.6
TPA of gastric gland Ed/100 mg	87.5 ± 7.6	56.8 ± 5.1*	71.9 ± 6.2

Table 2. – Changes in the considered parameters in rats with subacute carbon tetrachloride poisoning

** – significantly different values relative to the indicators of the control group;*

*** – significantly different values relative to the indicators of the experimental group 2*

In the main group there was a significant increase in the blood composition of CCK-8 and Gastrin-17 compared with the control group.

As part of the homogenates of the gastric mucosa and pancreatic tissue indicators of digestive hydrolases, under the influence of acute carbon tetrachloride poisoning correlated with those of the blood. So significantly increased relative to the control group in the composition of pancreatic tissue homogenate amylase and TPA. At the same time, pepsinogen-I indices in the composition of gastric mucosal homogenate significantly decreased in relation to the control group.

The experiments in rats in the 3 experimental groups showed that in animals the use of contrykal against the background of subacute carbon tetrachloride poisoning, there was a significant decrease in liver samples: ALT, AST, total bilirubin, compared with those in the 2nd experimental group (table).

As a result of the use of contrykal, against the background of subacute carbon tetrachloride poisoning, the indices of digestive hydrolases of the pancreas, pancreatic amylase and lipase in the blood significantly increased in relation to those data of the 2 experimental groups. At the same time, there was no significant increase in pepsinogen-I in relation to the 2nd experimental group (table).

At the same time, in the 3 experimental group there was a significant increase in the blood composition of CCK-8 and no significant decrease in Gastrin-17 compared to the 2nd experimental group (table).

Under the influence of the contrycal against the background of acute carbon tetrachloride poisoning, the indices of digestive hydrolases in the composition of the homogenates of the gastric mucosa and pancreatic tissue of the 3 experimental groups had no significant changes compared to the 2nd group, but correlated with those blood parameters.

The presented data demonstrate that in rats under the influence of acute carbon tetrachloride poisoning, an increase in the blood levels of amylase and lipase indicates an increase in the functional activity of the pancreas, which is also confirmed by an increase in the composition of pancreatic tissue homogenate amylase and TPA, as well as CCK-8. At the same time, a decrease in pepsinogen-1 in the blood and an increase in gastrin-17 indicators indicate a decrease in the function of the digestive glands of the stomach, which is confirmed by a decrease in TPA in the composition of gastric mucosal homogenate.

The reason for these changes is the marked increase in the concentration of CCK-8 in the blood, which is the result of a decrease in its utilization in the liver, under the influence of acute poisoning with carbon tetrachloride [9]. Due to the fact that the physiological role of CCK-8 is to stimulate pancreatic secretion [14], due to this, there is an increase in the indicators taken into account. At the same time, the increase in CCK-8 in the blood reduces the secretion of gastric acid. Since CCK-8 plays a crucial role in inhibiting stimulated secretion of gastric acid, changing the content of gastrin in blood plasma and somatostatin secretion [11].

In experiments in rats with the injection of contrykal against the background of subacute carbon tetrachloride poisoning, a decrease in the blood levels of amylase and lipase indicates a decrease in the functional activity of the pancreas, which is confirmed, although not a significant decrease in the composition of the pancreatic tissue homogenate amylase and TPA, as well as a marked decrease in CCK-8. At the same time, although not a significant increase in blood pepsinogen-1 and a slight decrease in indicators gastrin-17, as well as an increase in TPA in the composition of gastric mucosal homogenate, may indicate an increase in the function of the digestive glands of the stomach.

These changes are associated with a decrease in the concentration of CCK-8 in the blood and are the result of increased utilization of it in the liver, under the influence of contrykal on the background of acute carbon tetrachloride poisoning [9]. Due to the fact that the physiological role of CCK-8 is to stimulate pancreatic secretion [14], due to this, there is a decrease in the parameters taken into account. At the same time, a decrease in

CCK-8 in the blood reduces the secretion of gastric acid. Since CCK-8 plays a crucial role in inhibiting stimulated secretion of gastric acid, changing the content of gastrin in blood plasma and somatostatin secretion [11].

Thus, under the influence of acute carbon tetrachloride poisoning increases the functional activity of the pancreas, while reducing the functional activity of the digestive glands of the stomach. At the same time, the use of contrykal against the background of carbon tetrachloride poisoning reduces the functional activity of the pancreas, while increasing the functional activity of the digestive glands of the stomach, thereby contributing to the restoration of the activity of both the pancreas and the stomach.

We believe that the participation of the liver in the utilization of CCK-8 can be considered as an additional physiological modifying factor in the peptidergic mechanisms of regulation of the digestive glands, and in chronic hepatitis and cirrhosis of the liver is the main pathogenetic factor contributing to the development of these changes in the stomach and pancreas.

Conclusion. In toxic hepatitis, CCK-8 is the main factor contributing to an increase in the functional activity of the pancreas, and can contribute to the development of a hidden form of pancreatitis, while reducing the functional activity of the digestive glands stomach and lead to the development of a latent form of atrophic gastritis. The use of contrykal can help to restore functional activity of the pancreas and stomach.

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SUBJECTIVITY IN DEFECTS IN RENDERING MEDICAL AID

Abstract: Thus, a number of causes contribute to defects occurrence in various cases. Among defects causes subjective and organizational present the majority of cases. Among subjective causes the following facts prevail: incomplete examination of patients, inadequate qualification of medical personnel, careless treatment of patients. These defects were mainly observed in medical practice of obstetricians-gynecologist, surgeons, podiatrists, internists, traumatologists, neurosurgeons, paramedical personnel. With this subjective causes most often resulted in diagnostic and treatment defects, mistakes in administration and carrying out medical procedures (including irrational management of deliveries), defects in surgical treatment and organizational defects.

Keywords: Commission forensic medical examination, defects in the provision of medical care, subjective causes of occurrence, places of assumption.

Introduction. In countries with functioning Health Protection system the main attention is paid to the medical aid (MA) quality. At present the so-called Evidence-Based Medicine (EBM) appeared to be widely spread all over the world. EBM principles may be employed in evaluation of MA quality [1; 6; 11; 14; 17].

The quality control means methodic questions of development of quality criteria and standards and carrying out comparative analysis on their basis; and to provide quality means to achieve the necessary level of medical care and its improvement [5; 7; 12]. The following classification of unfavourable outcomes in connection with carrying out medical measures taking into consideration the cause of their origin is offered: 1. The character and severity of the disease itself or trauma; 2. Iatrogenic diseases; 3. Accidents; 4. Defects in rendering medical aid (prophylactic, medical-prophylactic, medical rehabilitating measures) (DMA); 5. Medical mistake; 6. Medical delict [2; 3; 4; 8; 13; 16]. Deep study of medical aid organization in a number regions showed that the main blunders in early diagnostics and treatment of the revealed patients were made at prehospital stage (PHS). The patients were not examined thoroughly and did not receive an adequate treatment in the period of undoubted curability in almost half of cases and in the future they will present the contingent of patient with chronic, often incurable diseases, filling in-patient departments [9; 10; 15]. Thus a number of causes contribute to the development of DMA. Many authors consider that the majority of DMA appears due to be objective causes and their comprehensive study is actual at present and that is the aim of this paper.

Materials and research methods. Conclusions of Forensic Medicine Commission of Expert Examination (FMCEE), carried out for professional infringements of the law in all regions Bureau and Chief Bureau of Forensic Medicine Expert Examination of Uzbekistan Public Health Ministry during the period from 1999 to 2008. Of 2.369 FMCEE concerning medical personnel, DMA were revealed in 4 9.4% (1171) of cases. Above-mentioned conclusions were thoroughly analyzed and appeared to be the material for study. In connection with above-mentioned conclusions the reports of 620 conclusions and 147 acts of Forensic Medicine Examination of corpses and alive persons, the other kinds of Forensic Medicine documents, the results of histological, chemical investigations'ets. were studied. In order to study the defects in rendering medical aid completely, taking into consideration peculiarities of medical practice, we developed modification of DMA classification, offered by Yu. I. Sosedko [7] in her work. Statistical processing of the received material, expressed in figures were carried out using the packet of statistical analyses of electronic tables Excel 2003 Microsoft office calculating average mistakes for mean arithmetic ($M \pm m$). Difference were considered to be reliable if $0.01 \leq P \leq 0.05$.

Results. Above-mentioned causes of DMA occurrence were conditionally generalized into 4 groups: exclusively subjective causes 1336(65.26%), organizational causes – 496(24.23%), objective causes – 156(7.62%), others – 59(2.88%). The revealed causes of DMA occurrence show that their number in 2000 decreased to 8,7% in comparison with the previous year, then increased gradually to 12.0% in 2003, then decreased to 10.9% in 2005 and to 6,6% in 2008.In percent correlation sharp prevalence of subjective causes in comparison with the other groups of causes is noticed. Among subjective causes the majority are presented by: insufficient qualification of medical personnel (25.6%) and inadequate examination of the patients (24.8%). Analyses

of DMA development in speciality aspect showed that they were mainly noticed in medical practice of obstetricians-gynecologists (25.0%), surgeons (16.8%), podiatrists (8.0%) and other(P < 0.05).

Investigation of causes of DMA occurrence among different specialities showed the following: careless treatment of patients was in the main presented in practical activity of the emergency care units physicians (EC) (35.3%), paramedical personnel(30.6%), podiatrists (23.3%), internists (17.0%), and other.

Example 1. *FMEEC Conclusion N59. T.T.– 50 years old fell down and received bodily injuries on his working place in May. He was twice treated in CRH for 8–12 days with diagnosis "Acute pyelonephritis". In 2 years he was treated for 10 days in CRH with diagnosis "Chronic lumbar-sacral radiculitis with left side monopareses". Only in a year the diagnosis "Compressive fracture of X thoracic vertebra body and tumor of the spinal cord" was revealed in clinical hospital. In spite of two performed operations the patient died. In timely complete examination and treatment of the patient it was possible to save his life.*

Insufficient qualification of medical personnel presented the majority of defects in medical practice of paramedical personnel(61.2%), reanimatologists (37.2%), traumatologists (34.6%), neurologists (27.0 and other. Inadequate examination prevailed in neurologists (54,1%), neurosurgeons (33.7%), traumatologists (28.1%), reanimatologists (21.5%), and other. Inter communication of DMA character and causes of their development show that they appeared due to subjective causes (65.26%), organizational (24.23%) and objective ones (7.62%). So development of subjective causes of diagnostic defects was often due to careless treatment of patients without correct diagnosis of the main disease (trauma) (13.5%) and its complications (21.1%) and also significant combining disease (4.6%); defects of treatment – mistakes in administration and performing medical procedures (11.2%), inadequate taking of medicines (5.6%), and other (P < 0.05). Insufficient qualification of paramedical personnel resulted in diagnostic defects – wrong diagnosis of the main disease (trauma) (14.9%) and its complication (23.1%), significant combining disease (5.2%); defects of treatment – mistakes in carrying out medical procedures (14.3%), defects of surgical treatment (9.4%), and other (P < 0.05). Inadequate examination results in diagnostic defects – incorrect diagnosis of the basic treatment(trauma) (16.5%) and its complications (24.8%), significant combining disease (7.7%); treatment defects result in mistakes in administration and performing medical procedures (including irrational management of deliveries) (8.5%), defects of surgical treatment (6.7%), and other (P<0,05). So in some specialities (obstetricians-gynecologists, surgeons) an increase of the studied signs is noted. In the aspect of specialities it was marked as following: obstetricians-gynecologists show careless treatment of patients with different forms of clinical gestosis, postdelivery bleeding, postdelivery sepsis, premature placental separation, early rupture of amniotic fluid sac, unwillingness to hospitalize pregnant women with beginning deliveries, inadequate care for women in labor with pathological pregnancy, late follow up of pregnant women.

Inadequate qualification of medical personnel is one of the most often DMA. This sign as a cause of DMA occurrence was noted in medical practice of obstetricians-gynecologists 110(21.0%), surgeons 86(16.4%), reanimatologists 45(8.6%), traumatologists 53(10.1%), paramedical personnel – 30(5.7%), and other (P < 0.05). Surgeons show conceit in examination and treatment of patients, unqualified diagnostic investigations, unqualified preparation of patient to the operations, absence of consultative assistance, incorrect evaluation of examination results, iatrogenic injuries during operative interferences, underestimation of the patient`s severe condition when he needs hospitalization and after operative interference. Reanimatologists-anesthesiologists have insufficient qualification in carrying out diagnostic investigations and medical interferences, in administration of medicamental treatment for diagnosis of the brain edema, pulmonary edema, steady pneumonia; long "waiting" tactics, underestimation of the patient`s severe condition, iatrogenic injuries in performing medical interferences, iatrogenic pathology in carrying out medicament therapy.

Example 2. FMEEC N6. T.A. 21 years old got bodily injuries and was hospitalized to medical sanitary unit. The diagnosis was: "Hypertonic crisis. Hypertonic disease of the III degree. Edema of the lungs and brain. Ischemic insult. Damage of cerebral circulation, right side hemipareses". In spite of performed medical measures there was a lethal outcome on the 5th day. The cause of the death was bleeding into the substance and ventricles of the brain, traumatic shock, fracture of nasal bones, VI, VII, VIII ribs on the left side and XI on the right one, the process of the 11 cervical vertebra, left radial and right tibial bones. These damages were not timely diagnosed due to insufficient qualification of the physician.

Incomplete investigation is most often the cause of subjective character in rendering medical aid. The received data show that such cause in DMA occurrence was observed in medical practice of obstetricians-gynecologists –116(22.8%), surgeons – 91(17.9%), grammatologists – 43(8.5%), internists – 41(8.1%), neurosurgeons and podiatrists in 34(6.7%), and other (P < 0.05). Reanimatologists anesthesiologists show incomplete examination in diagnosis of closed injuries of thoracic, abdominal cavities, cardiovascular and respiratory pathology during preparation and performing operations, in carrying out medical procedures, incomplete examination in

suspicion to alcohol intoxication, absence or incomplete use of consultative help, incomplete study of pathological course and also in diagnosis of complications of the main and combining pathology. The highest indexes show obstetricians-gynecologists and surgeons.

Conclusions. Thus, a number of causes contribute to DMA occurence in various cases. Among DMA causes subjective and organizational present the majority of cases. Among subjective causes the following facts prevail: incomplete examination of patients, inadequate qualification of medical personnel, careless treatment of patients. These defects were mainly observed in medical practice of obstetricians-gynecologist, surgeons, podiatrists, internists, grammatologists, neurosurgeons, paramedical personnel. With this subjective causes most often resulted in diagnostic and treatment defects, mistakes in administration and carrying out medical procedures (including irrational management of deliveries), defects in surgical treatment and organizational defects.

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PROSPECTS OF IVF EFFECTIVENESS IMPROVEMENT FOR PATIENTS OF OLDER REPRODUCTIVE AGE

Abstract: The studies examined the effectiveness of recombinant and urinary-derived gonadotropins use in stimulation cycles using gonadotropin releasing hormone (GnRH) antagonists in women of older reproductive age.

Keywords: in vitro fertilization, ovarian stimulation, reproductive age.

Introduction. Study of married couples infertility showed that in almost half of the cases (44.3–52.7%), the reason of infertility is woman reproductive system diseases; in 6.4–19.4% – the reason is pathologies of man reproductive system; and in more than one third of the cases (34.2–38.7%) infertility is the result of reproductive function pathologies of both partners [1; 5]. Age is a major factor in determination of in vitro fertilization (IVF) programs and embryo transfer (ET) effectiveness. It determines the number of obtained oocytes, the transferred embryos quality, and the frequency of assisted pregnancies outcomes. Complex IVF and PE programs significantly improve frequency and quality of pregnancies in patients over the age of 38, and also allow using their entire ovarian reserve. The lack of effective methods for restoring natural human fertility has inspired the development of new assisted reproductive technologies (ART), in particular (IVF), with their effectiveness ranging from 28.5% to 32.5% [2; 3]. In recent years, much attention has been paid to the development of methods aimed at increasing the effectiveness of IVF cycles [3; 4; 5].

Studies of a group of women over 40 years old by A. Fujimoto et al. (T. Fujiwara, Y. Osuga, T. Yano, O. Tsutsumi, Y. Taketani) revealed the following results: the birth rate of live-born, healthy newborns was 16% and was found only in age group from 40 to 42 years; no pregnancies occurred in patients over 43 years old. Duration of infertility, the partner age, the age at marriage, records of uterus surgery, and other parameters were statistically insignificant in the studied group. The authors concluded that with low FSH values, normal menstrual cycle, and no medical history of ovarian surgeries in women 40–42 years old, good results can be achieved.

As can be seen from the above, despite the expansive ART introduction, contributing to the conception in almost every third married couple with impaired reproductive function, the issues of increasing the effectiveness of expensive in vitro fertilization and embryo transfer continue to be extremely relevant [2; 3]. The effectiveness of IVF (measured in the frequency of pregnancies occurrence) currently does not exceed 35–40% with about a third of all pregnancies are terminated in the early stages due to unknown causes. This makes it important to research optimization of the examination and preparation of women with endocrine forms of infertility to the use of in vitro fertilization methods to increase their effectiveness.

Study Objective: to study the effectiveness of recombinant and urinary-derived gonadotropins use in stimulation cycles using gonadotropin releasing hormone (GnRH) antagonists in women of older reproductive age.

Materials and methods: The study used the ovarian stimulation protocol with GnRH antagonist. From 2–4 days of the menstrual cycle:

The 1st group of patients (main group) was administered with recombinant FSH-Puregon (Organon, Netherlands) or Gonal-F (Serono, Italy) (Fig. 1).

The 2nd group of patients (comparison group) was administered with urinary FSH-Menopur (Ferring, Germany) (Fig. 2).

The starting dose of gonadotropins in the first and second groups was 150–250 IU and depended on the ovarian reserve, the number of administration days ranged from 6 to 16 in the first group and from 6 to 12 in the second group. The daily dose was corrected according to ultrasound data, depending on the growth of follicles. Ultrasound monitoring was performed on the day of ovarian stimulation occurence, on the 5–6th day of stimulation, and then every other day before the day of the appointment of the ovulatory dose of hCG.

GnRH antagonists: Orgalutran (Merck, USA) or Cetrotide (Serono, Switzerland) were administered subcutaneously in a daily dose of 0.25 mg after leading follicle reached diameter of 13–14 mm. The final follicles maturation trigger, i.e. the ovulatory dose of hCG: Ovitrelle (6.5 thousand IU) (Serono, Switzerland) or Pregnyl (10 thousand IU) (Merck, USA) was prescribed after 3 follicles reach a diameter of more than 17 mm.

All patients were treated with Utrogestan 600 mg/day intravaginally before pregnancy was confirmed or excluded according to the number of the hCG β-subunit in the blood on the 14th day after embryo transfer. A pregnancy test was considered positive at a β-hCG level of more than 20 IU/L (biochemical pregnancy). Ultrasound diagnosis of clinical pregnancy was carried out 21 days after embryo transfer, after which further patient treatment plans were determined.

Results of the study: The duration of ovarian stimulation using recombinant gonadotropins (main group) was significantly higher than that when using urinary-derived gonadotropins (comparison group). For instance, in the main group, the duration of stimulation was 9.3 ± 0.2 days, and in the comparison group – 8.6 ± 0.3 days ($p < 0.05$). In addition, in the comparison group, the final follicles maturation trigger was introduced earlier than in the main group (10.5 ± 0.3 and 11.4 ± 0.2 day of the menstrual cycle, respectively; $p < 0.05$).

Ultrasound monitoring revealed that during gonadotropic stimulation, the number of growing follicles in patients of the main group exceeded the same parameter in the comparison group: 7.5 ± 0.5 and 5.7 ± 0.5, respectively ($p < 0.05$).

There were no statistically significant differences in the number of oocytes obtained during ovarian puncture, in the total dose of gonadotropins, the frequency of ovarian puncture, and the day of ovarian puncture in patients of the examined groups.

Table 1.– Parameters of ovarian stimulation by gonadotropins in patients of the examined groups (M±m)*Parameter*

	Main Group	Comparison Group	p
Course dose of gonadotropins, IU	2035.4 ± 93.9	1947.6 ± 131.4	
Duration of stimulation, days	9.3 ± 0.2	8.6 ± 0.3	< 0.05
Number of growing follicles	7.5 ± 0.5	5.7 ± 0.5	< 0.05
Introduction day of the final follicles maturation trigger, day of menstruation cycle (DMC)	11.4 ± 0.2	10.5 ± 0.3	< 0.05
Frequency of ovarian puncture,%	97.8	93.8	
Day of ovarian puncture, DMC	13.3 ± 0.3	12.8 ± 0.3	
Average number of oocytes obtained by ovarian puncture	6.4 ± 0.5	5.6 ± 0.7	
Frequency of ovarian punctures with no oocytes obtained,%	7.6	6.3	
Frequency of cycle cancellation (lack of follicle growth during gonadotropic stimulation of the ovaries),%	1.1	0	

Table 2.– Dependence of ovarian response to gonadotropin stimulation in the IVF / IVF + ICSI protocol on hormone levels and age. (M ± St)

Parameter	"Weak response" of the ovaries	4 or more oocytes acquired	P
Age, years	38.8 ± 0.5	37.6 ± 0.3	< 0.05
FSH at 2 DMC, nmol/L	7.8 ± 0.4	6.4 ± 0.2	< 0.01
AMH	1.2 ± 0.2	2.2 ± 0.2	< 0.005

Table 2 shows the probability (OR) of obtaining a sufficient ovarian response and the risk of obtaining a "weak" ovarian response when punctured in IVF/IVF + ICSI protocols in older reproductive age women of the study groups (OR). It can be seen that the chance to get 4 or more oocytes in the main group is slightly higher than in the comparison group (OR = 1.35, $p < 0.05$).

Table 3.– The probability (OR) of obtaining a certain number of oocytes during puncture in IVF/ IVF+ICSI protocols in older reproductive age women in the studied groups (OR)

Oocytes obtained by puncture	Studied Group		OR	p
	Main	Comparison		
1–3	32	13	–	> 0.05
	34.8%	41.9%		
4+	60	18	1.35	< 0.05
	65.2%	58.1%		

On the 14th day after the transfer of the level of betahCG in the blood, the biochemical pregnancy occurred in 18 (24%) women of the main group and 9 (32.1%) women of the comparison group. After 1–2 weeks, ultrasound shown the gestational sac in 21.3% (16) women of the main group and 28.6% (8) women in the comparison group. No statistically significant differences in pregnancy rates between groups were found.

Table 4. – The effectiveness of the treatment per study groups

Pregnancy rates per embryo transfer		Main Group	Comparison Group	Total
Biochemical pregnancy	n	18	9	27
	%	24	32.1	25.9
Presence of the ovum as shown on ultrasound (coefficient of implantation)	n	16	8	24
	%	21.3	28.6	23.3
Single delivery	n	7	4	11
	%	9.3	14.3	10.7
Twin delivery	n	1	0	1
	%	1.3	0	0.9
Miscarriage (ovum on ultrasound)	n	2	0	2
	%	12.5	0	8.3

Figure 1 shows the changes of FSH, AMH in the blood and the frequency of pregnancy in women of three age groups. It should be noted that in the age group of 37–39 years the pregnancy rate was higher than in the age group of 34–37 years and in the age group of 40–43.

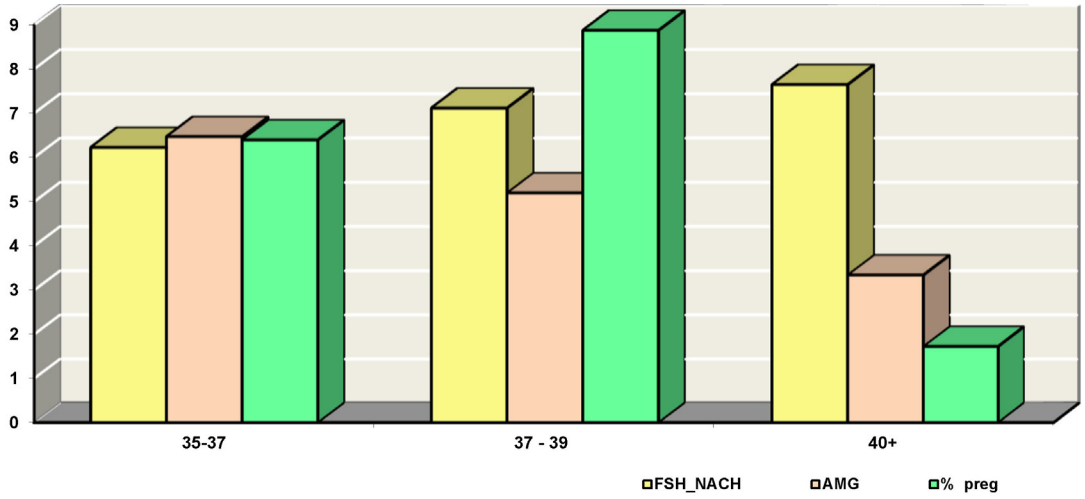

Figure 1. Changes of FSH, AMH in the blood and the frequency of pregnancy in women of three age subgroups

Comprehensive assessment of pregnancy probability in cycles of IVF/ IVF+ICSI in patients of older reproductive age

The method of constructing classification trees has developed a scale for obtaining a total index of clinical pregnancy in the IVF/IVF+ICSI protocols in women of older reproductive age.

The transitional value was the score of 3, which can be considered as a threshold. Patients with score from 4 to 5 have the chance of clinical pregnancy increased by 21.8 times compared with patients who have score of 0–3; with a prognostic score of 6–7, the chance increases by 120 times ($p < 0.001$) compared with patients who have score of 0–3.

For the biochemical pregnancy occurrence in the process of building classification trees, the following scale was developed:

Table 5. – Calculing scale for the total prognostic index of clinical pregnancy occurrence in women of older reproductive age in IVF/IVF+ICSI protocols

Parameter	Value	Score
1	*2*	*3*
Age, years	Age ≥ 40	0
	Age < 40	1
Artificial abortions in past medical history	Yes	0
	No	1

1	*2*	*3*
Ovarian failure	Yes	0
	No	1
Tubectomy in past medical history	Unilateral	0
	No	1
	Bilateral	2
FSH, IU/L (2 DMC)	≥ 6.5	0
	4.5–6.5	1
	< 4.5	2

Table 6. – Calculating scale for the total prognostic index of biochemical pregnancy occurence in women of older reproductive age in the IVF/IVF + ICSI protocols

Parameter	**Value**	**Score**
Age, years	Age ≥ 40	0
	Age < 40	1
Artificial abortions in past medical history	Yes	0
	No	1
Ovarian failure	Yes	0
	No	1
Chronic adnexitis	No	0
	Yes	1
Duration of embryo cultivation	2, 4, 5 days	0
	3 days	1
FSH, IU/L (2 DMC)	FSH ≥6,5	0
	4.5J	1
	FSH<4.5	2

Also, the transitional value of 3 can be considered a threshold. When the score is 4–5, the chance of a biochemical pregnancy increases by 20 times ($p < 0.001$) compared with patients with score of 0–3; at a score of 6–7, by 159 times compared with patients with 0–3.

Conclusion: In summary, in patients of older reproductive age, IVF protocols are characterized by a high frequency of weak (35.3%) and extremely weak response (33.3%) of the ovaries to gonadotropic stimulation; its efficiency and the quality of *in vitro* fertilization of oocytes is reduced by the transferred surgical interventions on the organs of the reproductive system (unilateral or bilateral cystectomy by 2 times; unilateral or bilateral tubectomy, myomectomy by 1.5 times); ovarian failure (by 1.5 times), clomiphene-resistance (by 2 times), no history of previous childbirths (by times).

The number of oocytes obtained during ovarian puncture, the quality of fertilization and the development of embryos in vitro have a negative correlation with the basal level of FSH and a positive correlation with the concentration in the blood of the anti-Muller hormone; the blood content of inhibin B correlates with the number of type C embryos on the third day after fertilization.

In patients of older reproductive age, IVF protocols use gonadotropin-releasing hormone antagonists, recombinant FSH medications and urinary-derived gonadotropins have equal efficacy in stimulating the ovaries, fertilizing the oocytes and increasing the frequency of pregnancy.

Compared to protocols with recombinant FSH, IVF protocols with urinary-derived gonadotropins are characterized by a high rate of embryo development (*with higher number of blastomeres*) (on the 3rd day after fertilization, the morula stage occurs in 17.1% and 6.9% cases, respectively), greater frequency of embryo transfer into the uterine cavity on the 5th day of development (7.6% and 2.2%), cryopreservation at the morula stage (50.0% and 27.9%) and blastocyst stage (18.2% and 1.5%).

In IVF protocols with urinary-derived gonadotropins, LH in blood of the patients on the day of the introduction of the final oocyte maturation trigger is 2 times lower than that in IVF protocols with recombinant FSH and has a high negative relationship with the quality of fertilization and embryo development in vitro.

In IVF protocols with urinary-derived gonadotropins, the duration of ovarian stimulation is shorter when compared

with recombinant FSH. Additionally, the thickness of the endometrium during the transfer of embryos into the uterus with urinary-derived gonadotropins is greater than with the use of recombinant gonadotropins.

In IVF protocols for patients of older reproductive age, the frequency of pregnancy is determined by the calculating scale for the total prognostic index of the of clinical pregnancy occurrence in women of older reproductive age in IVF/IVF+ICSI protocols. The transitional value that can be considered as a threshold was score of 3. Score from 4 to 5 increases the chance of clinical pregnancy by 21.8 times compared with patients who have score of 0–3; with a prognostic score of 6–7, the chance of pregnancy increases by 120 times ($p < 0.001$) compared with patients who have score of 0–3.

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PECULIARITIES OF X-RAY SEMIOTICS IN EARLY AGE CHILDREN WITH PNEUMONIA

Abstract: The features of radiological semiotics of pneumonia were studied depending on the period of gestation at birth. In children born prematurely with pneumonia, radiographic signs characteristic of the continuing immaturity of the lung tissue are revealed. Characteristic for prematurity, low-intensity foci against the background of immature lung and relatively poor, and slow dynamics of inverse changes confirms the view that the risk of developing chronic pulmonary pathology prevails precisely when there is a history of prematurity and a clear correlation of inflammatory changes in the lungs with perinatal pathology and lung maturity and the body as a whole.

Keywords: pneumonia, immaturity, term of gestation, early age, radiography.

Diseases of the respiratory system are widespread among the child population and have a large proportion in the structure of the incidence, especially is the first 3 years of life. A common form of respiratory organs failure in children in all age groups is pneumonia.

Guided by the opinion [3; 6] of continuing signs of immaturity in premature babies and up to 3–4 years of age, the opportunity was used to investigate the presence of these signs in pneumonia in young children, depending on the gestational age. Acute pneumonia in children has clinical and morphological features due to the immaturity of the lung tissue and the response of local immunity [1]. The diagnosis of pneumonia is considered verified only in cases where the focal inflammatory lesion of the lungs is confirmed radiographically [2].

The purpose of the study is to study the features of radiological semiotics in pneumonia in young children, depending on the period of gestation at birth.

Material and research methods. A clinical X-ray examination of 110 young children with pneumonia was performed. Survey radiography of the chest was carried out in a straight line and, if necessary, in lateral projections, in an upright position, with maximum inspiration or at the height of a crying child to improve the contrast of the pulmonary fields with gonad screening. X-ray examination was performed on the apparatus of the brand KH0 50F – "Toshiba" (Japan). During chest radiography in children we adhered to the following technical specifications: voltage of 50–55 kV, current of 100–150 mA, exposure time 0.03–0.1 seconds. The effective equivalent dose (conditional dose of uniform irradiation of the whole body) per 1 image was 0.02–0.04 mSv, in accordance with the Radiation Safety Standards.

Depending on the age and duration of gestation at birth, the children surveyed comprised the following groups:

A_1 – children aged 1 month to 1 year, from full-term history (42);

A_2 – children aged 1 month to 1 year, from the history of preterm (36);

B_1 – children aged 1 to 3 years, from the history of full-term (15);

B_2 – children aged 1 to 3 years, from the history of preterm (17).

The results of the study and their discussion. The features of radiological semiotics of pneumonia were studied depending on the period of gestation at birth. Analysis of radiological manifestations and comparison of changes in acute pneumonia in children aged 1 month to 1 year, as well as in children from 1 year to 3 years of age showed that satisfactory parameters of pulmonary ventilation were better manifested in groups of children born full-term (groups A_1 and B_2). At the same time, in children with prematurity in history (groups A_1 and B_2), hypoventilation of the lungs (78% and 65%, respectively), including the frosted glass symptom, was dominant.

As for such a reliable radiological symptom of pneumonia, as shadowing, it is revealed that in all groups, limited shadowing dominated on radiographs (79%, 72%, 80%, 65%), i.e. the shadows, the area of which corresponded to a part of the lobe or segments of lungs. According to the structure, shadows usually had a heterogeneous character (79%, 69%, 80%, 76% respectively), more often with indistinct shadows (98%, 97%, 80%, 71%). Shadowing of the homogeneous structure was revealed less frequently. On radiographs for pneumonia between the ages of 1 and 3 years, along with shadowing, having weak intensity and indistinct contours, we also observed shadows of medium intensity (67%, 41%) with relatively sharp contours (20%, 29%), especially prevalent in term babies. This X-ray manifestation of some consolidation of the pulmonary parenchyma is most likely due to a tendency to chronic inflammation in these groups of children. Identification in isolated cases of the indicated symptoms in the group of full-term children may be explained by the severity of the patient's condition due to premorbid background (hypotrophy, rickets, exudative-catarrhal diathesis).

In parallel to the limited shadowing of a certain part of the examined children (10%, 39%, 20%, 12%), in the medial zones of the lung fields, single scattered the small-focal shadows, which also had indistinct contours, were often visualized. The common multiple small focal shadows were more often visualized on radiographs in children with prematurity in history. So, in children of group A_2, they were revealed in 61% of cases, and in group B2, in 41% of cases. In children from 1 year to 3 years, from the history of full-term, this picture was not typical. It should be noted that focal shadows very often tended to merge, forming foci of shadowing.

Shadowing of the lung fields are often combined with areas of limited compensatory swelling of the adjacent sections of the lungs. Individual bullous swellings were noted with almost the same frequency in all studied groups of patients (40%, 39%, 47% and 47%).

Analysis of the x-ray morphological picture of the pulmonary pattern in all the examined groups revealed the prevalence of the characteristic symptom of the inflammatory process as an increase in the pulmonary pattern (100%, 75%, 67%, 88%). The pulmonary pattern along the lungs on both sides was enhanced due to swelling of the fibrous stroma along the vessels. In limited areas, reticulation was determined due to edema of the reticular stroma. The degree of detectability of such radiological signs of pulmonary immaturity, such as the limited reticular deformity of the pulmonary pattern and the symptom of "air bronchogram", was more common in children with a history of prematurity. Thus, the change in the pulmonary pattern of the net type dominated in the A_2 and B_2 groups (92% and 88%), as opposed to the A_1 and B_1 groups (38% and 47%). There was often a more homogeneous lesion of the lungs with multiple clear lace-like dense foci leading to the periphery.

The symptom of "air bronchogram" prevailed in children aged 1 to 3 years (80% and 71%) than in children aged 1 month to 1 year (24% and 50%), which most likely explains certain chronic character of inflammation in the airways. The resistance of the X-ray picture of the lungs is noted in the form of alternating areas of low transparency of the lung tissue, more often the middle-medial sections, of coarse interstitial pattern (fibrosis) and hyperaerial areas. The impoverishment of the pulmonary pattern in minor cases was visualized in a group of children with prematurity in history (8% and 12%) and was not typical of full-term babies.

Attention was drawn to a significant increase in the roots on both sides, revealed in all the examined groups of children. If the focal shadows were located in segments, the projection of which coincided with the root and root zone, the structure of the root changed dramatically. Additional shadow in the root zone due to involvement in the process of interstitial tissue very often created a picture of the expansion of the root zone.

In general, it can be noted that in children with pneumonia born prematurely, radiographic signs characteristic of the continuing immaturity of the lung tissue are revealed, namely, moderate pulmonary hypoventilation, common small-focal shadows, limited net deformity of the pulmonary pattern and the symptom of "air bronchogram". Moreover, at the age of 1 year to 3 years, the above symptoms are somewhat less marked, which is consistent with the available information about the response from the interstitial tissue in age dynamics [7].

The generalization of the results showed that in the older groups of children the pneumonic process proceeds less rapidly and captures a smaller area of the lungs, that is most likely, associated with the maturation of lung tissue. Characteristic for prematurity, low-intensity foci against the background of immature lung and relatively poor, and slow dynamics of inverse changes confirms the view that the risk of developing chronic pulmonary pathology prevails precisely when there is a history of prematurity and a clear correlation of inflammatory changes in the lungs with perinatal pathology and lung maturity and the body as a whole.

We would like to note that the above symptoms (intensification and deformation of the pulmonary pattern, reduced transparency of the pulmonary fields of the frosted glass type, small focal shadows), in their turn, are radiographic signs of the early stages, the so-called interstitial lung diseases, which have recently attracted attention of not only clinicians, but also radiologists, morphologists due to the increasing prevalence [4; 5; 7]. As the process progresses, some of the observed children show signs of interstitial fibrosis, appearance of cavities, and a picture of the cellular lung is formed. Such information gives us the reason to assume that presence of such signs in children born premature does not exclude the probability of an age predisposition to interstitial lung diseases. This is consistent with the emphasis that in the general children's population there is a fundamentally separate age group – newborns and infants and it is in this group that there are interstitial lung diseases that have no equivalents in older children and adults, but are probably related to lung function in the next years of life [8].

Conclusions. Long-persisting signs of immaturity of the lung tissue in children born prematurely leave an imprint on the process of the further development of respiratory tract diseases in young children and do not exclude the probability of an age predisposition to interstitial lung diseases. X-ray examination for presence of continuing signs of immaturity in premature babies and up to 3–4 years of age for pneumonia, having a wide range of indicators, rich in morphological information, will contribute to the timely correction of complex treatment.

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ACTUAL PROBLEMS OF INFECTIOUS DISEASES IN OBSTETRICS

Abstract: The urgency of the problem of obstetric and gynecological infections is determined by their high prevalence and pronounced adverse effects on the reproductive function of women, the course and outcome of pregnancy. The article summarizes the data of modern scientific, methodological and normative literature covering various aspects of infectious and inflammatory diseases important in obstetrics and gynecology. The actual epidemiological data are given, the modern ideas of pathogenesis, ways of infection and risk factors, clinical manifestations of infections and their complications, treatment and prevention are stated.

Keywords: infections, reproductive system, etiology, pathogenesis

Infectious diseases of the mother play a leading role in infertility, miscarriage and miscarriage, and the cause can be both severe systemic infectious diseases and asymptomatic bacterial and viral infections of the genital tract. Premature infants have a high rate of stillbirth, early neonatal mortality and disability [6]. The role of infection in the development of gestosis has been revised and this factor is very important. In fact, the pathogenesis of gestosis is currently considered from the standpoint of systemic inflammatory response with endothelial dysfunction, cytokine cascade, dysfunction of immune cells, vascular system, hemodynamics and the development of multi-organ failure [3].

The problem of inflammatory diseases in gynecology, postpartum inflammatory processes and sepsis remains topical. From year to year, sepsis takes the leading place in the structure of maternal mortality, with post – abortion sepsis-more often than postpartum [7]. Chronic inflammation of the genitals leads to a decrease in the quality of life of women due to the development of chronic pelvic pain syndrome, infertility, miscarriage, ectopic pregnancy and neurotic conditions. Thus, the problems of infections become crucial in obstetrics and gynecology [1].

Currently, the etiological structure of infectious diseases of women, as well as intrauterine infection of the fetus and newborn has changed. These changes relate to both opportunistic and pathogenic flora. Dominant in recent years, gram-negative microbial flora in the inflammatory foci of the sexual sphere was replaced by coccal (which was typical for the 40–50-ies) and this led to an increase in the number of purulent processes. Formed particularly resistant coccal flora, insensitive to broad-spectrum antibiotics. Characteristically, along with staphylococci, a lot of pathology was to determine strep D Enterococcus that are resistant even to antibiotics of the reserve. Consistently held its position among the etiological factors of inflammatory diseases of the nonspore anaerobes (peptococcus, Peptostreptococcus, Bacteroides, fuzobakterii, veillonella etc.), and their detection remains an insurmountable challenge for health care practice [8].

However, it is in recent years has increased dramatically the role of pathogens of sexually transmitted diseases: chlamydia, Mycoplasma, Ureaplasma, herpes simplex viruses, cytomegalovirus, fungi. Along with the well-known, well-studied representatives of conditionally pathogenic genital bacterial flora, these pathogens, and with them the viruses of rubella, enteroviruses and Toxoplasma, made TORCH-complex – is well known to obstetricians, neonatology and Perinatology. It is a complex of pathogens that can cause intrauterine infection of the fetus. Infections, sexually transmitted infections, an essential part of this list and built him significant linkage [2].

The need for comprehensive treatment of women with urogenital infection during pregnancy to prevent infection of the placenta and fetus became apparent after studying the risk of intrauterine fetal infection in women with specific infection. The examination of 200 infected pregnant women at 22–40 weeks of gestation and 96 newborns [4] revealed that in women with Mycoplasma(Ureaplasma)-chlamydial infection the rate of infection of the placenta is 74.2%, in viral infection – 21.8%, in Mycoplasma-chlamydia-viral Association – 63%, while there is no nonspecific microflora in placental tissue. Pathomorphological changes in placental tissue, membranes and umbilical cord

in women with specific urogenital infection largely depend on the type of pathogen. Mycoplasma (Ureaplasma) and herpetic infections potentiated the formation of compensatory-adaptive processes in the form of terminal villi hypervascularization in moderately pronounced basal lymphocytic deciduitis.

Alterative and dystrophic reactions were manifested by arteriosclerosis, the formation of calcifications in the placenta and were characteristic of chlamydial and cytomegalovirus infection. Amniotic fluid in the vast majority of women with urogenital infection were sterile, only 0.7% revealed Mycoplasma, 1.4% – cytomegalovirus and herpetic infection. Features of the microelement composition of amniotic fluid in pregnant women with urogenital infection is a high level of strontium, contributing to the development of placental insufficiency, and increased glucose levels, reflecting metabolic disorders in the fetus [9].

According to some authors, the fetus is most often infected with intranatally conditionally pathogenic flora of the lower genital tract (66%), myco – and Ureaplasma (19.7%), chlamydia (10.4%). Antenatal infection occurs much less frequently-viruses in 1.4%, Mycoplasma-in 0.7%, chlamydia-in 2.1% of newborns. The main condition for the infection is an infection of the placenta, Feto-placental insufficiency and infectious pathology of the vagina [5; 7].

Prognostically reliable criteria for the risk of intrauterine infection of the fetus are specific bacterial and viral infection in the mother, the threat of termination of pregnancy, colpitis, pathology of amniotic fluid, fetoplacental insufficiency, the lack of comprehensive treatment during pregnancy.

As data on intrauterine infection accumulate, its Association with women's somatic health becomes apparent. Women at risk of inflammatory diseases in the postpartum period have gastrointestinal, cardiovascular and respiratory diseases 1.9, 1.7 and 1.6 times more often than healthy puerperas, as well as the threat of abortion, gestosis and anemia 3.3, 3.6 and 1.7 times respectively. Childbirth is 2.7 times more often complicated by abnormal contractile activity of the uterus, 2.2 – premature discharge of amniotic fluid and 2.5 – pathological blood loss. However, a factor determining the development of inflammatory diseases after childbirth, along with the above, is the presence of chronic chlamydial, mycoplasmic [10], ureaplasmic, herpetic and cytomegalovirus urogenital infection combined with activation of urinary tract infection in the first trimester and recurrent colpitis or gestosis in late pregnancy, as well as a combination of chronic specific infection, abnormalities of uterine contractility and gestosis [4].

The high degree of infection of the endometrium and postpartum inflammatory complications are certainly associated with intrauterine infection of newborns, which was detected in 44% of children of women who had postpartum inflammatory complications, and in 32.8% who did not have them.

Implementation of intrauterine infection according to clinical and microbiological data was proved in 4.6% and 2.9% of children, respectively, the rest had a high risk of intrauterine infection. this was manifested by umbilical cord infection in 31.1%, auricle infection in 58%, as well as complications in the early neonatal period – intrauterine growth retardation – in 12.7%, hemorrhagic syndrome – in 21.9%, neurological symptoms – in 37.5%, jaundice syndrome – in 11.5%, which should be regarded as the consequences of placental insufficiency and hypoxic complications[7].

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TO THE PECULIARITIES OF DIAGNOSIS AND TREATMENT OF CEREBELLAR TUMORS

Abstract: This study includes data from a comprehensive examination and treatment of 35 (21 women, 14 men) patients, the average age of patients was 30 years (from 3 to 69 years). The results of the treatment of cerebellar tumors depend on the use of modern surgical methods and their radicalism.

Keywords: cerebellar tumors, medulloblastoma, hemisphere, astrocytoma, ependymoma.

Relevance. The relevance of diagnosis and treatment of cerebellar tumors is due to the prevalence of these pathologies, the severity of the course and the lack of effectiveness of common treatment methods. Among neuro-oncological diseases in children, cerebellar tumors range from 70.6% to 73.6%, according to the histological structure of them, medulloblastomas range from 29.0% to 48.9%, astrocytomas from 32.1% to 36.0%, ependymomas from 1.4% to 18,0% [1; 9].

The severity of prognosis in patients with cerebellar tumors are due to the development of hydrocephalic-hypertensive and dislocation syndromes. The development of hydrocephalus during tumor localization in the cerebellum is more common than with other localization and is caused by occlusion of the cerebrospinal fluid [3; 7; 8].

Neuroimaging methods such as computed tomography (CT) and especially magnetic resonance imaging (MRI), which appeared in the 1970 s. and 1980 s, made a major breakthrough in non-invasive studies of the localization and structure of brain tumors, the patterns of their growth and blood supply, relationship with the surrounding tissues, the dynamics of their development [2; 4].

Surgical tactics, if possible, consist in radical removal of the tumor with subsequent recovery of the liquor outflow. With the help of liquor shunting operations, although it is possible to achieve control over hydrocephalus, however, after these operations, in 70–95% of cases the condition of the patients becomes drainage-dependent and in 1/3 of the patients the development of one or another complication is observed [5; 6].

Studying the results of applying various therapeutic and diagnostic approaches to well-verified clinical material helps determine the effectiveness of existing methods of diagnosis and treatment of cerebellar tumors.

Purpose of the study. The aim of our study was to study the diagnosis and treatment of cerebellar tumors.

Materials and research methods. This study includes data from a comprehensive examination and treatment of 35 (21 women, 14 men) patients. The average age of patients was 30 years (from 3 to 69 years) who were in inpatient treatment in the neurosurgery department of the clinic of Samarkand Medical Institute for cerebellar tumors from 2012 to 2014. All patients underwent a comprehensive examination, including brain CT, (MRI) and contrasted CT and MRI.

The results of the study and their discussion. For the diagnosis of cerebellar tumors, MRI was performed to all 35 (100.0%) patients, CT to 8 (22.8%) patients and contrast imaging of the brain to 9(25.7%) patients. CT and MRI, depending on the structure of the tumor itself, in 14(40.0%) was cystic, in 5(14.3%) solid, in 6(17.1%) cystic-solid and in 10 (28.6%) infiltrative (figure 1).

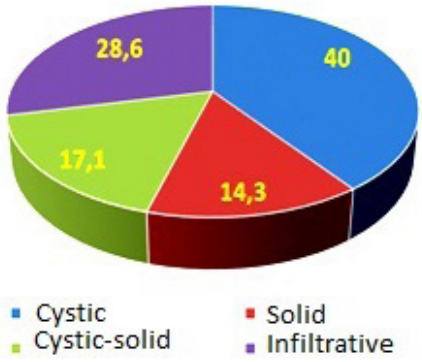

Figure 1. CT and MRI depending on tumor structure

According to localization, in 13(37.0%) it was localized in hemispheres, in 10(28.5%) patients in the cerebellar worm, in 8(22.8%) patients in the cerebral-cerebellar angle, in 4(11.4%) patient in the IV-th ventricle (Figure 2).

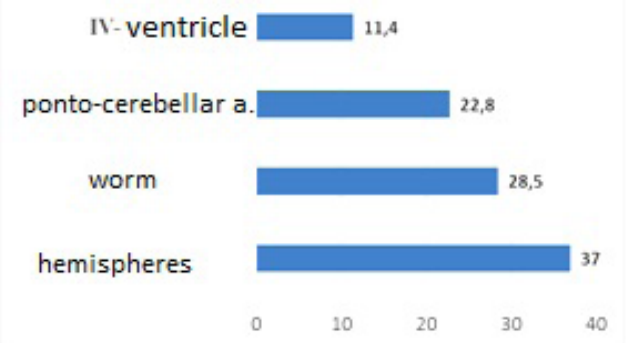

Figure 2. Tumor localization

All patients underwent surgical treatment, the essence of which was as much as possible in the radical removal of the tumor, depending on the operability of the tumor itself, followed by recovery of the liquor outflow.

Depending on the location of the tumor, we used the following prompt access: in 22(62.8%) patients, a midline skin incision and resection of the occipital bone scales, in 13(37.2%) patients, a paramedian skin incision on the left or right, and a resection of the occipital bone on the left, of these, 5 patients (14.3%) had Torkildsen ventriculocystomy surgery in order to normalize liquorodynamics.

Histological examination of these tumors most frequently revealed medulloblastomas (42.9%), followed by astrocytomas (37.1%) and ependymomas in (20.0%) (Figure 3).

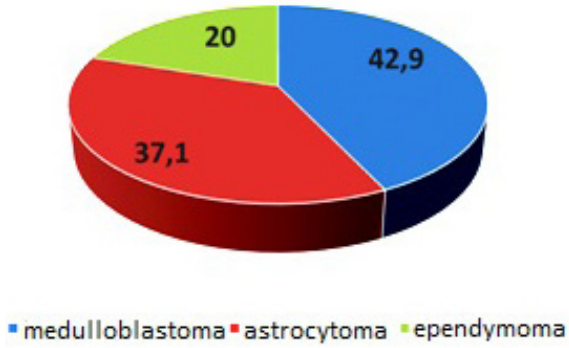

Figure 3. Histological structure of cerebellar tumors

It should be noted that out of 35 operated patients, total tumor removal was achieved in 26(74.3%), subtotal removal in 7(20.0%) and biopsy in 2(5.7%) patients.

Postoperative mortality was observed in 6(17.1%) patients, and it dominated after subtotal removal of the tumor (11,4%), and in patients after total removal of the tumor and biopsy, only one case was fatal.

Conclusions:

1. The main methods in the diagnosis of cerebellar tumors are MRI and CT methods, which allow to determine the structure, morphological features, the presence of infiltration, cysts and edema with their qualitative and quantitative assessment.

2. Among cerebellar tumors, cystic (40.0%), solid and infiltrative (by 28.6%), relatively less cystic-solid (17.1%) tumors are more often detected. These tumors are predominantly located in the hemispheres (37.0%) of the worm (28.5%), then in the ponto-cerebellar angle (22.8%) and the IVth ventricle (11.4%).

3. According to the histological structure, medulloblastomas prevail among cerebellar tumors (42.9%), followed by astrocytomas (37.1%) and ependymomas (20.0%). The results of treatment of cerebellar tumors depend on the use of modern surgical methods and their radicalism.

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TO THE QUESTION OF CLASSIFICATION AND PREVENTION YATROGENIC DAMAGE TO VESSELS

Abstract: Develop a classification of iatrogenic damage to blood vessels and their consequences.

Keywords: Uniform classification of iatrogenic damage and its consequences, qualitative and quantitative characteristics of all their variants.

So far, in domestic and foreign literature, studies of iatrogenic vascular pathology are rather few. In this regard, the intensification of research to create a unified classification and the development of adequate preventive measures to reduce the level of iatrogenic vascular damage.

It should be noted that the choice of surgery depends on: the prevalence of the pathological process; localization of associated lesions of surrounding tissues and others. At the same time, the choice of tactics of surgical treatment has always been active and independent of the time of the occurrence of iatrogenic injury and aneurysm.

Therefore, a waiting position in their treatment is fraught with serious complications, in the form of: thrombosis; rupture of aneurysms, etc.

Our experience in studying this issue was the basis for developing a classification of iatrogenic vascular damage.

This classification includes the following provisions:

– patients with partial disability after correcting iatrogenic vascular damage, temporarily;

– patients with complete disability due to iatrogenic damage, due to complications such as: ischemic contracture; trophic ulcers; gangrene and amputation of extremities and organ extirpations. At the same time, the types, forms and nature of the means used were taken into account.

Most often, iatrogenic vascular damage occurs during angiographic studies, somewhat less frequently during angiosurgical and general surgical operations. At the same time, an insignificant percentage in the total amount is: obstetric-gynecological and neurosurgical interventions.

However, about half of the vascular damage occurs due to angiographic and angiosurgical interventions: puncture; catheterization; the Ilizarov apparatus; hernia repair; removal of veins; reposition of bone fragments and insertion of the needles became their cause. These factors, naturally, contributed to an increase in the proportion of interoperative vascular iatrogeny.

Our experience shows that the nature of damage to stabbed and cut wounds of vessels of iatrogenic etiology are common.

Thus, the analysis of iatrogenic damage to the vessels by the anatomical location made it possible to establish the frequent wounding of the vessels in the thigh area. The vessels in the pelvic area and retroperitoneal space were significantly less frequently damaged. The causes of these complications were: lack of knowledge on syntopy of the elements of the neurovascular bundle and the error of surgical tactics on the use of tools for surgical interventions on vessels. At the same time, the following clinical signs are observed: bleeding with and without shock; hematomas of various shapes; thrombosis with complete occlusion of vessels and vascular stenosis with chronic hemodynamic insufficiency.

At the same time, on the vessels there are: false aneurysms; fistula and their displaced forms.

It should be noted that the prevalence of thrombosis and hematomas in the clinical picture of iatrogenic vascular damage is mainly due to errors in angiographic studies.

When examining patients with iatrogenic aneurysms, it is not always possible to distinguish the outcome from other vascular lesions. At the same time, local swelling is visible in the area of the damaged limb vessel. In addition, depending on the duration of iatrogenic aneurysms, they can be formed or unformed.

Long-existing aneurysms, especially for large sizes, are clearly visible upon inspection. The skin above the swelling is usually of a normal color, but redness, infiltration or thinning of the skin is sometimes noted. Large, tense aneurysms sometimes cause necrotic changes in the skin.

An indispensable method for examining a patient is palpation. This method revealed a large percentage of patients with aneurysms. The consistency of the aneurysm was tightly elastic or tight. At the same time, an important role is played by thrombosis or calcification. Aneurysm size ranges from 0.5 to 10 cm in diameter. They are round or oval. Pulsation is absent or weak; this is due to the following reasons: fatigue, wall calcification or thrombosis of its cavity. The pulsation of the aneurysm, as a rule, catches systolic tremor over swelling.

The method of auscultation is one of the key in the diagnosis of iatrogenic aneurysms. At the same time, systolic murmur is often heard. Thrombosis of the aneurysmal sac with varying degrees, muffled the systolic murmur until its cessation.

Based on the above, we established the clinical symptoms of diagnosing the formation of vascular aneurysm:

– pain in the aneurysm, in the form of pulsating tumor-like formations in the initial stage. At the same time, the symptoms are observed by: arising compression; ischemia; imbibition surrounding soft tissue and nerve trunks. Along with them, complaints associated with ischemic events were noted with the localization of iatrogenic aneurysm on the extremities. These complaints include: fatigue; intermittent claudication; general weakness, hypersensitivity to cold factors, convulsive phenomena, mainly in the calf muscles.

– ischemic nature, usually appearing at the initial stage as: angiospasm; stenosis and occlusion of the main artery. Pain associated with involvement in the pathological process of the nerve trunk in the form of: damage and compression, which are of varying intensity and shooting at the limb. And also, symptoms in the form of: paresis; paralysis; hoarseness voices, compression of the return vagus. At the same time, the large size of the aneurysm, often worries the patient. Cervical aneurysm according to Horner's symptom associated with damage to the sympathetic nerve trunk. In addition, pressure of the main vein and related disorders of the venous outflow, the distal limb, were observed.

At the same time, there were complaints about the feeling of fullness and strengthening of the venous pattern.

Therefore, a well-assembled history contributes to the correct diagnosis of iatrogenic vascular damage and optimization of the choice of treatment tactics.

As a typical example, we present the following medical history.

Patient H. B., 39 years old, (IB No. 3732) entered by gravity.

Complaints at admission: edema of the lower limb; heaviness and shortness of breath on exertion and general weakness.

The patient considers herself a patient since April 2017. On April 21, 2017, the planned operation "percutaneous microdiscectomy" was performed for hernia of the lumbar spine. During the operation at the stage of access to the spine, abundant bleeding from the working tools arose (before the discharge from the(RSCN). At this stage, the operation was stopped and the tools were removed. During the day, hemoglobin progressively began to fall. In this connection, 04.22.2017 with suspicion of internal bleeding, the patient was transferred to RSCEME, where diagnostic laparoscopy was performed. During the operation, a retroperitoneal hematoma was detected.

An outpatient patient was examined by MSCT of the abdominal aorta from 05.30.2017: signs of an arteriovenous fistula between the right common iliac artery and the right common iliac vein were found. With ultrasound of deep veins of the lower extremity: deep veins are passable; Valve apparatus wealthy. On both sides in the lower third of the leg is defined edema.

The general condition at admission is satisfactory, the consciousness is clear, the position is active. Sick plump. The skin is a normal color, except for local status. Musculoskeletal system without deformities. In the lungs vesicular breathing, no wheezing. Heart sounds are rhythmic, clear. HELL 120/90 mm. Hg Art. Heart rate 82 per minute The abdomen is soft, painless. Liver at the edge of the costal arch.

Symptom "tapping" negative. Physiological functions are not violated.

When viewed from the left lower limb is increased in volume compared to the right. Palpation of edema of the lower limb, painless. Pulsation at all identification points is determined. Noise over the main arteries there.

Examinations: hemoglobin-112g/l, leukocytes-5.9, platelets-240, tochevina-3.5 mmol/l., Creatinine-49 mmol/l, glucose-6.5 mmol/l. The remaining indicators in the normal range. ECG: sinus tachycardia, horizontal position E.O.S. HR-100ud\min. P-copy of organs gr. cells: Lung fields without fresh focal and infiltrative shadows. The heart lies broadly on the dome of the diaphragm, enlarged in diameter.

Aorta protrudes. EchoCG: KDO-139ml., EF-58%. Disturbance of local kinetics was not detected. Immunoenzyme an. blood: HBsAg and HCV neg. (–). Diagnosis: Iatrogenic arteriovenous fistula between the right common iliac artery and the vein on the right.

Patient, 06.27.2017, in a planned manner, performed a laparotomy operation. Produced audit of the retroperitoneal space. Under intubation anesthesia, complete midline laparotomy was performed. The intestine is removed in the wound, to the right. Access to the retroperitoneal space is made.

In the projection of the terminal part of the abdominal aorta and the continuation of the right iliac region (along the iliac vessels) there is a rough systolic jitter. A pronounced adhesions process and periprocess in the area of the terminal part of the abdominal aorta and the right iliac region were found. Inflamed and thinned walls of dilated and convoluted venous collaterals are noted, with contact with which bleeding is noted. All the above forms a pulsating conglomerate with systolic tremor. The right ureter is intimately soldered to the back of the conglomerate, which is impossible to mobilize and push back from the inflamed conglomerate.

Selected abdominal aorta below the renal arteries, outside the zone of inflammation. With a trial clamping of the abdominal aorta, systolic tremor disappears. Further, the attempt to extract the acute and blunt by the iliac arteries (OPA,

NPA and VPA) from the inflammatory conglomerate was not crowned with success. The pulsation on the iliac arteries on the right is very weak and practically can not be felt in the conglomerate. This is due to arteriovenous discharge of arterial blood into the venous system through OPV. Differentiate anatomical structures (abdominal aorta, inferior vena cava, iliac arteries and veins) in the scar and inflamed tissues with relatively "disturbed" anatomy was not technically possible. The progress of the operation and the intraoperative picture were reported by telephone to the director of the center, Academician F. G. Nazirov. Given the high risk of intraoperative bleeding and the technical impossibility of mobilizing anatomical structures, it is recommended that the operation be completed with a revision of the retroperitoneal space. Made a reorganization of the abdominal cavity. Hemostasis. A suture was made on the posterior leaflet of the parietal peritoneum, layer-by-layer suturing of the wounds of the anterior abdominal wall. Aseptic dressing.

In the postoperative period, the patient received antibacterial, anti-inflammatory therapy.

After surgery: hemoglobin-120 g, hematocrit-38%, ESR-6 mm, Urea-3.3 mmol, Creatinine-40 mmol, Glucose-6.1 mmol, PTI-88 mg%. In the postoperative period, wounds heal by primary intention. The patient is discharged for further observation by the surgeon and cardiologist at the place of residence.

Recommended: Endovascular interventions (installation of Endocraft).

In order to prevent iatrogenic vascular damage, it is necessary, when upgrading the qualifications of doctors, to pay great attention to the training of features and the main method of providing emergency care to such patients. In addition to the uniform classification of iatrogenic vascular damage, the frequency of damage to the following vessels should be taken into account:

1. Facial artery and vein. 2. Temporal artery and vein. 3. Posterior artery and vein 4. Common carotid artery. 5. The external carotid artery. 6. Vertebral artery. External jugular vein. 8. Internal jugular vein. 9. Subclavian artery and vein. Axillary artery and vein. Aorta. 12. Superior vena cava. 13. The pulmonary artery and vein. Intrathoracic artery and vein. Unpaired vein. Semi-unpaired vein. Celiac trunk. 18. Hepatic artery. 19. The common artery and vein. 20. External iliac artery and vein. 21. Internal iliac artery and vein. 22. Common femoral artery and vein. 23. Deep femoral artery and vein. 24. Superficial femoral artery and vein. 25. Popliteal artery and vein. 26. Anterior tibial artery. 27. The posterior tibial artery. 2. Taz.

Table 1.

I. Depending on the type of intervention:	II. Depending on the nature of the form of funds:	III. Depending on the date of occurrence:	IV. By anatomical location:	V. By the clinical picture:	VI. For complications in the vessels:	VII. By the nature of the damage:	YIII. Okhod:
Endovascular Angiographic. Angiosurgical. General surgical. Traumatic. Oncological. Obstetric- gynecological. Neurosurgical. Therapeutic. Oftolmalagicheskie. Otoloringological.	Puncture. Injection. Sounding. Catheterization. Plastic vessels. Autovenous shunting. Prosthetics. Ligation of vessels. Paravasal manipulations. Removal of vessels. Removal of the organ. Venesection. The overlay of the Ilizarov apparatus. The imposition of the needle and pin.	Acute (occurring at the time of medical intervention). Remote (arising after some time after medical intervention).	Head. The neck. Subclavian area. Anterior mediastinum. Posterior mediastinum. Abdominal cavity. Frontal space. Crotch. Leverage. Local area. Forearm. Brush. Inguinal area. Femoral triangle. Thigh. Shin area. Shin. Stop. Taz.	Bleeding with shock. Bleeding without shock condition. Hematomas of various forms. Thrombosis with complete occlusion of vessels. Stenosis of the vessel with chronic hemodynamic insufficiency	False aneurysms. Arteriovenous fistula. Pulsating hematomas Mixed clinical forms.	Stabbed. Cutted. Tom.	Remediation. Partial loss of ability to work. Complete disability. Death.

Methods for the treatment of iatrogenic vascular damage:

1. Side seam. 2. Circular seam. 3. Autogenous plastics. 4. Autovenous shunting. 5. Prosthetics. 6. Skeletization. 7. Thrombectomy. 8. Dressing. 9. Anti-aogul treatment. 10. Anti-shock therapy. 11. Disintegration of blood substitute. 12. The expansion of the fistula. 13. Elimination of aneurysm. 14. Amputation. 15. Detoxication therapy 16. Regional perfusion. 17. Hyperbaric oxygen therapy. 18. Providing specialized surgical care. 19. Rentgenendovascular complete occlusion of vessels.

Full recovery and temporary disability after successful correction of iatrogenic vascular damage, respectively, should be attributed to favorable and encouraging results.

Necessary measures to eliminate the occurrence of iatrogenic damage should be considered tamponade or finger pressing of the vessel, the maximum reduction in time to provide specialized assistance and timeliness of the latter. High efficacy of reconstructive surgery for iatrogenic aneurysm and fistulas using endovascular complete occlusion of the vessels. At the same time, we often applied it to remote locations of iatrogenic aneurysms and fistulas.

To date, there is no consensus on iatrogenic vascular injuries and there is no uniform classification. Given the urgency of this problem, we attempted to develop this group of vascular damage. The classification is based on a number of clinical, etiological, anatomical and topographical criteria. Our proposed classification of iatrogenic vascular damage is based on a thorough study of domestic and foreign data on this issue, as well as our many years of observation of patients with traumatic vascular damage.

It must be emphasized that the development of a unified classification of iatrogenic vascular damage is a pressing issue. At the same time, clinical symptoms and outcome have their own characteristics. Depending on various criteria, we have proposed the following classification:

Creating a single form of documentation for classification, treatment and prevention measures is, in our opinion, a priority task that requires urgent solutions.

Findings

1. A single classification of iatrogenic vascular damage should contain the main qualitative and quantitative characteristics in all their variants.

2. The main causes of vascular damage are insufficient knowledge of the topography of tissues in the operated area, errors in the operative technique and the use of general surgical instruments during vessel manipulation.

3. Early diagnosis and qualified assistance is the main direction in reducing the level of complications caused by various interventions on the vessels.

4. Conducting thematic seminars with: students of the institutes of advanced training of doctors, senior students of medical universities in anatomy and emergency vascular surgery, which is an effective measure for the prevention of iatrogenic vascular damage.

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OPTIMIZATION OF THE DIAGNOSIS AND SURGICAL TECHNIQUE OF THE TRAUMATIC ARTERIOVENOUS FISTULA

Abstract: The purpose of the study is to optimize the diagnosis and surgical treatment of traumatic arteriovenous fistula.

Keywords: optimization, diagnostics, surgical tactics, treatment, arteriovenous fistula, fulfillment logic.

Introduction

Surgical treatment of traumatic arteriovenous fistula (TAVS) is one of the topical problems of modern angiology [1; 2; 3]. Until recently, vascular injury was considered the prerogative of wartime. However, the events of recent decades have shown an increase in vascular damage in peacetime, which can be up to 2% in the overall structure of injuries [1; 4].

Despite this, at present, the frequency of post-traumatic aneurysms and fistulas reaches 15–28% among all vascular injuries [5]. In medical practice, for endovascular interventions for injuries, aneurysms and arteriovenous fistulas, intravascular stents are increasingly being used [6]. In place of the arteriovenous anastomosis, a traumatic rupture of artery with fistula formation is observed. Fistula and large venous aneurysms are completely blocked by transvenous embolization. At the same time, the patency of the posterior connecting artery is preserved [7].

Open intervention is the method of choice in the treatment of arteriovenous fistula. X-ray endovascular method can be an alternative to surgical [8].

In 9 patients, a stent was applied with a coating about the aneurysm of the subclavian artery and arteriovenous fistula, in 2 patients in the postoperative period thrombosis occurred [9]. It must be emphasized that TAVS manifests itself in various clinical symptoms and may be difficult to detect. Thus, the authors report rare observations of non-pathogenic arteriovenous fistulas in the pelvic region, which were detected according to angiography 14 and 20 years after the injury. Therefore, the use of angiography makes it possible to better diagnose TAVS [10]. However, rentgenendovascular interventions for TAVS are rarely performed [11].

In this connection, a traumatic arteriovenous fistula is an indication for surgery early treatment after injury. Due to anatomical features and severe concomitant diseases, open surgery in patients with arteriovenous fistulae, as a rule, are accompanied by great technical difficulties, therefore rentgen-endovascular interventions are promising, since among them there aretive moments – low invasiveness, low incidence of postoperative complications and a short postoperative rehabilitation period [4; 12; 13; 14]. Tsigankov V. N. et al. [15] emphasize that the anatomical features of open interventions on the subclavian arteries, especially in the first segment, are associated with largemi difficulties. In recent years, with the introduction of modern technologies in the treatment of TAVS, endovascular interventions are widely used. Therefore, endovascular intervention for the treatment of this localization of TAVS is the most promising treatment method. The purpose of this study was to optimize the diagnosis and surgical treatment of traumatic arteriovenous fistula.

Material and methods. In order to effectively address this issue, we carried out certain studies. So, in the clinic under the supervision there were 30 patients with TAVS, to study the question of its correct diagnosis and the choice of the optimal tactics of surgical treatment. In this case, first of all analyzed the causes of TAVS. For reasons of occurrence, TAVS patients are distributed as follows (tab.1). As can be seen from table 1, mainly in 13 (43.3%) patients, the causes of TAVS are the piercing and cutting means.

Along with the reasons, we studied patients by sex and age. Information on the distribution by sex and age composition of patients with TAVS are presented in (table 1).

Table № 1.– The distribution of patients by causes of traumatic arteriovenous fistula (TAVS)

№	Causes of TAVS Number of patients	Total:	
		abs	%
1	*2*	*3*	*4*
1.	Piercing and cutting tools	13	43.3

1	*2*	*3*	*4*
2.	Gunshot wounds (bullet, shot)	2	6.6
3.	Car accidents	2	6.6
4.	Other	12	40.0
5.	Total:	30	100.0

Along with the reasons, we studied patients by sex and age. Information on the distribution by sex and age composition of patients with TAVS are presented in

Table 2.– The distribution of patients with traumatic arteriovenous fistula by sex and age

№	Age	Number of patients		Of them	
		abs	%	Men	Women
1.	up to 20 years	8	26.6	6	2
2.	21–30 years	10	33.3	10	–
3.	31–40 years	3	10.0	3	–
4.	41–50 years	4	13.3	4	–
5.	50 years and over	5	16.6	4	1
6.	Total:	30	100.0	27(90%)	3(10%)

As the analysis of the data in (Table 2) shows, a large percentage of patients with TAVS are observed in male-27 (90%) and 63% fall on the most able-bodied age from 20 to 49 years. In addition, we analyzed data from patients with TAVS on the location and lesions of peacetime arteries. Surgical access to the TAVS provides a good approach to the fistula, that is, quite wide, given the restoration of the subsequent motor function of the operated limb. The incision of the skin and subcutaneous tissue on the limbs was made rectilinearly along the projection of large vessels, less often at an angle. In 3 patients, high technologies were used in the operation.

Figure 1. Place the puncture-cut wound in the thigh area, on the left

At the same time, endovascular full balloon occlusion of arterial vessels was performed. There were a balloon catheter with dimensions 6 × 60 mm, a balloon catheter with extension to complete occlusion for vascular patency. At the same time, the pressure in the cylinder to 9 atm. at RBP 10 atm. Contrast Unigexol-350–100 ml. According to the statement from 09/07/2016. On September 18, 2016, the patient was in the vascular department of the RSSC and was operated on in a planned manner 09.09.2015g. Carried out the elimination of the false aneurysm of the su-

perficial femoral vein, on the left. In addition, an arteriovenous fistula between the superficial femoral vein and artery has been separated. An autovenous patch was performed on the superficial femoral vein and resection of the superficial femoral artery. The femoral – popliteal autovenous shunting is performed on the left (Fig. 2–4). The patient was discharged in a relatively satisfactory condition. In the last 6 months, the patient notes the above complaints. In the last 6 months, the patient notes the above complaints. When reentering the vascular department of the RSCH, the patient's condition was relatively satisfactory. Consciousness is clear. Normal physique and moderate fatness. The skin and visible mucous membranes are clean, normal color. In the lungs, vesicular breathing on both sides, no wheezing. Heart sounds are muffled, rhythmic. HELL 110/70 mm RT. Art., pulse 84 beats/min. The belly of the usual form, is involved in the act of breathing. Palpation is soft, painless. The liver and spleen are not palpable. Pokolachivanie lumbar region painless, on both sides. Physiological functions are not affected. When viewed from the left thigh, it is set to increase in volume, relative to the right. The pulsation on the right n/a and arteries of the foot clear. On the left n/a pulse on the inguinal fold, distal is not defined. There are old postoperative scars on both thighs, with no signs of inflammation (on the right there is an autovene fence, a fragment of the GSV trunk) (Fig. 1). Systolic tremor is determined on the medial surface of c / s of the left thigh. On the remaining identification points, the ripple is determined. Over the projection of the main arteries, there is no noise.

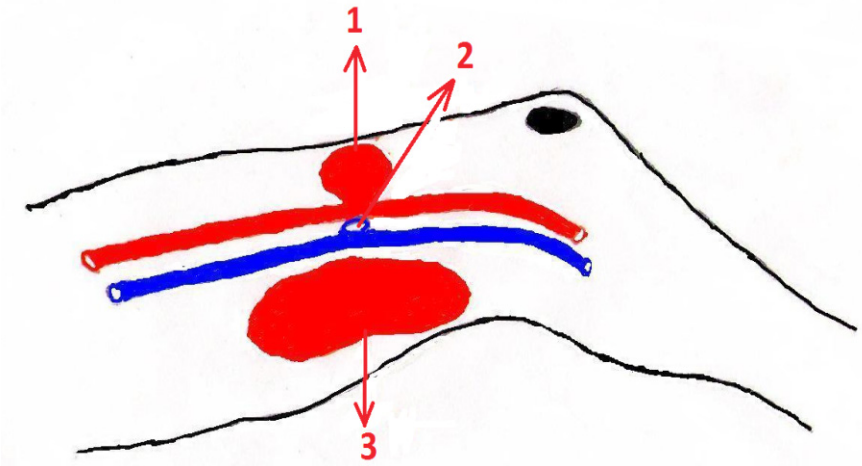

Figure 2. Scheme TAVS superficial femoral artery and vein, left.
1 – aneurysm; 2 – AVS; 3 – extensive hematoma

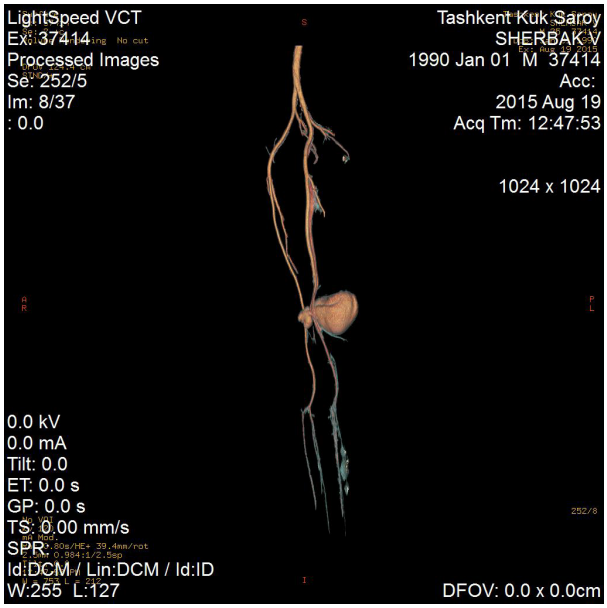

Figure 3. MSCT: Post-traumatic aneurysm and arteriovenous fistula between the superficial femoral arteryan dvein, left

Laboratory examination of the patient: OAK – Hb 162 g/l, Erythrocytes – 5.5 × 1012 /l., Leukocytes 4.9 × 10 9 /l. Biochemical blood test: sugar 6.1 mmol/l, creatinine – 82 μmol/l, urea – 4.7 mmol/l, sodium 145 mmol/l, potassium 5.0 mmol/l, total protein 78 g/l, AST 23 μmol/l, ALT 14 μmol/l, total bilirubin 43 μmol/l; Coagulogram: PTI-100%, Fibrinogen-2660 mg%, thrombotest V, hematocrit-53%; OAM: rel. density 1030, protein -avs, glucose – avs, ep units in the field of view, Leukocytes units in the field of view, Erythrocytes unchanged 0–0–1; ECG: sinus rhythm, heart rate 66–68 f/min. Vertical position E.O.S; Chest x-ray, without features; EchoCG: CVD-170 ml, KSO-77 ml, PP-93 ml, PVF-55%. Valve system, intact. USDG n / a: LSBD right-1.0, left – 0.5. Ultrasound of the liver: the liver is not enlarged, fine-grained. IAP is not expanded. Choledoch 0.4 cm, Vienna Porte 1.0 cm. The patient was made MSCT (22.11.2016.) – occlusion of the prosthetic Department of the PBA, on the left. Next, a contrast agent is injected into the popliteal artery at the level of the crack in the knee joint. From the middle third of the thigh at the level of the onset of occlusion, the venous phase is contrasted and an enlarged femoral vein is observed (Fig. 5).

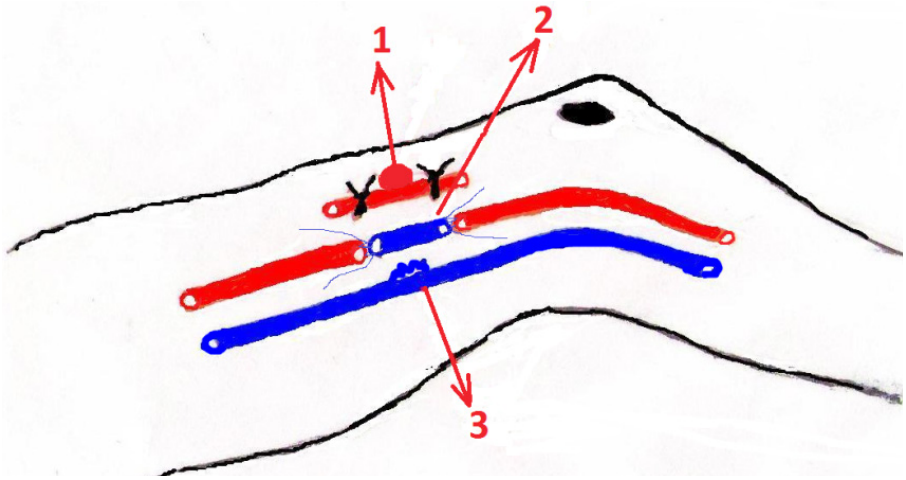

Figure 4. The scheme of imposing an autovenous patch on the femoral vein and autovenous shunting on the superficial femoral artery. 1 – resection of the aneurysm; 2 – autovenous shunting; 3 – patch the femoral vein

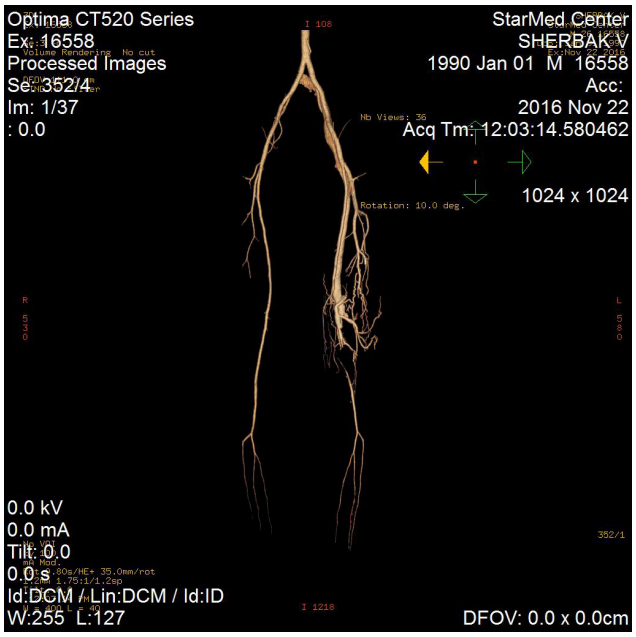

Figure 5. Postoperative recurrence of TAVS superficial femoral artery and vein, left. 5 patients with TAVS showed signs of venous insufficiency. It is a clearing of the skin of the saphenous veins. 3 patients had a pulsation in this area. During auscultation of the TAVS area, systolic murmur was heard in 5 patients, diastole – systolic murmur and tremor in 28 patients (90.3%). Thus, it was 11; till 2 o'clock – 11; from 3–6,5 hours and more to 8 patients. Important diagnostic methods for TAVS are: radiological; Ultrasound 11; USDG-6; angiography-15; MSCT-10; duplex research-1

At 12.12.2016 the patient underwent selective arteriography with access through the right femoral artery, selective contrast enhancement of PBA and HAB was performed. When contrasting PBA with c/s of the thigh, blood is discharged through small branches into the femoral vein. Also, with selective contrasting of the arterial trunk, blood is discharged into the femoral vein through the small arteries into the HAB system. Given the presence of AV fistulae, in the PBA system, and the HAB system, it is not advisable to embolize the AV fistula from the HAB system. The cause of recurrence is the discharge of blood into the femoral vein, remaining in the small invisible arteries of the HAB.After consultation, the patient was discharged home.

5 patients with TAVS showed signs of venous insufficiency. It is a clearing of the skin of the saphenous veins. 3 patients had a pulsation in this area. During auscultation of the TAVS area, systolic murmur was heard in 5 patients, diastole – systolic murmur and tremor in 28 patients (90.3%). Thus, it was 11; till 2 o'clock – 11; from 3–6,5 hours and more to 8 patients. Important diagnostic methods for TAVS are: radiological; Ultrasound 11; USDG-6; angiography-15; MSCT-10; duplex research-1; Echocardiography-1.

Results

Currently, reconstructive – reconstructive operations on vessels are widely introduced, and doping of TAVS is carried out quite rarely. If necessary, use angiography. It should be noted that the epicenter of the tremor is usually a fistula projection. Among the indications for doping TAVS, its caliber is sufficient (no more than 1 cm). For imposing on the TAVS double ligature, extremely close to the artery and vein, its length is not less than 2 cm. In 2 cases, the fistula is dissected between two ligatures. Excision or also called TAVS dissection, we performed in 16 patients with recent and old cases. According to localization (arteries), these operations were distributed as follows: 3-carotid, 1-iliac, 3-hip, 3-calves, etc. We had a double indication for this method: first, when the fistula was located between non-trunk or paired vessels; secondly, when it was difficult to suture it was necessary to legitimize the TAVS. Depending on the relevant circumstances, we performed the reconstructive surgery using traditional methods (lateral, circular, autoural, prosthetic). Based on the above, and taking into account the relevant circumstances, we performed a side seam – 5 patients with TAVS; by location: 2-femoral, 2-popliteal, 1-aortic arch, and anonymous vein. In 2 cases, the fistula walls were calcined. If the artery defect in the operation was half or more than the diameter of the artery, then the side seam was not used, since this could lead to a narrowing of the artery lumen. In such cases, a circular suture or autovenous shunting was used. In all cases, after completion of the lateral suture operation, the pulsation of the distal artery was clearly determined. The circular suture on the arteries in TAVS was applied in 5 cases, including femoral-4, popliteal-1. After surgery, the distal pulse was determined well. When TAVS with "experience" of more than 20 years (in 3 cases), atherosclerotic plaques stenotic distal part of the artery.

In cases where it was impossible to impose a ligature on the fistula with the TAVS, a plastic-restorative surgery was used for the lateral or circular suture. In 3 cases, the graft was a 3-autovent and 1-synthetic prosthesis. In 4 cases when the artery defect was significant, we used a transplant patch (3-autovenous and 1-synthetic). In 2 cases, transplantation was necessary for TAVS with great experience.

Discussion

In our study, of all 30 operated patients with TAVS, the patency of the main veins was restored in 4 cases. Including ligature imposed on fistula-16; lateral suture – 5; circular suture – 5 and 4 cases, when the artery defect was significant, we applied a transplant patch (3-autovenous and 1-synthetic) to the patients. Surgical intervention for venous aneurysms in TAVS was determined individually by us after mobilization of the adductors and abducers and dissection of the arteriovenous fistula. After the removal of TAVSA (approximately 2–3 years), the need for surgical intervention arose, continued to exist if there was venous insufficiency. Of these, 3 patients used high-endovascular temporary full occlusion of vessels (EEAS) during the operation.

Table 3.– Type and nature of reconstructive restorative operations for traumatic arteriovenous fistula

№	Type of operation	Number of patients Type of surgery%	
		abs	%
1	Doping fistula	16	53.3
2	Side seam	5	16.6
3	Circular stitch	5	16.6
4	Automated Shunting	3	10.0
5	Prosthetics	1	3.3
6	**Total:**	30	100.0

As a result of medical interventions, the blood flow of the operated limb of patients significantly improved. According to the subjective sensations in patients, the discomfort disappeared, many of whom experienced him for several years, constantly. The pulse on the foot was clear, pink, the color of the skin on the leg after the operation sharply decreased, this was due to the phenomenon of venous insufficiency on the limb. We have established signs of vascular lesion in patients with TAVS: venous drawing-1; tense dilated veins-6; swelling of limbs-3; trophic ulcers-2: after surgery-1. There were no forced amputations and deceased patients. In 27(90%) patients, the wound healing was primary, in 3(10%) by secondary intention. Thrombosis was noted in 1 case. The performed thrombectomy restored blood flow, with a distinct distal pulsation. In 11 patients before the operation there were complaints of pain in the region of the heart, feeling of interruptions. After the operation, when interviewing them, they noted the joyful feeling that "now they are not cores", i.e. the disappearance of negative sensations in the heart. In 9 patients, the pulse became rhythmic, its frequency returned to normal. In the first days after surgery, the pulse was increased and the temperature was elevated, in 5 patients, after 10–20 days they returned to normal. If rapid breathing was observed in 7 patients with TAVS, then after elimination of the fistula, only in 2. In addition, we studied the long-term results of treatment of TAVS, by types of operations. They are presented in (table 4).

Table 4.– Long-term results of treatment of traumatic arteriovenous fistula

№	Type of operation	Total	Results of treatment			Observation period		
			good	Satisfied full body	uncomfortable	1–3 year	4–5 year	6 years or more
1	Ligature	6	4	1	1	1	1	4
2	Side seam	2	2			1		1
3	Circular stitch	1	1					1
4	Autovena	1		1		1		
5	Prosthesis							
6	**Total:**	10	7	2	1	3	1	6

Long-term results were obtained after reconstructive-restorative operations in 10 patients. Among those operated on for TAVS, 70% had good results; satisfactory in 20%; unsatisfactory at 10%. In this case, a carefully collected history allows us to establish the presence of TAVS. In this case, for an objective assessment and treatment of TAVS, we developed a therapeutic and diagnostic algorithm for TAVS. Algorithmic language is a textual description of the algorithm, but this is not yet a programming language. For our description of the most appropriate method is a flowchart based on the integration of commands. The examination includes: history, complaints, external examination; – palpation – in the presence or absence of a dense, soft, painful, painless education; size of education; – auscultation – in the presence of the absence of systolic or systodioastolic noise on the projection of the aneurysm; If a pulsating hematoma is suspected in the presence of a dense, painful formation with systolic or systolic and diastolic noise above it, hemodynamic indicators are evaluated (decrease or increase in blood pressure, heart rate, pulse rate, etc.). With a long history of TAVS, hemodynamic instability is "significant" hypertension or hypotension, with or without tachycardia and tachycardia and with a decrease in hemoglobin. At the same time, it is necessary to take into account the clinical signs: pallor of the skin, a decrease or increase in the pulse rate on the radial artery. With fresh TAVS, hemodynamic stability – "insignificant" signs are recorded at normal blood pressure, heart rate, and pulse of the radial artery. With a high risk of cardiovascular diseases, ECG changes occur – dystrophic changes in the myocardium, severe LV with systolic or systolodiastolic overload.

Findings

1. When TAVS squeezed veins, leading to venous stasis. Therefore, it is necessary to take them into account in the differentiated diagnosis of venous thrombosis with their different localization.

2. MCT – angiography is the most optimal non-invasive method for diagnosing TAVS, as well as assessing the status of outflow and blood flow pathways.

3. For the category of patients with TAVS, the tactics of surgical treatment are implemented in stages: 1st stage – endovascular temporary total occlusion of vessels; 2nd – the stage of the choice of operational access; 3-stage-dissociation of arteriovenous fistula and 4-stage surgical reconstruction of blood vessels.

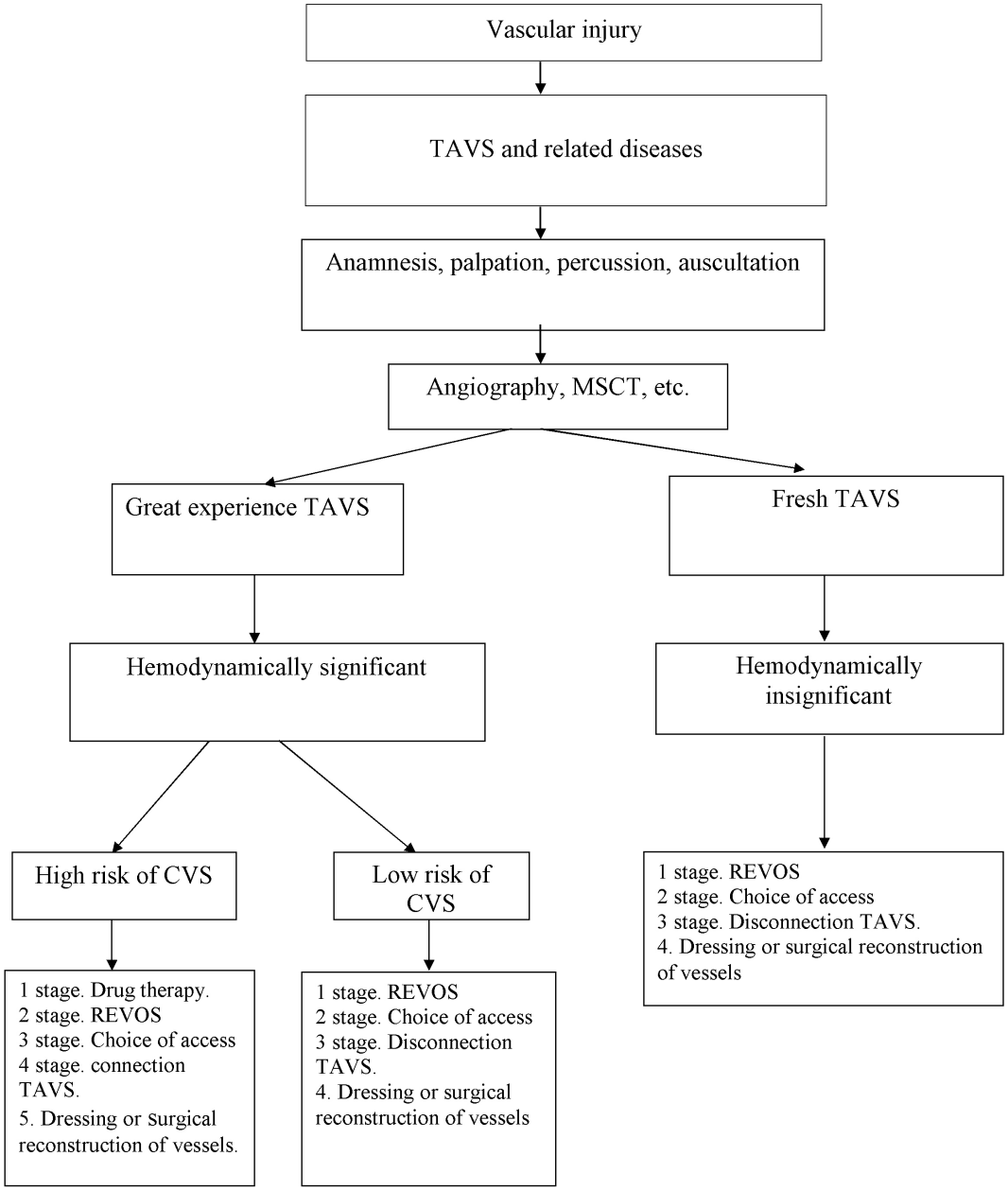

Figure 6. Algorithm for diagnosis and treatment of traumatic arteriovenous fistula (TAVS)

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ALGORITHMIC APPROACH TO THE SELECTION OF SURGICAL TREATMENT OF TRAUMATIC ARTERIAL ANEURYSMS

Abstract: To study the surgical treatment of traumatic arterial aneurysms.

Material and methods. In the hospital we have studied 69 patients due to traumatic arterial aneurysms (TAA). Of them males were 55 (80.3%), females – 14 (20.5%). At present time ligation of TTA is performed rather seldom. The various types of reconstructive-restorative surgeries on the vessels have been widely introduced now. For early diagnosis of traumatic arterial aneurysms, dopplerography, ultrasound, angiography and MSCT are used along with clinical examinations.

Results: The lateral suture was applied 6(9.3%) with TAA in the following localization: brachial artery – 2(3.1%); femoral – 3(4.6%); ulnar-1(1.5%). If the artery defect is half its diameter or more, then the lateral suture is not used, since this can lead to narrowing of the lumen of the arteries. In such cases, a circular suture or plastic is used.

The circular suture was used in 15(23.4%) patients, of which: radiation –2(3.1%); subclavian – 2(3.1%); femoral – 5(7.8%) vessels. In cases where it was impossible to impose a ligature at TAA, the lateral seam or circular seam had to be resorted to plastic surgery. So, in: 14(21.8%) – autovenous shunting was performed; 7(10.9%) used synthetic prosthetics.

Conclusion: In the immediate postoperative period, 64 patients were examined. Of these, 57(89%) were good; 7(10.9%).–Satisfactory results. In 48: (75%) patients, wound healing was primary, 7(10.9%) healing occurred by secondary intention.

For 8 (12.5%) patients, high-endovascular temporary full occlusion of the vessels was used in the operation.

Keywords: diagnostic algorithm, traumatic aneurism, surgical treatment.

Introduction

Surgical treatment of traumatic arterial aneurysm is an urgent problem of vascular surgery [1; 3; 5; 6; 7; 11; 12; 14; 15].

Surgical treatment of vascular injuries and their consequences has a 2000-year history. Despite this, some issues remain insufficiently resolved and require their further development [7]. Until the beginning of the 20th century, surgical interventions for traumatic vascular injuries and their consequences were mainly palliative [6]. Damage to the main arteries is a serious injury, due to the high frequency of local and general complications found in 15.4–48.4% of cases. The trauma of the subclavian artery is a rather rare form and is about 2% [16]. When there are punctured, stabbed wounds with a narrow wound canal, closed blood clots and injuries to the subclavian artery, they can lead to traumatic aneurysms or traumatic arteriovenous fistulas. The frequency of occurrence of peripheral aneurysms ranges from 3.4 to 6.7% [4; 9]. Despite the relative rarity of peripheral aneurysms, which is a formidable pathology, it represents a real threat of loss of the limb and even the life of the patient [2]. Diagnosis of this disease is recognized by ultrasound duplex scanning, since using this method not only aneurysm is visualized, the presence or absence of blood clots, as well as the ability to assess the inflow and outflow of blood vessels [13]. The algorithm has been developed for false aneurysms of the femoral arteries (LABA), which allows to increase the effectiveness of interventions [10].

At the same time, vessel ligation was the main method used to stop bleeding and save the life of the victim, while causing a large percentage of amputations [15].

Materials and methods

In the clinic, under our supervision there were 69 patients for traumatic arterial aneurysms (TAA). The causes of aneurysm were as follows: stab wounds of blood vessels – 16 (23.5%); gunshot wounds of blood vessels with shot and bullet – 2(2.9%); blunt vascular injuries – 14 (20.5%); injuries of World War II-1 (1.4%) and others-37(54.4%). Among them: men-55 (80.3%), women-14(20.5%). At the same time, we analyzed patients with TAA by age and sex. Table 1 shows the results of the analysis of patients with TAA by age and sex.

Table 1. – The distribution of patients by sex and age

The age of patients	Including		Quantutiy of patients
	Men	Women	
Till 15 years	11	3	14(20.2%)
16–20 years	5	–	5(7.3%)
21–30 years	12	4	16(23.1%)
31–40 years	9	5	14(20.2%)
41–50 years	5	2	7(10.1%)
51 years or more	13	–	13(18.8%)
Total:	55(79.7%)	14(20.2%)	69(100%)

As can be seen from table number 1, in most cases, TAA were observed in male patients of active working age from 15 to 40 years. In addition, we analyzed patients with TAA for damage to the arteries and their localization in different parts of the body.

Table 2 shows the distribution of patients with TAA, depending on the lesion of the arteries and their localizations, in different parts of the body.

The most frequent localization of aneurysms is observed in: the femoral artery – 21(30.4%); radial artery-7(10.1%); subclavian artery – 6(24.2%); popliteal artery – 3(4.3%); brachial artery – 9(13%).It should be noted that during the initial examination, in 69 patients with traumatic arterial aneurysms, the following clinical signs were noted: pain and tumor-like lesions-48(69.5%); thinning, redness, limb infiltration – 3(4.3%); swelling of the distal extremities – 8(11.5%); movement restriction-7(10.1%); – numbness-5(7.2%). TAA has a round or oval shape, with sizes ranging from 1.5 to 25 cm. At the same time, swelling and pulsation of the vessels in 35(50.7%) patients are noted. During auscultation of aneurysms, in 37(53.6%) patients, systolic murmur was monitored. In addition, there were neurological symptoms, transient in 6(8.6%) patients; ischemic events – 4(5.7%). At the same time, in 41 patients (59.4%) the blood pressure of TAA was normal; 28(40.5%) patients increased.

For the early diagnosis of traumatic arterial aneurysms, along with clinical examinations, dopplerography, ultrasound, MSCT and angiography were used.

Results and discussion

In the clinical setting, 69 patients were under our supervision. Of these, 64(92.7%) patients underwent reconstructive-restorative interventions; 13(20.3%) – operations on an emergency basis, due to suppuration and rupture of the aneurysm. Operations were performed in 16(25%) patients 1–2 days after their receipt.

After 5 months of injury and the occurrence of TAA, 45(70.3%) patients underwent surgery with favorable results. In addition, 5(7.8%) patients were operated on a year after the injury. The nature of surgical interventions is described in (Table 3).

Table 3. – Types of surgical interventions

Localization TAA	Ligature	Side seam	Circular seam	Autove–nous	Prosthetics	%
1	*2*	*3*	*4*	*5*	*6*	*7*
Common sleepy	1	–	–	–	–	1(1.5%)
Axillary	1	1	1	1	–	4(6.2%)
Tibial	5	–	–		–	(7.8%)
Subclavian	1	–	2	2	1	6(9.3%)
Shoulder	–	2	3	1	1	7(10.9%)
Radiation	5	–	2	–	–	7(10.9%)
Elbow	–	1	–	–	–	1(1.5%)
Zaushnaya	1	–	–	–	–	1(1.5%)
Femoral	3	2	5	8	3	21(32.8%)
Popliteal	–	–	1	2	–	3(4.6%)
Left facial artery	1	–	–	–	–	1(1.5%)
Abdominal aorta					2	2(3.1%)
The jugular vein			1			1(1.5%)
Superior thyroid artery	1					1(1.5%)

1	*2*	*3*	*4*	*5*	*6*	*7*
Ileal vein	1					1(1.5%)
Total:						
Всего:	21	6	15	14	7	64(100%)

In (table No. 3), various types of reconstructive-restorative operations are presented: the imposition of a ligature – 21(32.8%); lateral suture –6(9.3%); circular suture – 15(23.4%); autovenous shunting – 14(21.8%); vascular prosthetics – 7(10.9%) patients. In support of the above, consider the case history of one patient with TAA.

Under local anesthesia to the femoral arteries on both sides, introducer shears 6F are installed. At the same time, endovascular temporary full balloon occlusion of the arterial vessels was performed. At the same time, a balloon catheter with dimensions 6 × 60 mm was used; for expansion to complete occlusion and vascular permeability. Occlusion occurred at balloon pressure up to 9 atm with RBP of 10 atm. Contrast Unigexol-350–100 ml (1 bottle of 100 ml). At the same time, 3 thousand hereditary heparin was introduced (Fig. 1).

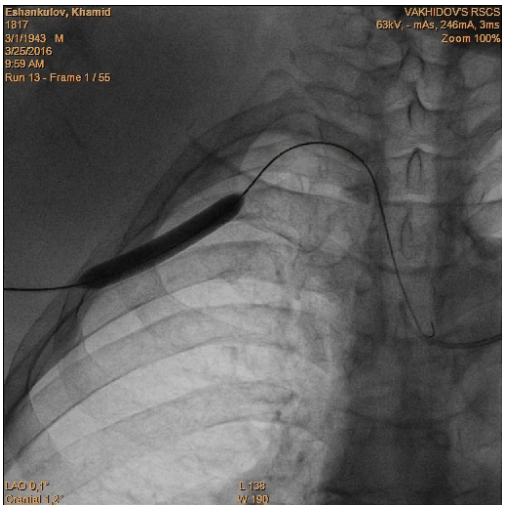

Figure 1. Rentgenendovascular complete occlusion of the right subclavian artery

So, Patient Eshonkulov Kh. 73, complaints about: the presence of education in the supraclavicular region on the left; numbness of the right upper limb; lack of movement of fingers of the right cyst, general weakness. According to the patient, 4 months ago he was injured, as a result of a fracture of the clavicle on the right and rib fractures. The patient was treated by a traumatologist. The last 20 days before contacting us, he had the above complaint.

The patient received MSCT angiography (from March 16, 2016). Diagnosis: Occlusion of the right subclavian vein. Stenosis of the right subclavian artery. CT scan is a feature of the right upper and subclavian area and extends to the right axillary region. On examination, it was established: the general condition is satisfactory; normal build; integuments of normal color; peripheral lymph nodes are not enlarged; in the lungs vesicular breathing, on both sides; percussion over the lungs pulmonary sound; muffled heart tones; HR80 beats per minute. HELL 120/80 mm. mercury column; the abdomen is soft, of the usual form, participates in the act of breathing. On palpation, the abdomen is soft, the liver and spleen are not enlarged. Symptom tapping negative on both sides; physiological functions are not disturbed. When viewed, the upper and lower limbs of the same perimeter. There is no edema. Pulsation at all identifying points is determined. In the supraclavicular region, on the right, there is a pulsating formation – with dimensions of 10 × 12cm – motionless; painless, the skin above it is not changed. In the right lower limb, the activity of the movement of the cyst of the fingers is absent and the sensitivity is reduced. At auscultation over formation systolic noise is listened.

Examination: Complete blood count: HB-113 g/l. Erythrocytes-3.8 × 1012 / l. Leukocytes-5.7 × 109 /l. Urinalysis – protein-0.099, epitol. unit / pr leu /unit Biochemical blood test: Sugar-6.8. ECG: sinus rhythm. HR-90; The horizontal position of the EOS; Dystrophic manifestations in the myocardium. Roentgenoscopy: Lung fields, without fresh focal infiltrative shadows. The roots of the lungs are hard. The domes of the diaphragm and sinuses are free. Heart and aorta, within age changes. EchoCG: FV 69%. KDO 79 ml. CSR 24 ml. UO 55ml. Severe LVH with systolic overload. Ultrasound: false aneurysm of the subclavian artery, right. Dopplerography: on both sides of the main anti-blood flow. Amplitude saved.

At the first stage, under endotracheal anesthesia, endovascular occlusion of the subclavian artery was performed, a skin incision of the supraclavicular region up to 15 cm long was made. right above the aneurysm. The anterior wall of the false aneurysm is marked by a sharp and blunt way. Then, the wall of the false aneurysm was opened and about 300 g of an old blood clot was removed from it. Further, during the revision, a defect of the anterior wall of the subclavian artery with a diameter of up to 0.3 cm is installed. The defect of the artery is restored, with a lateral suture on the subclavian artery, with a 5/0 prolan thread. Removed occlusion balloon from subclavian artery. The seam is carried out, tight. The aneurysm bed is drained through a separate skin incision. Hemostasis dry. Imposed layered seam on the wound. Aseptic sticker produced. Immediate and long-term results are good. Doppler blood flow on both sides of the great vessels is normal and the amplitude is preserved (Figure 2–7).

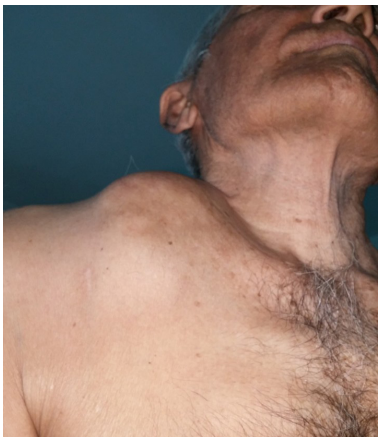

Figure 2. General view of the patient

Figure 3. MSCT of the right subclavian artery

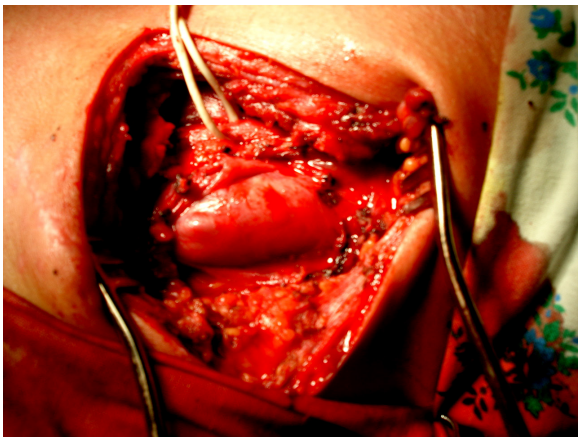

Figure 4. Traumatic aneurysm of the subclavian artery, right

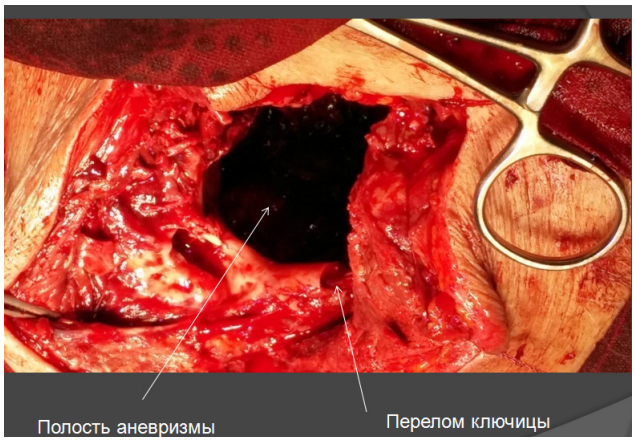

Figure 5. Fracture of the right clavicle and aneurysm cavity

Figure 6. Remote thrombotic masses

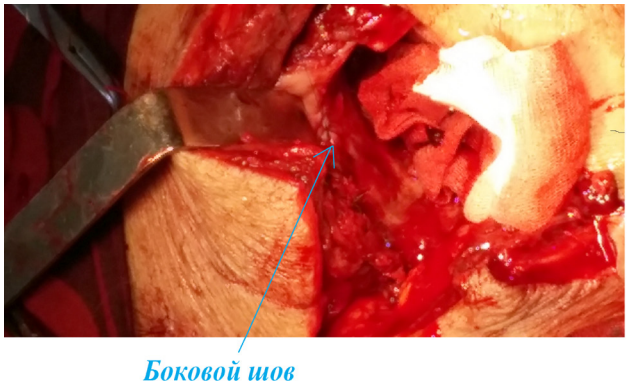

Figure 7. Lateral suture in the right subclavian artery

With TAA, the time interval since the damage to the vessel is of great importance. Among the observed patients with TAA, their absolute majority – 48(75%). All of them were operated on for a period of not more than one month from the moment after the traumatic damage to the vessels. It should be noted that conducting a reconstructive surgery on vessels after 1 year is extremely difficult. Currently, TAA alloying is rather rare. Nowadays, various types of reconstructive surgery on vessels are being widely implemented. This is confirmed by the data below. Thus, the lateral suture was applied in 6(9.3%) with TAA in the following localization: brachial artery – 2(3.1%); femoral – 3(4.6%); ulnar-1(1.5%). If an artery defect is half its diameter or more, then the side seam is not applicable, since this can lead to narrowing of the artery lumen. In such cases, a circular suture or plastic was used.

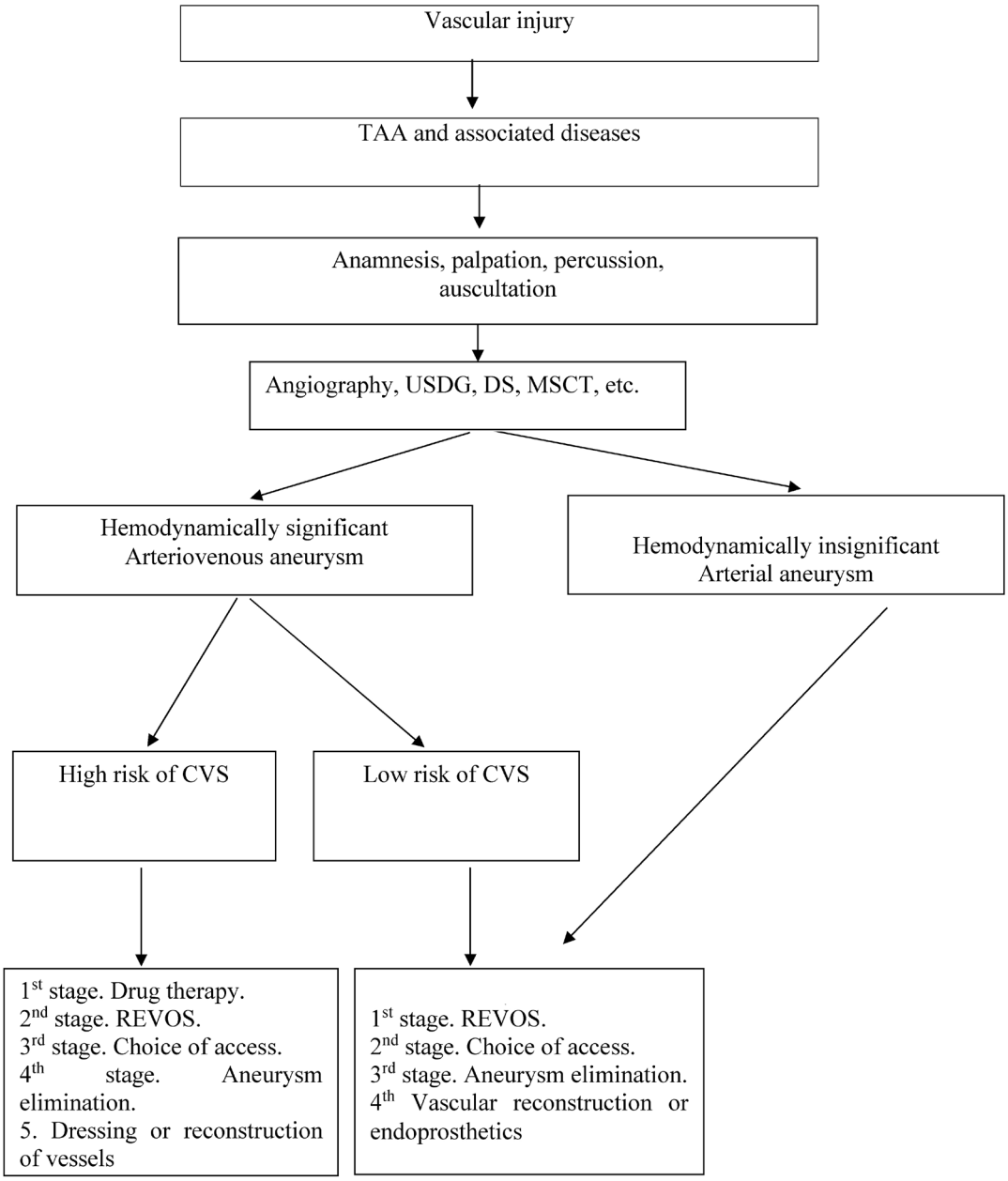

Figure 8. Algorithm for diagnosis and treatment of traumatic arterial aneurysms (TAA)

In this case, a circular suture was used in 15(23.4%) patients, of which: radiation –2(3.1%); subclavian – 2(3.1%); femoral – (7.8%) vessels. In cases where it was impossible to impose a ligature, side seam or circular seam with TAA, it was necessary to resort to plastic surgery. Thus, in: 14(21.8%) cases, an autovenous shunting was performed; 7(10.9%) – used synthetic prosthetics. At the same time, autovenous shunting was used on the following vessels: axillary – 1(1.5%); subclavian – 2(3.1%); humeral – 1(1.5%); popliteal – 2(3.1%); femoral – 8(12.5%). From them: extraanatomic shunting was performed to one patient. Prosthetics of vessels was carried out by patients in: subclavian – 1(1.5%); femoral – 3(4.6%); brachial arteries-1(1.5%). For 8(12.5%) patients, high technologies were used in the operation. At the same time, complete balloon occlusion of the arterial vessels was performed.

In order to prevent DIC of blood and thrombosis of vessels with a large volume of aneurysm, taking into account changes in the parameters of the hemostasis system before and after the operative period, heparinotherapy 150 IU/kg, fresh frozen plasma (FFP) from 5 to 15 ml/kg were used.

It should be noted that TAA with complications associated with aneurysm wall rupture was observed in 46.2%) patients with severe bleeding. In addition, thrombosis was detected in patients – (partial and complete) 19(29.6%),

fresh blood clots in the aneurysm – 1(1.5%); tearing aneurysm-2(3.1%), infection of blood clots-4(6.2%), removal of prosthesis-1(1.5%).

In 10(15.6%) patients associated with suppuration and aseptic inflammation, and infiltrates in the area of postoperative wounds, recovery was delayed. In 5(7.24%) patients, surgical interventions were not performed, due to contraindications of their health status and patient failures.

In the immediate postoperative period, examinations were performed in 64 patients: 57(89%) are good and 7(10.9%) are satisfactory.

In 48(75%) patients, wound healing was primary, in 7(10.9%), healing occurred by secondary intention.

In line with the above, in order to effectively diagnose and optimize (select) the surgical treatment of traumatic arterial aneurysms, we have tried, on the basis of an algorithmic approach to the problem being studied, to propose an algorithm for their implementation.

Algorithmic language is a textual description of the algorithm, but this is not yet a programming language. For our description, the most appropriate is the flowchart method based on the integration of select and repeat commands.

Inspection includes – anamnesis, complaints, external examination;

– palpation – on the presence or absence of a dense, soft, painful, painless formation; the size of education;

– auscultation – for the presence / absence of systolic or sistolodiastolic noise on the projection of the aneurysm;

If a pulsing hematoma is suspected in the presence of a dense, painful formation with systolic or systolic and diastolic noise above it, hemodynamic indicators are evaluated (decrease or increase in blood pressure, heart rate, pulse rate, etc.).

Hemodynamic instability with "significant" hypertension or hypotension, with or without tachycardia and with a decrease in hemoglobin. At the same time, it is necessary to take into account the clinical signs: pallor of the skin, a decrease or increase in pulse rate on the radial artery.

Hemodynamic stability or "insignificant" signs are recorded by normal arterial pressure, heart rate and radial artery pulse.

With high risks of cardiovascular disease, there is a change in ECG – dystrophic changes in the myocardium, severe LVH with systolic or systolodiastolic overload. Low risk of CVS is not observed in ECG changes and dystrophic changes in the myocardium and LVH with systolic or systolodiastolic overload.

Findings:

1. The most effective treatment for TAA is their early diagnosis using a diagnostic and treatment algorithm.

2. In inflammatory processes of the surrounding tissue, it is necessary to perform autovenous shunting and vascular prosthetics.

3. The best method of surgical treatment is a plastic vascular reconstructive surgery using endovascular temporary occlusion of the vessels.

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THE IMPACT OF PESTICIDES ON ORGANISM. THE MANIFESTATIONS OF THE ACTION OF PESTICIDES ON ORGANS AND SYSTEMS

Abstract: On the basis of literature data, the question of the effect of pesticides on the human body was analyzed. Pesticides are one of the most important inventions of our time, affecting the life of humankind. But their downside is in accumulation in the environment and in the human body along food chains. The analysis of available literature data indicates the relevance of this topic, since elucidation of the characteristics of cell proliferation, differentiation, structure and metabolism under the action of pesticides is a necessary attribute for establishing adaptive reactions of the body to the effects of pesticides and developing ways to correct them.

Keywords: pesticides, anthropogenic pollution, manifestations, impact.

Pesticides can enter the body through the respiratory system, the skin and the alimentary route with food and water, while such well-soluble lipid pesticides as organophosphate compounds (OPC) and organochlorine compounds (OCC), phenols, cyanides and some salts begin to be absorbed into the blood already in the upper digestive tract. The intake of pesticides in the body is accompanied by their interaction with the chemical components of cells and body fluids, which leads to a change in the functions and structure of the internal organs and the organism as a whole.

One of the specific indicators of the toxic action of pesticides is the inhibition of the activity of enzyme systems: the activity of erythrocyte acetylcholineterase, serum and tissue cholinesterase, and mitochondrial redox enzymes.

Thus, under the action of OPC, cholinesterase loses its inherent catalytic activity. Daily administration for 30–60 days with food to white rats acetorate (ortene) at a dose of 60 mg /kg resulted in a decrease in the activity of tissue succinate dehydrogenase and glutathione in the liver and blood.

Many pesticides do not have selective toxicity, but affect the body as a whole. However, the anatomical and physiological characteristics of the liver and its detoxification function determine the greatest contact of this organ with harmful factors. The results of many toxicological and morphological studies have shown a significant effect of most pesticides on the liver. So, with a 5-month intragastric administration of chlorophos in the liver, pathological changes of varying severity were observed: central necrosis in the lobules, the phenomenon of postnecrotic cirrhosis, hemorrhage.

The action of OPC and OCC causes a violation of protein-forming, neutralizing and other functions of the liver.

Acute intoxication with chlorophos (300 mg/kg) is accompanied by an increase in the content of phospholipids in the mitochondrial membranes of the liver of experimental rats. Changes in the content of phospholipids are considered as the result of their catabolism. In the animals on the background of a long daily (for 9 months) administration of chlorophos through the mouth (0.01 LD50), it caused more pronounced biochemical and ufological changes in the liver. A pronounced decrease in the antitoxic function of the liver, an increase in the activity of alanine aminotransferase and sorbitol dehydrogenase in the blood serum of rats was revealed. After 6 months, widespread cirrhotic changes and fatty degeneration of the liver were determined.

There is evidence of a negative effect of butifos on the functional state of the liver, as well as on the activity of some liver enzymes and blood of experimental animals.

With the long-term administration of hexachloran in small doses, despite the absence of visible signs of intoxication, significant changes are revealed in the liver of animals. The mass of the liver increases mainly due to hypertrophy of hepatocytes, the number of dual-core cells increases. Biochemically and histochemically, the tendency to an increase in the content of RNA, glycogen and protein in the liver tissue are determined, and the content of enzymes of the microsomal fraction in it also increases.

The experimental material showed that pesticides have similar biological properties and cause qualitatively identical

morphological changes. For example, 6 days injection with Mileran (20 mg/kg), the spermatogonia quantity sharply decreased.

Analysis of the research results of 15 chemical compounds (mainly pesticides) showed that 9 of them negatively affected the gonads in low doses: blockade of gonad proliferation and differentiation occurs, which is accompanied by the development of destructive changes in spermatocytes and spermatids. It is assumed that pesticides have an inhibitory effect on the endocrine function of the gonads.

Important are studies of the reactions of blood cells and hematopoietic tissue to the action of pesticides. Hematopoietic tissue refers to tissues with a high capacity for renewal, which maintains a stable balance between the formation and destruction of blood cells, and the effect of pesticides can lead to disruption of the mechanisms for maintaining this balance, which manifests itself in the form of changes in peripheral blood.

Thus, paraphenididine and metatrifluoromethylaniline cause changes in erythrocyte metabolism and the formation of methemoglobin. Nitrofor leads to a decrease in hemoglobin level by 14%. Phthalafos, mercaptos and others increase the hemoglobin level and the number of red blood cells in the peripheral blood, cause neutrophilia with a left shift, eosinopenia and lymphopenia. Triethylenemelanin changes the cellular composition of the bone marrow, reducing the number of polychromatophilic normocytes. Under the influence of methylsystox there is an increase in the number of erythroblasts, which indicates bone marrow irritation.

A similar change in red blood, coupled with symptoms of anemia, is observed with chronic effects of butyphone, aniline, nitrobenzene and their derivatives. In case of chronic poisoning with glyphtor, there is leukocytosis with eosinophilia and decrease in the activity of cholinesterase, peroxidase, as well as a decrease in the antitoxic function of the liver.

A decrease in the number of red blood cells, monocytes, eosinophils and the level of hemoglobin was detected in 37 workers exposed to aromatic isocyanates and tertiary amines. At the same time, a decrease of glycogen and an increase of RNA in leukocytes, hypochromic anemia, erythropenia, methemoglobinemia, reticulocytosis, thrombocytopenia, and a tendency to leukopenia are found in those who work on contact with aniline, dimethylaniline, tolol and nitro derivatives, and their derivatives with nitro derivatives, are found.

The peripheral blood of persons who had a contact with anti-treflan showed a decrease in the percentage of hemoglobin by 12.6%, the number of erythrocytes by 17.3% and the development of leukocytosis, mainly due to the staple neutrophils and segmented forms, neutrophils appeared hypersegmented nuclei, there was an increase in the content of eosinophils in the blood to 5–8%. The functional activity of neutrophils changed, as evidenced by a decrease in the amount of lipids and glycogen in them, a decrease in the activity of cytochrome oxidase and peroxidase enzymes. The revealed violations of cytochemical parameters indicate violations of the functional activity of leukocytes. Such a diverse, chemical effect helps to reduce the body's reactivity and increase overall morbidity.

Conclusion

Available data suggest that pesticides with long-term effects on the organism can lead to serious changes in many systems. At the same time, this problem has been studied insufficiently and requires further scientific research. Its solution would allow in risk groups, first of all in children living in agricultural regions, to carry out effective biomonitoring of the concentration of toxic substances, to carry out programs of screening studies included in the system of regular medical check-ups. Such measures are designed to ensure the early detection and treatment of the toxic effects of pesticides, as well as to determine a system for the prevention of associated damage to the organs.

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RETROSPECTIVE ANALYSIS OF COMPLEX TREATMENT OF PATIENTS WITH UTERINE SARCOMAS

Abstract: The results of a retrospective analysis of 52 patients with uterine sarcomas are presented. The methods of complex treatment and their prognosis in patients with uterine sarcomas are analyzed. It has been established that the presence of a residual tumor in the pelvis after non-radical surgery significantly worsens the prognosis of the disease. Endometrial stromal sarcoma and poorly differentiated uterine leiomyosarcoma occur more aggressively.

Keywords: uterine leiomyosarcoma, endometrial sarcoma, treatment.

Relevance. Uterine sarcomas are malignant mesenchymal tumors, their frequency among all malignant tumors of the uterus is 2–6% and less than 1% among malignant tumors of the female genital organs. To date, according to the literature, knowledge of the prognostic characteristics of uterine sarcoma is considered the key to understanding the development of the disease, which is extremely important for assessing the individual prognosis and probabilistic response to therapy [3; 5; 8]. The main clinical symptoms of uterine sarcomas are uterine bleeding of varying intensity (observed in 70–80% of cases), an increase in abdominal volume, abdominal pain, putrid vaginal discharge, weakness, anemia [2; 6; 9].

Questions of treatment tactics for uterine sarcomas remain controversial to date. All authors agree that only one operation should be performed in an amount not less than hysterectomy with appendages. In none of the types of malignant tumors of the genitals, there are so many medical diagnostic errors leading to non-radical treatment, as in uterine sarcomas [1; 4; 11]. The literature data point to the ineffectiveness of radiation therapy as an independent method of treating patients with malignant mesenchymal tumors of the uterus. However, in some cases, the use of this method in combination with surgery and chemotherapy, as well as taking into account the histological form of the tumor, improves the long-term results of treatment [2; 5; 10]. The effectiveness of antitumor drug treatment is also different.

The high malignancy of sarcoma, the rapid progression of the process and the propensity for metastasis determine the need for radical surgical treatment, adjuvant chemotherapy and radiation therapy [3; 7]. In 60% of patients, uterine sarcoma is diagnosed in advanced stages, and therefore the problem of early diagnosis of this disease is extremely urgent.

The purpose of the research: analysis of methods of complex treatment and its prognosis in patients with uterine sarcomas (US).

Material and research methods. Patients were treated in the tumor department of the reproductive system of Samarkand branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology from 2014 to 2017.

For all patients, analysis and statistical processing of case histories were performed. The obtained results were processed by the variation statistics methods on the Pentium IV personal computer using the Microsoft Office Excel 2003 software package. For statistical analysis used the criteria of student-Fisher.

The study included 28 patients leiomyosarcoma (LMS), 16 patients – endometrial stromal uterine sarcoma (ESUS), 2 patients – carcinoma of the uterine sarcomas (CUS) and 6 patients, 4 of which with LMS and 2 is operated with the ESS cancer institutions. According to these studies, all patients underwent laparotomy, hysterectomy with appendages.

According to the data of this study, all patients were divided into 3 groups: 1-group-6(11.5%) patients who received only surgical treatment; 2-group –24(46.2%) patients who received the combined treatment (operation + AChTh); 3-main group – 22(42.3%) patients who received complex treatment (surgery + 4 courses of AChTh + combined radiation therapy).

The distribution of patients by age groups: 30–39 years 4(7.7%), 40–49 years old 28(54%), 50–59l-17(32.7%), 60 years old and above –3(5.6%). We know of the 4 main histological types of uterine sarcomas according to the Samarkand branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology the most common uterine leiomyosarcoma – 73%(38 out of 52). 14 patients (36%) were younger than 50 years old, and 3 patients (9%) were over 60 years old, the remaining 21 patients (55%) aged 50–59 l. At the 2nd place was endometrial stromal sarcoma of the uterus, macroscopically similar to the exophytic form of endometrial adenocarcinoma in 9 patients (17%), poorly differentiated uterine sarcoma was detected in 3 patients (5.7%) and uterine carcinosarcoma –2 cases (3.8%).

The problem of early diagnosis of uterine sarcoma still remains unsolved in gynecology. The preliminary diagnosis was based on the grounds of complaints and clinical signs. The main diagnostic methods for suspected lesions of this malignant tumor were the following: 1 – complete and full blood count, biochemical blood test, coagulogram; 2 – in order to identify the morphological features of various variants of the uterine body sarcomas, differential diagnosis and identification of the capabilities of the morphological method, a scraping from the uterine cavity, a biopsy from a recurrent and from a metastatic tumor were carried out; 3 – conducted ultrasound and x-ray examination, which are necessary to obtain information about the size of the tumor and the degree of its germination in neighboring organs; 4 – MRI and CT examination were performed to determine the structure of the tumor and identify metastases in distant organs; 5 – excretory urography to determine the presence of tumor germination in the organs of the excretory system (state of the renal excretory function, n / 3 ureters permeability, bladder wall); 6 – irrigoscopy to clarify signs of tumor invasion into the rectum.

The results of the study. According to a retrospective analysis of patient histories, a preliminary diagnosis was made on the basis of complaints from patients and the following signs of illness: acyclic bleeding was observed in 36 patients (69%); an increase in the size of the abdomen due to the rapid growth of a tumor or myoma node in 11 patients (21%); anemia of varying severity in 16 patients (30.8%); deterioration of the patient's condition with a combination of several symptoms in 44 patients (84.6%); relapses after removal of polyps and submucous nodes in 3 patients (5.7%); recurrent tumor of the cervical stump after supravaginal amputation of the uterus in 2 (3.8%). When studying the results of general blood tests of patients with uterine sarcomas, we found that in almost all patients the disease was complicated by varying degrees of severity of anemia.

In the period before the operation for histological verification all patients were produced by indications scraping of the uterine cavity, and biopsy of recurrent of metastatic tumors. Based on this study, only 18 patients had a primary diagnosis before surgery (fractional scraping of the uterus, polypectomy, biopsy from a recurrent tumor) and amounts to 34.6%. This indicates that tumor cells are not always determined by scrapings.

Ultrasound is a routine method for diagnosing uterine sarcoma. An ultrasound study, if there is a rapid growth of myoma node, will give us the opportunity to suspect uterine sarcoma. In addition, necrosis in the center of the myoma node, tissue heterogeneity, degree of echogenicity and density are considered ultrasound for early diagnosis of uterine sarcomas. According to the results of the study, all patients underwent an ultrasound study in the pre-operative period. Suspected uterine sarcoma was diagnosed by ultrasound in 38 patients (82%).

An X-ray study method was used primarily to conduct chest x-rays to all patients, to clarify the state of the lungs, whether there are metastases in the lungs. A distant lung metastasis was detected in 2 patients in the pre-operative period. In 32 patients, radiological criteria of chronic bronchitis were revealed. It is difficult to accurately diagnose uterine sarcoma prior to surgery or biopsy of a tumor tissue.

According to an MRI study, the clinical diagnosis of uterine sarcoma was established in 42(80.8%) patients who were confirmed in a postoperative histological study. Diagnosis of

uterine sarcoma in the period of menopause is that, against the background of a suddenly changing, rapidly growing benign tumor of the uterus, a degeneration into uterine sarcoma can be suspected. In patients of the first group who did not undergo chemotherapy due to severe extragenital pathology, a histological form of endometrial protromal sarcoma of the uterus revealed a relapse after 62 ± 5 days (in 6/6 patients). Patients of the second group (24 = 100%) who received the combined treatment – operation + autoscopic chemotherapy (AChTh), with the histological form of ESUS in 3/24(12.5%) and with poorly differentiated LMS in 4/24(16.7%), a relapse was detected after 92 ± 7 days. 11/24(45.8%) patients had a relapse after 120 ± 6 days. In 6(25%) patients after 142 ± 7 days were admitted with distant metastasis

In the main group, which consisted of 22 patients, after the combined therapy (operation + AChTh + combined radiation therapy), 18 months after the combined treatment, distant metastasis (multiple metastasis in the lungs) was revealed in one patient, with a histological form of poorly differentiated endometrial sarcoma. In addition to the above, as a result, due to the performed non-radical operation in non-oncological institutions, 6 patients were admitted with continued tumor growth in a short time (from 32 to 70 days). Of these, two had complications in the form of bilateral ureterohydronephrosis of 2–3 degrees, and in the first stage, prior to chemotherapy, they were forced to deliver percutaneous nephroconeostomy on both sides and for a long time to prepare the patient for a course of chemotherapy, to improve biochemical parameters. Two patients had liver metastases in the postoperative period in the coming months (up to 64 days).

Conclusion. The high malignancy of uterine sarcoma, the rapid pace of tumor progression, the tendency to frequent local recurrences indicate the need for a radical operation. The presence of a residual tumor in the pelvis after non-radical surgery significantly worsens the prognosis of the disease. Despite the combined and complex treatment methods, endometrial stromal sarcoma and poorly differentiated uterine leiomyosarcoma is more aggressive than uterine leiomyosarcoma and carcinosarcoma. In the post-operative period, the administration of adjuvant polychemotherapy (AChTh) to affect subclinical metastases, which at the time of treatment may be outside the anatomical zone of the tumor, gives us the opportunity to improve the results of surgical intervention. A timely radical surgery, supplemented by adjuvant chemotherapy in combination with radiation therapy, a comprehensive approach to the treatment of US, improves long-term results of treatment, prolongs a recurrent period, survival and quality of life of patients. Early diagnosis of uterine sarcomas even before the operating period allows us to carry out not only radical, but also organ-preserving operations in patients of reproductive age.

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NON-ALCOHOLIC FATTY LIVER DISEASE – SOME ASPECTS OF PREVENTION

Abstract: Non-alcoholic fatty liver disease (NAFLD) is a nosological unit that has become known in the medical community relatively recently. The first mentions of it in the specialized literature appeared in 1980, when H. Ludwig et al. the term "nonalcoholic steatohepatitis" (NASH) was first introduced (Podymova S. D., La Brecque et al., 2014). Up to 80% of obese and up to 20% normal-weight people might develop it. It is estimated that 24% of the worldwide population is affected in 2017. NAFLD is the leading cause of chronic liver disease as of 2017.

Keywords: NAFLD, NASH, NAFLD treatment, liver disease.

Currently, NAFLD is considered as one of the leading causes of chronic liver disease in the world. This is probably due to the fact that a patient with NAFLD often had more serious diseases – type 2 diabetes mellitus (DM-2), metabolic syndrome, etc. For a long time, hepatosteasis was not given much importance, despite the fact that doctors knew about it. It has been established that insulin resistance underlies these metabolic diseases, and their compensation does not eliminate NAFLD. Moreover, NAFLD worsens the course of the underlying disease. Therefore, interest in its study has grown substantially. A large amount of heterogeneous data has already been accumulated concerning both the theoretical basis of the NAFLD pathogenesis, as well as important clinical features of the disease course, diagnosis and treatment (Volkova N. I., Porksheyan M. I., 2017).

Clinical manifestations: visceral obesity, signs of impaired glucose metabolism, dyslipidemia, and arterial hypertension. Rarely: fatigue, aching pain or discomfort in the right hypochondrium. If NAFLD leads to the liver cirrhosis, symptoms of liver failure and/or portal hypertension appear: an increase of the abdomen size, edema, hemorrhagic syndrome, encephalopathy (McCullough A.J. [8]). Diagnosis of NAFLD often reveals obesity in patients.

There are no standard approaches to the treatment of NAFLD. Since NAFLD is often combined with obesity, type 2 diabetes and hyperlipidemia, it is necessary to correct these conditions, and therefore treat the metabolic syndrome (Lazebnik L. B., Zvenigorodskaya L. A., 2009). Modern guidelines on the effects on the components of metabolic syndrome emphasize that lifestyle changes are the main way to correct metabolic risk factors.

Treatment of NAFLD includes a gradual reduction in body weight, a balanced diet therapy with restriction of fats and carbohydrates, as well as physical exertion (Polunina T.E. [5]). The development of steatosis and steatohepatitis is a multimodal process, so today several treatment regimens are being investigated at once, such as the treatment with thiazolidinediones (TZD). It is proved that the use of vitamin E at a dose of 400 mg per day can improve liver histology. The possibility pioglitazone treating of NASH patients is being considered. Currently, the properties of a new potentially highly effective drug GFT505, a double agonist of PPAR α and δ receptors, are being studied (T. E. Polunina [5]). Omega-3 polyunsaturated fatty acids are the first drugs for treating elevated triglycerides in NASH patients, but it's too early to consider them as the drugs of choice for NAFLD/NASH treating. Statins are recommended to be prescribed to correct dyslipidemia in NAFLD/NASH patients, however, data from clinical studies on the effect of statins on NAFLD are not obtained. S-adenosylmethionine is formed from methionine in the process of ATP-dependent reaction catalyzed by methionine-adenosyltransferase, and participates in the process of transmethylation in the body. S-adenosylmethionine is usually used in a dose of 400 mg 2 times a day (Kalhan S. C., Edmison J., Marczewski S., et al., 2011). The antioxidant effect of S-adenosylmethionine is taken into account in the treatment of NAFLD; however, there is currently no convincing evidence of its positive effect on the biochemical and histological picture of NASH (Ivashkin V. T., [4] Prof., Ed.). The effectiveness of ursodeoxycholic acid in the NAFLD treatment, NASH in particular, has been proven. At a dose of 15–30 mg per kg of body weight daily for 24–48 weeks, ursodeoxycholic acid

has been proven to decrease serum transaminase activity (Zun Xiang, Yi-peng Chen, Rui-fen Ma., Et al. [9]). However, there is no convincing evidence of its positive effect on necroinflammatory changes and liver fibrosis, as well as on the long-term prognosis of NAFLD patients (Ivashkin V. T., [4] Prof., Ed.). Essential phospholipids have antioxidant, anti-inflammatory effects and restore the integrity of cell membranes. The use of phospholipids for NAFLD treatment reduces liver steatosis (according to ultrasound) and the level of serum transaminases. Depending on the ratio of linoleic and linolenic acids, essential phospholipids may have additional properties (for example, lipid-lowering) (Vyushnova E.S., Mayev I.V., Babina S.M., 2010; Myazin R.G., [6]). Convincing data on the long-term positive effect of essential phospholipids on the course of NASH are also not yet obtained at the moment (Ivashkin V. T., [4] Prof., Ed.).

Treatment regimens for NAFLD patients are based on pathogenesis, therefore the most important tasks for this category of patients are:

1. Metabolic disorders correction:
   - weight loss (diet and physical activity);
   - increased sensitivity of cellular receptors to insulin (metformin, thiazolidinediones);
   - decrease in triglycerides level (fibrates, statins);
   - a decrease in the concentration of TNFα (pentoxifylline);
   - antihypertensive therapy (angiotensin II receptor antagonists);
2. Oxidative stress treatment:
   - antioxidants and hepatoprotectors (vitamin E, silibinin, betaine, N-acetylcysteine, ursodeoxycholic acid, α-lipoic acid);
3. Intestinal microbiocenosis restoration (eubiotics, probiotics, prebiotics).

Diet. A diet for obese patients implies a decrease in the overall energy value of the diet. Daily caloric content is selected individually depending on body weight, age, sex, level of physical activity using special formulas.

It has been proven that weight loss of 5–10% is accompanied by a decrease in hepatosplenomegaly, ALT, AST activity and correlates with regression of hepatic steatosis (Feldstein A. E., et al, 2006). It should be noted that rapid weight loss can lead to the development of "acute" NASH with the formation of portal fibrosis, central necrosis on the background of a significant increase in inflammatory activity due to an increase in FFA in the liver against the peripheral lipolysis background (Hamaguchi M., Koima T., Takeda N., et al, 2005). For obese and NAFLD patients, weight loss is effective: 500 g per week for children and 1600 g per week for adults (Ratziu V., Goodman Z., Sanyal A., [3]).

In addition, all patients with NAFLD recommended:

- limiting fat intake to 25–30% of the total energy value of food; the ratio of polyunsaturated and saturated fatty acids (FA) in food is more than 1;
- reducing consumption of foods high in cholesterol (no more than 300 mg per day) – excluding by-products (liver, kidney), caviar, egg yolk, smoked sausages, fatty meats and dairy products;
- exclusion of products prepared as a result of food processing such as frying, deep-frying, etc.;
- enrichment of food with vitamins and natural prebiotics;
- for patients with IGT and type 2 diabetes, a diet with the exception of simple and restriction of complex carbohydrates is relevant, which contributes to achieving metabolic control.

Physical activity. A prerequisite for the treatment of NAFLD patients is physical activity. It has a positive effect on weight loss and insulin sensitivity, and this increases the flow of FFA into muscle tissue, where it oxidizes, thereby reducing insulin resistance. The degree of insulin resistance reduction, as a rule, correlates with the intensity of physical exercises, which are recommended to be carried out at least 3–4 times a week, lasting 30–40 minutes.

The work of recent years proved the fundamental possibility of drinking mineral waters to influence the course of metabolic processes in lipid and carbohydrate metabolism violation in patients of different nosological groups, including those with NAFLD associated metabolic syndrome. The possibility of differentiated use of mineral waters and an aqueous solution of bischofite depending on the stage of the disease, the severity of metabolic disorders, concomitant diseases, such as digestive pathology, type 2 diabetes and hypertension, has been demonstrated.

I. B. Zabolotnaya agrees with the opinion of V. K. Frolkova et al. on the prospects of further studies of natural factors, in particular mineral waters, with a different way of realizing their biological potential for developing indications for use in the treatment and prevention of the NAFLD pathogenesis.

Preventive measures include nutrition, daily physical activity, the exclusion of unjustified use of drugs.

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SOME ASPECTS OF THE RESISTANCE OF HIV INFECTION TO NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS

Abstract: The results showed that the most common mutation of M184V does not in itself lead to pharmacological resistance of HIV, and among the complexes of thymidanalogous mutations, M41L and D67N dominated leading to the development of low-level resistance to all nucleoside reverse transcriptase inhibitors.

Keywords: HIV infection, nucleoside reverse transcriptase inhibitors.

The widespread prevalence of HIV infection worldwide causes the enormous social, economic and demographic significance of this disease. The number of HIV-infected people in the world according to WHO data for 2017 exceeds 30 million people.

Currently, HIV infection is a priority health care issue. The number of HIV-infected patients with clinical manifestations of the disease requiring specific treatment increases annually.

The history of antiretroviral therapy for HIV began in 1987, when the first drug that suppressed viral replication, azidothymidine, was approved. In subsequent years, a number of drugs of the same pharmacological group were developed – nucleoside reverse transcriptase inhibitors (NRTIs). However, after a certain time, it was found that treatment with one or two drugs does not produce the desired effect due to the rapid emergence of mutant forms of the virus with reduced sensitivity to antiretroviral drugs (ARVs). HIV replication. The combination of three or four drugs (the so-called highly active antiretroviral therapy – HAART) made it possible in many cases to suppress the multiplication of the virus. The use of HAART has contributed to a significant reduction in mortality among HIV-infected patients, but it did not eliminate the problem of resistance of the human immunodeficiency virus [1; 3; 5; 9].

And in most cases, the ineffectiveness of therapy is associated with the development of HIV resistance to antiretroviral drugs. Highly active antiretroviral therapy, which should be given to a patient for life, may not be effective due to the development of resistance to antiretroviral drugs. Due to the high degree of genetic variability of HIV, the active replication of the virus and the need for long-term use of ARV drugs, the emergence of HIV resistance is inevitable. Resistance potentially develops to all ARV drugs and may manifest as early as 14–28 days after administration of the drug. The spread of HIV resistance to ARV drugs leads to a decrease in the effectiveness of therapy, an increase in mortality from HIV / AIDS and an increase in the cost of antiretroviral therapy [2; 5; 9].

Studying the level of HIV resistance to ARVP is an important and integral component in the provision of quality care for HIV-infected patients. Detection of resistance is necessary to analyze the transmitted resistance of the virus in order to minimize its spread, as well as timely planning and taking measures to prevent the circulation of resistant strains [2; 5].

A complex has been undertaken in the country to limit the effects of the negative effect of virus resistance on the patient's body.

Analyzing the data of HIV-infected patients receiving various treatment regimens, taking into account resistance to antiretroviral drugs, may clarify some still unclear issues in the management of such patients, optimize the strategy of antiretroviral therapy and increase its effectiveness.

Purpose of the study. Determination of resistance to reverse transcriptase inhibitors.

Material and methods. Analyzed 200 plasma samples of HIV-positive patients. The study included patients with the experience of receiving ART for at least a year. Studies on the identification of mutations associated with HIV resistance to ARVP included the determination of nucleotide sequences of the human immunodeficiency virus genome. Processing of sequencing data, obtaining a consensus sequence and further analysis was carried out using the Stanford University database (http: // hivdb. Stanford. Edu) to determine the mutation profile of HIV resistance to various ARVs.

The results of the study. Analyzed 83 samples of patients in whose blood the HIV viral load was detected. The analysis showed that in the study group, mutations of resistance to nucleoside reverse transcriptase inhibitors (NRTI resistance mutations) contained a number of mutations.

The analysis of resistance to individual drugs showed that the average and high degree of resistance to most drugs from the group of nucleoside reverse transcriptase inhibitors was de-

tected with approximately the same frequency. So, sensitivity to tenafovir was maintained in 49(59%) patients, in 16(19.2%) patients there was a low level of resistance to this drug. The average degree of resistance was found in 8(9.6%) of the blood samples examined, despite the fact that these patients did not take a regimen containing tenafovir. And only in 10 (12%) patients, in the AVR scheme of which tenafovir was obtained, the results indicated a high resistance of HIV to the drug.

In 5 samples in the highly resistant group, a K65R mutation was found associated with a decrease in sensitivity to tenafovir and didanosine (3–4 times). Patients who found this mutation had low rates of DM 4 cells that did not exceed 110 copies / ml, a high level of HIV-RNA (OR [95% CI] and the duration of the first-line regimen (lamivudine, tenafovir, efavirenz) for more than 12 months In studies [4; 7], it was shown that with the introduction of tenofovir into clinical practice, the K65R mutation causing resistance to this drug became the subject of close attention. However, taking tenofovir in combination with didanosine and abacavir significantly increased the likelihood veniya mutation (especially while receiving three drugs), whereas the joint receiving zidovudine and lamivudine reduced the risk of this phenomenon [6; 10; 11].

In the samples we studied, a sensitivity analysis to emtricitabine was also carried out, despite the fact that this drug is not used in the country. So, in 65(78.3%) samples from 83 studied patients receiving therapy for at least a year, full sensitivity was found, in 3(3.6%) patients a moderate degree of resistance was found and in 5(6.0%) samples a high degree of resistance. In this group, a large percentage of M184V mutations was observed in almost all patients (70%). M184V is the most common mutation in the reverse transcriptase gene that overcomes the effects of emtricitabine and lamivudine. M184V also slows down the onset of resistance and increases susceptibility to zidovudine, tenafivir. Also in the group with high resistance to emricitabine, there were found complexes of timidin-tax mutations (TAM), which are non-polymorphic mutations – D67N, K70R. They reduce susceptibility to the entire group of NNIOT, contributing to the unblocking of the primer (for example, removal of nucleotides, pyrophosphorolysis) [8; 9; 11].

Zidovudine sensitivity has also been investigated. This drug has been used in the country since 2006 and is the most commonly used in AVT schemes. So full sensitivity was found in 70 (84.3%) patients from 83 examined. Only 3 had a low degree of resistance, 6 had a medium resistance, and 3 had a high degree of resistance. In samples with a high degree of resistance to zidovudine, TAM mutations were identified: M41L D67N T215Y. Together, M41L and T215Y provide high resistance to zidovudine and stavudine, as well as low to medium resistance to abacavir, didanosine, and tenafovir. D67N reduces susceptibility mainly to zidovudine and stavudine [4; 9; 11].

Conclusion. On average, each patient identified 1.35 mutations of HIV mutations. The most common mutation was M184V, which was not isolated pharmacologically resistant to HIV. Among TAM Thus, the results suggest that among patients receiving ARV therapy for at least a year, a number of mutations occur, which need to be studied as clinically significant.

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INFLUENCE OF SOME PROTON POMP INHIBITORS, CYTOPROTECTIVE AGENTS AND THEIR COMBINATIONS ON CONDITION OF GASTRIC MUCOSAL BARRIER IN INDOMETHACIN INDUCED GASTROPATHY

Abstract: In experimental model of Indomethacin Induced Gastropathy, treatment with Proton Pomp Inhibitors(PPIs) and Cytoprotective agents influence on process of mucosal defense differently. Omeprazole decreases, rabeprazole, de-nole and pepsan-P increase, while sucralfate does not impact on synthesis of mucosal barrier. Thus, combination of omeprazole with cytoprotective agents is not expedient. Administration of rabeprazole with de-nole as well as pepsin-P has shown the best pharmacological synergism.

Keywords: indomethacin induced gastropathy, proton pomp inhibitors, cytoprotective agents, treatment.

Over the last decades safe usage of non steroid anti-inflammatory drugs (NSAIDs), prevention and treatment of gastrointestinal complications are under great attention [3]. Considering the pathogenesis of NSAID-gastropathy, nowadays there are two group of drugs for treatment and prophylaxis: anti-secretor and cytoprotective drugs. H2 histamine blockers are not the best choice for this purpose, taking into account that they are inferior than proton pomp inhibitors [1]. PPIs take a leading position among all the drugs for treating gastropathies, therefore they are comfortable for use, effective and safe compared to other group of medications[2]. Analyses have shown that there is no answer to the question-"Which PPIs are the most efficient in therapy of gastropathy and do they all influence on process of cytoprotection in a same way?"

Usually, alongside with PPIs, misoprostol, de-nole and sucralfate are used for therapy. Misoprostol is synthetic analog of prostaglandin E2 which was intended to cure and prevent NSAIDs- induced gastropathy. However, misoprostol significantly inferior than PPIs and not excluded from several side effects as practice and latest guidelines show. It puts their usage as a first line drugs under question [3].

Efficacy of de-nole and sucralfate in treatment of NSAIDs induced gastropathy was proven in clinical trials by R. Malagela and co-authors [4], A. E. Karataeva and co-authors [5].

At the same time, lacks information about compared effectiveness of cytoprotectors and their usage in combination with PPIs in therapy [4]. In this aspect efficacy of new cytoprotector Pepsan-P appeals great attention.

Aim of the study: To investigate influence of some PPIs, cytoprotectors and their combinations to the condition of mucosal barrier of the stomach in indomethacin induced gastropathy (IIG).

Materials and methods: Experiment is conducted on white male rats of mixed population with body mass of 150–200 gr. NSAID gastropathy is induced by indomethacin via oral insertion in dosage of 2,5 mg/kg within 5 days [6]. Research run in 14 animal groups: 1stgroup.– intact, 2nd group.-animals with IIG,3rd group.-animals with IIG without therapy; 4–8th groups.–animals with IIG receiving omeprazole, rabeprazole, de-nole, sucralfate, pepsan –P. 9–14th groups-animals with IIG receiving combination of PPIs and cytoprotectors- omeprazole with de-nole; omeprazole with sucralfate; omeprazole with pepsan-P; rabeprazole with sucralfate; rabeprazole with de-nole; rabeprazole with pepsan-P respectively.

Each group had 6 rats. Drugs were inserted orally in form of water suspension within 10 days on following dosage: omeprazole 50 mg/kg [7], rabeprazole 5 mg/kg [8], de-nole 10 mg/kg [9], sucralfate 400 mg/kg [10], pepsan-P 1500 mg/kg [11]. Condition of the mucosal barrier explored via amount of insoluble glikoproteins (IGP) in suspension from mucosal liquid of stomach. Content of sialic acid measured by L. I. Linevik method [12], amount of fucosa by method of P. D. Rabinovich and co-authors [13]. Concentration of common protein tested by method of O. H. Lowry and co-authors [14].

Results and explanation: Table 1 illustrates the effects of some PPIs and cytoprotectors on amount of insoluble glikoproteins of mucosal layer of stomach in indomethacin induced gastropathy.

It is evident from provided information that indomethacin noticeably decreases synthesis of mucosal barrier components, such as IGP. Group of animals with IIG had 3 times less amount of sialic acid and fucosa, 1,5 less amount of total protein in suspension of gastric mucosa. Usage of omeprazole decreased synthesis of IGP. In this group observed following results: decrease of sialic acid to 40.6%, fucosa to 39.0%

and total protein to 27.4%, compared to non –treated group (IIG+H2O). Effect of rabeprazole was totally vice versa, it stimulated synthesis of IGP. Sialic acid concentration raised to 62.2%, fucosa to 106.9% and total protein to 35.7%.

Almost same results were with de-nole usage. Sialic acid level grew for 87,8%, fucosa for 94.9% and total protein for 40.7% differently from non-treated group.

Table 1.– Effects of some PPIs and cytoprotectors on amount of insoluble glikoproteins of mucosal layer of stomach in indomethacin induced gastropathy.

Animal groups	Sialic acid (mkg/ml)	fucosa (mkg/ml)	Total protein (mkg/ml)
Intact	3.66 ± 0.24	6.45 ± 0.48	16.52 ± 0.99
IIG	1.29 ± 0.16	2.34 ± 0.14	10.48 ± 0.83
IIG+ H2O	1.48 ± 0.10	2.18 ± 0.15	10.12 ± 0.79
IIG+ omeprazole	0.88 ± 0.07*	1.33 ± 0.09*	7.35 ± 0.29*
IIG+rabeprazole	2.40 ± 0.14*	4.51 ± 0.15*	13.74 ± 0.60*
IIG+de-nole	2.78 ± 0.21*	4.25 ± 0.15*	14.24 ± 0.60*
IIG+sucralfate	1.69 ± 0.14	2.53 ± 0.18	9.83 ± 0.79
IIG+pepsan-P	2.23 ± 0.12*	3.92 ± 0.22*	13.21 ± 0.95*

*Note: * – P < 0.05 from group of non-treated (IIG + H_2O)*

Group of animals treated with sucralfate had no significant changes compared to the group of without treatment, such as decreased amount of total protein and increased level of sialic acid, fucosa.

Use of pepsan-P showed stimulating effect on mucosal barrier. In this group level of IGP changed: sialic acid to 50.6%, fucosa to 79.8% and total protein grew to 30.5%.

Taking into account results of monotherapy, effectiveness of combined use PPIs with cytoprotectors presents great promises.

Results of use in combination omeprazole and rabeprazole with cytoprotectors and their effect on amount of IGP of gastric mucosal layer in IIG is shown in (table 2).

As it is evident from presented information, combination of omeprazole and de-nole inhibits stimulative effect of the latter. Apparently, combined therapy has no difference than monotherapy with omeprazole. Using omeprazole with sucralfate also does not have a stimulative influence on mucosal barrier IGP.

Table 2.– Effects of combined usage of omeprazole and rabeprazole with some cytoprotective agents on level of IGP of mucosal barrier in IIG.

Animal group	Sialic acid (mkg/ml)	Fucosa (mkg/ml)	Total protein (mkg/ml)
IIG+ H_2O	1.48 ± 0.10	2.18 ± 0.15	10.12 ± 0.79
IIG + omeprazole + De-nole	0.91 ± 0.07*	1.24 ± 0.11*	7.53 ± 0.60*
IIG + omeprazole + sucralfate	0.80 ± 0.06*	1.15 ± 0.12*	6.89 ± 0.42*
IIG + omeprazole + pepsan-P	1.32 ± 0.11	1.85 ± 0.14	9.26 ± 0.72
IIG + rabeprazole De-nole	3.10 ± 0.18*	6.29 ± 0.26*	15.80 ± 0.55*
IIG + rabeprazole + sucralfate	2.54 ± 0.18*	4. 37 ± 0.23*	14.12 ± 0.85*
IIG + rabeprazole + pepsan-P	3.80 ± 0.29*	7.18 ± 0.58*	16.45 ± 0.96*

*Note: * P < 0.05 from the group of non-therapy(IIG + H_2O)*

In the group of omeprazole with pepsan-P, the content of sialic acid increased by 58.0%, fucose by 39% and total protein by 26.0% compared to the indicator of the monotherapy group with omeprazole. At the same time, there was only a significant increase in sialic acid and fucose. According to the data presented in the table, it can be seen that in terms of the stimulation of the protective barrier, the best combination is cytoprotectors with rabeprazole.

In the treatment of IIG with a combination of rabeprazole and de-nol, synergism of the pharmacodynamic interaction was observed. In this group, the content of sialic acid increased by 109.4%, fucose by 188.5%, total protein by 56.0% of the indicator of the group without treatment. Therapy with rabeprazole has shown following results: the increase in IGP fractions was 62.2%, 106.9% and 35.7%, respectively (P < 0.05).

In simultaneous use of rabeprazole and sucralfate, the stimulating effect of rabeprazole remained almost unchanged (P > 0.05).

The combination of rabeprazole with pepsan-R is the most effective. In this group, the pharmacodynamic synergism

of the drugs was more significant than in the rabeprazole and de-nol group. The content of sialic acid increased by 156.7%, fucose – by 229.3%, total protein by 62.5% compared to the group without treatment. These results were significantly superior than results of monotherapy with rabeprazole.

As it can be seen that, the proton pump inhibitors such as omeprazole and rabeprazole act in different directions on the synthesis of IGP. The inductive effect of rabeprazole convincingly indicates the superiority of the action of the drug on the mechanisms of synthesis and development of the mucous barrier, with regard to the stimulating effect of de-nola on the IGP, it must be assumed that this is due to its two main pharmacodynamic effects. Firstly, de-nol forms a type of protective barrier that prevents absorption of H + ions and promotes faster regeneration of damages in mucosal layer. Secondly, de-nol stimulates the local synthesis of prostaglandin E2, which helps to increase the synthesis of the mucosal barrier [15]. There are debate on the effect of sucralfate on the synthesis of IGP in some literature. Our results are consistent with the data of K. Stiener and co-authors. [16], F. Halter [17] and J. C. Soule [18], who argue that the cytoprotective features of sucralfate are determined solely by its local "protective" mechanisms. B. L. Slomiany and co-authors. [19] found in their investigation that under the action of sucralfate, the content of IGP in the gastric mucosa increases by 19.0%. However, other authors have questioned this point of view [20].

In our studies, the stimulating effect of pepsan-P on the synthesis of IGP has been established. Probably, this effect of the drug in the treatment of IIG is linked to its other remarkable features. As it is known that pepsan-P has a noticeable antacid, anti-inflammatory and antioxidant effect [21]. It inhibits the release of histamine from the mast cells in the mucous membrane of the esophagus and stomach, reducing the formation of thromboxane A2 and reactive oxygen ions, therefore as a result reduces the local inflammation process.

It can be assumed that the pharmacodynamic synergism of rabeprazole with cytoprotectors is due to their similar effect on impaired mechanisms of mucosal barrier synthesis, at the same time, the combined use of omeprazole with cytoprotectors multidirectional, because of the prevail pharmacodynamic effect of omeprazole and the absence of synergism.

Conclusions:

1.Proton pomp inhibitors and cytoprotectors influence on mucosal defense process of stomach in indomethacin induced gastropathy differently.

2. Omeprazole decreases, rabeprazole, de-nole and pepsan-P increase, sucralfate does not impact on synthesis of mucosal barrier. Combined usage of omeprazole with cytoprotectors does not change inhibitive effect of omeprazole on mucosal barrier secretion.

3. Combination of rabeprazole with de-nole and pepsan-P shows pharmacological additive synergism, whilst combined usage of rabeprazole with sucralfate has no any pharmacological change in effectiveness.

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THE CHARACTERISTICS OF LYMPHATROP PATIENTS WITH LOW-TEMPERATURES IN THE PULMONARY CONSEQUENCES

Abstract: The article analyzes the results of lymphatic therapies used in patients with acute inflammation of the eye and the eye and the injured eye. Treatment procedures made in FBRRCEM. From 2015 to 2017, 1569 patients with nerve injuries have been examined by an ophthalmologist. Of these, 494(31.4%) patients with side injuries were injured, those with nervous system disorders, severe patients with acute inflammation around the eye orbit, and 11(0.7%) in the resuscitation department. In addition to general treatment procedures, local lymph nodes were used and analyzed. Except for general treatment in the emergency system, the use of immediate local lymph node treatment has helped improve the quality of hospital emergency care and reduce complications.

Keywords: lymphatic catarrhal injury, bone injury, orbital bone fracture, eye rupture, orbital phlegmon, high leprosy syndrome.

It is known that in the last 10 years there has been an increase in the number of bodily injury by 33% of the overall mortality. When analyzing the type of injury, the number of bodily injuries is increasing. These injuries are particularly challenging for patients, for a fixed period of time in the hospital, a high level of disability, and death. At present, WHO estimates that 8–14% of patients with side injuries are the 3rd with a death rate, and the death rate under the age of 40 is the 1st. Eye loss can be dramatically reduced, so do not lose weight or bloody wounds, it is only life-threatening.

Lymphatic therapy is a convenient method of treatment that can cause pain for the patient not to have a serious pain in the eye, a reduction in the recovery period, and a reduction in the injuries.

Material and treatment results. Out of 1569 patients wounded by neuropathy in 2015–2017, the ophthalmologist has been examined. Of these, 494(31.4%) patients with double wounded injuries were injured, that is, those injured in the nervous system and injuries. 51(10.3%) patients were treated with lymphocyte lesion and damaged by leprosy. The combined traumatic brain injury and the obstructive nerve paralysis resulted in 25(5%), 12(2.4%) eyes with severe retinopathy, sharp injuries, 3(0.6%) eye obstruction, orbital 11(2.2%) patients were treated with lymphocytes.

Among the patients with combined traumatic brain injury, 25 (5%) had paralysis of the nerves of the III, IV, and VI pairs of eyes.

9 nerves (1.8%) III nerves – nervous moving muscles;

IV nerve – rectus nerve;

Severe neuromuscular nerve paralysis was detected in 10(2.2%) patients.

In addition to nerve surgery procedures, lymph nodes were sent to the lymph node for treatment of paralysis and to improve the synapse nerve impulsivity (Figure 1, 2).

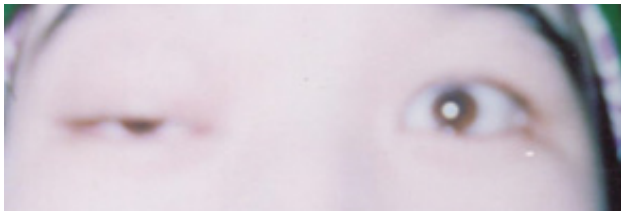

Figure 1. (The future)

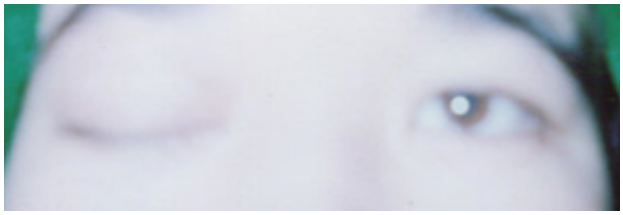

Figure 2. (5th day after hospital stay)

Out of 25 patients with paralyzed swelling, 16 had a 100-hour swab for 3 days, and six had 5 eyes at 50.

In 2 patients, paralytic chips did not change.

In the absence of localized lymph nodes, the mean duration of the nerve activity was about three months, but after lymphotropic medications for the recovery of local nervous activity, the average duration was reduced by 1.5 months.

Brain splashes. Linear breakage of the abdomen bone. Retrobulbar cavity hematomas. Severe leak syndrome (ezophthalm, ptosis, midrias, ophthalmoplegia).

Twelve (2.4%) patients were treated with cerebral trauma and severe diarrhea. Of the 12 patients (16.6%), children (66.6%) were elderly and eight were middle-aged and 2 were elderly (16.6%).

Upon arrival, 6 had a sharp vision and a finger in front of the patient. In the case of gastrointestinal tract, giphoea, a hemophthalmus in the gonorrhea, was observed in the preceding cell. No eye contact has been identified. In addition to general therapies for nerve surgery, local lymphoprotein dytinone, mildronat. In addition to the above-mentioned substances, steroid drugs were also sent to lymphthropic for 3 days. The 3-day sharpness was 0.01, gifema, hemophthalm, a certain amount of absorbed, partially pink reflex in the eye, 5 per day sharpness increased to 0.5.

In children and adolescents, it was reported that in 3 out of 10 patients (83.3), visual acuity was 0.01. The gyphema in the previous cell was absorbed in a certain amount of hemophthalm in the body of the bottle. Partially pink reflex appeared in the eye. On the 5th day gifema, hemophthalm, was absorbed. A complete pink reflex was detected in the eye and ophthalmoscopy of the KND.

Two patients (16.6%) were seldom absorbed in the elderly, due to which the presence of diabetes mellitus, diabetes mellitus, hypertension, and diabetes mellitus slowed the recovery process.

9(1.5%), fracture of the orbital wall with preservation of the eye obstruction, 3(0.5%), linear fracture of the orbit wall, anterior hemispheres, obstruction of the orbital wall bone, 3(0.5%) patients were treated with eye care. After VHF in the vision, lymphocytopenia was conservatively treated from the local lumbar spine.

Even though the orbital wall bone fracture, vision in patients with cerebral palsy, and eyesight have not been completely reversed, the primary surgical treatment of conservative treatments has been restored safely. Subsequently, these patients were subjected to subatrophy, but no complications or second case of sympathetic inflammation were detected.

The Orbita phlegmon treated 11 patients (2.2%) for 3 years with sepsis. Of the 11 patients treated, 7(63.6%) were adults and 4(36.4%) were children (Figure 3. 4).

Seven children, orbital phlegmon, were treated for rhinogenic etiology, diagnosed with pediatric intensive care unit, LOR, and children's rehab on the recommendation of schoolchildren.

The purulent process in the geymorova cavity has passed to retrobulbar spacing. The retrobulbar space was cut open from the upper and lower extremities of the orbital, the pus was removed, and the drain was placed. An antibiotic drug substance was sent to the lymphocytes.

Seven patients (63.6%) were enrolled to the school inspectorate, LOR for the 5th day (Figure 3, 4).

Four (36.3%) were sent to continue the treatment at the dentist and school supervision, with the 6th day improvement.

Figure 3. Orbital phlegmon rhinogen etiology. The future

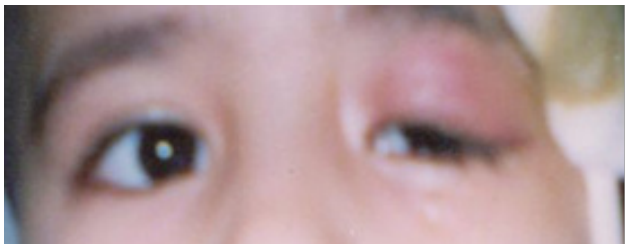

Figure 4. 5th day after treatment

Summary

The use of immediate localized lymph nodes in patients with acute inflammatory diseases of the eye obstruction with visual impairments in eye obstruction:

1. Increasing the duration of the davo effect and the shortening of the duration.
2. Lympathropic therapy does not have the risk of injury.
3. High concentration of the drug in the burned oven.
4. The complete exposure to the visualization pathway.
5. Lymphatic system rehabilitation
6. Dosage of drug 1 time, daily, and course of treatment will decrease dose.

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SOME PSYCHOVEGETATIVE FEATURES OF PATIENTS WITH FACIAL NEURALGIA IN ASPECT OF SEXUAL DIMORPHISM

Abstract: This work shows presence and expressiveness of the syndrome of vegetative dystonia (VDS) and anxiety in the emotional sphere in 372 patients suffering from idiopathic form of neuralgia of the trigeminal nerve (TNN). It was found that intensity of the accompanying psychovegetative disorders in TNN prevailed in the group of women and in the age over 45 years irrespectively of the gender of patients. In the group of men the degree of the VDS and anxiety in the emotional sphere prevailed in the right form of damage, and in the group of women was type of the left lateral damage. The authors suggest that the data obtained should be taking into account during choice of vegetotropic and psychotropic drugs in the range of complex therapy of TNN.

Keywords: psychovegetative, features, patient, facial neuralgia, sexual dimorphism, trigeminal nerve, vegetative dystonia, epileptiform neuralgia.

Until recently in diagnostics and treatment of many diseases including neurologic, the sex factor was not given special meaning. Researches on action of new medicinal preparations were often carried out only on volunteers-men and features of their influence on female organism were lost sight [3]. In many publications there were no indications on a sex of examined persons, in others to conserve "cleanliness of experiment» the women [9] were intentionally excluded. At the same time experience shows that one diseases is more characteristic for men, whereas others for women [4]. Severities of disease course, its outcome, response to treatment are also in many cases depended on the patient sex [1; 8; 10; 11].

The real boom in studying of a problem of sexual differences has begun hardly more 10 years ago after wide introduction in practice of magneto-resonant tomography when morphological differences of men and women brain have been found out. Doctors, scientists, psychologists and sociologists have presented an overall picture specifying accurate sexual differentiation [5–7, 15].

It is considered to be that the main differences of men from women are features of genesial system. However the brain [12] is an organ defining development of organism by male or female type. In a blastogenesis there is a brain differentiation on male or female type that is shown in certain anatomic, morphological features, in various distribution of receptors, establishment of different communications in a brain. It finally, defines differences in functioning of a brain of men and women. According to the majority of the given epidemiological studies, women more often than men show complaints to various by character pains. Thus they have pains more frequent and long [13]. Not always it is possible to explain these differences by biological factors. It is known, that migraine, facial pain (neuralgia of V nerve), dorsodynias and breasts of the woman suffer more often. Chronic paroxysmal hemicrany is exclusive prerogative of women. Differences in metabolism of a brain and biological mechanisms of transfer of a pain may be the reasons. Researches on animals have revealed differences in the analgetic response having shown possibility for involving of estrogenic dependent mechanisms. However the most powerful contribution to character of implication of a painful syndrome often brings the mental factor. The stress and painful stimulus cause more expressed emotional response in women at enough similar changes in somatic, nervous and suprarenal adrenal systems. Men and women have differences in perception of a pain. Men use more opioids (Morphinum) after operations than the woman. Thus according to experimental data at females painful threshold is lower and strain of muscles is higher [2].

These signs often associate with painful syndromes which is often met at women (migraine, strain headache, miofascial painful syndrome, myalgia including fibromialgiya). However, even if to admit that men and women variously react to a pain, it is impossible to explain it only by differences in painful thresholds. The issue on the importance of psychovegetative characteristics of painful syndromes in aspect of a sexual dimorphism demands studying [14].

The aim of the research was to analyze the clinical and psychovegetative (PV) characteristics of epileptic neuralgia (EN) in men and women.

Material and methods. Under our observation there were 372 patients, suffering idiopathic EN form including 234 women and 138 men. We carried out continuous retrospective and prospective study on materials of the Bukhara regional Multidisciplinary Medical Center and municipal hospital of a city of Bukhara. Taking it into account already from the very beginning it is possible to notice EN women suffer in 1,7 times more. The age analysis carried out by us has shown that as a whole EN as in group of women and men meets at those older 45 years with authentic prevalence in female group. At the same time in group of men the tendency to greater presentation in age groups is noted at younger 45 years, and on presentation the patients are older 35 years the men almost twice pass ahed women. The analysis of the party of a lesion has revealed also characteristic differences. As a whole irrespective of a sex authentically were more often right-hand EN in comparison with left hand. And the analysis in the general groups of women and men has shown about identical presentation of the right and left hand forms of a lesion. However the age analysis has revealed that among patients to 45 years, right-hand EN occurs more often than in similar age group of women, at the same time of senior 45 years some prevalence of right-hand forms of disease in group of women becomes perceptible.

For studying of PV disturbances we used screening questionnaire and the scheme for revealing and mark estimation of a syndrome of a vegetative dystonia (VD). developed in MMA of I. M. Sechenov under the guidance of academician A. M. Vein and Spilberger test for estimation of presence and expression of reactive and personal uneasiness. The statistical analysis of figures was carried out by nonparametric methods with use of Vilcocson-Mann-Witni criterion.

Results and discussion. The received results are presented in (tables 1 and 2). From (table 1) it can see that as by results of Spilberger test and by data of screening researches about presence and expression VD between groups of men and women there are essential differences. It is noticed the fact that as a whole in group of women there is tendency to prevalence of uneasiness in emotional sphere. Thus it was revealed the authentic difference on reactive uneasiness especially in age group older 45 years. On personal uneasiness authentic differences on age group younger 35 years was revealed. Comparison of presence and expression of VD in the studied groups reveals authentically more expressed prevalence of point characteristic of VD in group of women as a whole in all age groups. These differences are especially visible in the age from 35 to 45 years.

Table 1. – Features of PV disturbances at EN patients Depending on sex and age

Age	Spilberger test (points)		VD (points)	
	RT	LT	Questionnaire	Scheme
Group as a whole	42.8* 39.6*	46.5 45.5	46.8** 35.2**	59.5** 36.3**
to 35 years	42.5 42.8	50.5* 47.0*	49.3*** 35.0***	64.8* 52.0*
36–45	45.0 43.0	49.0 49.0	45.8*** 18.0***	60.6*** 22.5***
46–60	41.0* 32.9*	40.0 40.6	45.3* 40.5*	53.1** 34.5**

Note: in numerator – data for group of women, in denominator – for group of men
*Sign * – reliability of differences between groups of men and women. One – P < 0.05; two – P < 0.01; three P < 0.005*

Table 2. – The side of a lesion and PV EN features at men and women

Research methods		Men		Women	
		Right hand EN	Left hand EN	Right hand EN	Left hand EN
VD (points)	questionnaire	37.2** Δ	25.2** Δ	48.0**	45.6**
	Scheme	40.0** ΔΔ	32.6** ΔΔ	60.4**	58.6**
Spilberger (points)	RT	42.1 Δ	37.1** Δ	42.0	43.6**
	LT	49.4 Δ	41.6* Δ	47.2	45.8**

Note: sign Δ – reliability of differences between the sides of a lesion in groups of men and women. One – P < 0.05; two – P < 0.01.
*Sign * – reliability of differences between groups of men and women with the identical side of a lesion*

Interesting data are received by comparison of VD expression and uneasiness in emotional sphere depending on the lesion side. As seen from (table 2), in group of men the tendency to larger expression both uneasiness and VD is distinct at right-hand lateralization process. In group of women at larger VD expression and uneasiness between subgroups with right-hand and left hand lateralization process statistically significant difference was not revealed. At the same time the accurate tendency to prevalence of VD expression and uneasiness becomes perceptible at left hand lateralization process in a subgroup of women after comparison with similar group of men.

Conclusions:

1. Expression of accompanying PV disorders at EN prevails in group of women.

2. As a whole degree of expression of accompanying PVe disturbances at EN prevails in the age older 45 years.

3. In group of men degree of expression of VD and uneasiness in emotional sphere prevails at the right-hand form of a lesion, and in group of women at left hand lateralization.

4. The obtained data is required to consider at appointment vegetotropic and psychotropic drugs within the limits of complex EN therapy.

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EXPERIENCE IN THE TREATMENT OF PATIENTS WITH ODONTOGENIC JAW CYSTS

Abstract: In the practice of the dental surgeon, odontogenic cysts make up 78–96% of the total number of cysts and 7–12% of the total number of diseases of the jaws. These figures indicate the relevance of the problem of treating this pathology. The priority tasks of surgical treatment of patients with odontogenic cystamias are the restoration of bone structure and the preservation of the function of the teeth. The main method of surgical treatment remains cystectomy with resection of the root apex. The disadvantages of cystectomy include the reduction of the function of the teeth in the area of the cyst, reinfection and residual bone cavities, which reduce the strength of the bone. Disruption of the integrity of the bone in the surgical area is often associated with prolonged healing, the outcome of which is incomplete or incomplete restoration of bone tissue.

Keywords: odontogenic jaw cysts, cystotomy, cystectomy and two-step operation, platelet-rich plasma, osteoinductive properties.

The upper and lower jaw is often found in the practice of the dental surgeon. To date, effective methods of surgical treatment have been developed, including the use of various osteoplastic materials for filling bone cavities. This applies mainly to small sized cystic formations, when shown precystoectomy, platelet-rich plasma,

Improving the treatment of odontogenic jaw cysts continues to be a pressing problem in surgical dentistry. This is due to the wide prevalence of the disease, the possibility of such complications as cyst suppuration, the development of osteomyelitis, deformity of the jaws, loss of teeth, the occurrence of a pathological fracture and even the so-called central jaw cancer from the epithelium of the cyst wall, as well as frequent relapses after surgical treatment.

Currently, there is no consensus in the literature about the optimal shape of the incision of the mucous membrane of the alveolar margin of the jaw during operations for odontogenic cysts. One of the important tasks of the surgical treatment of peritoneal cysts of the jaws is the preservation of teeth located in the area of the cyst and adjacent to it, the restoration of their full function [1; 2; 4]. The presence of an infected root protruding into the cyst cavity dictates the need to resect the tip of the tooth root simultaneously with the removal of the cyst sheath. Sometimes during the resection of the apex of the tooth root there is a question about retrograde filling of the canal. Currently, there is no consensus in the literature about which filling material should be preferred. At the same time, the frequency of complications associated with poor-quality retrograde root canal filling remains high enough.

In assessing the size of the bone defect formed after the removal of odontogenic cysts, the working classification of abdominal defects of small, medium, large size and extensive [2; 4] was used. The main operative interventions in the treatment of extensive jaw cysts are cystotomy, cystectomy and two-step surgery. Indications for cystotomy are large cysts of the upper jaw, sprouting into the maxillary sinus with the destruction of the bone bottom of the cavity of the bottom and the palatal plate, extensive cysts of the lower jaw with significant thinning of the bony walls of the jaw, the patient's old age or the presence of severe concomitant diseases. Indications for cystectomy are cysts of small size within 1–2 intact teeth, an extensive mandible cyst, in which there are no teeth in its zone and a sufficient thickness (up to 1 cm) of the jaw is preserved, a large cyst on the upper jaw, with preserved bony wall bottom of the nasal cavity and maxillary sinus. The choice of cystotomy or cystectomy in the treatment of extensive jaw cysts is discussed by many authors. Some are supporters of cystotomy, considering that cystectomy is a traumatic operation with the possibility of damage to adjacent intact teeth, damage to the neurovascular bundle, pathological mandible fracture, probability of opening the maxillary sinus and nasal cavity, the possibility of autolysis of a blood clot in the bone cavity [6].

Others advocate cystectomy, arguing that cystotomy is a non-radical intervention in which cavities are formed, defects that require long postoperative care associated with the periodic change of iodoform tampons, sometimes wearing obturators for 1–1.5 years. All this contributes to the deterioration of the cleansing of the oral cavity with the oral fluid and creates conditions for the reproduction of microorganisms. The above, as well as the deformation of the external contours of the face have a negative impact on the quality of life of patients in the early and late postoperative period.

However, after cystectomy, the question arises about the restoration of bone formation with bone-plastic material, since with large bone defects and with suppuration of cysts of the blood clot organization often does not occur, it becomes infected and lysed. The experience of clinical observations showed low efficiency of some materials, especially with significant sizes of bone defects, since they are not always completely replaced by bone, but encapsulated by connective tissue, support chronic inflammation, increase bone resorption or partially rejected [1]. In this regard, the correct choice of osteoplastic materials for filling the bone defect in case of extensive jaw cysts plays a leading role for the favorable rehabilitation of patients.

According to the literature, one of the most effective means of increasing the regenerative capacity of tissues when applied topically, today is the patient's blood plasma, enriched with platelets. According to recent studies, platelets contain high concentrations of growth factors – tissue hormones that initiate regeneration processes:

– **the main growth factor** is β FGF, which affects the growth of all cell types in a wound, stimulates the production of extracellular matrix components, accelerates the processes of angiogenesis, proliferation of capillary endothelial cells, and their migration into collagen;

– **transforming growth factors** – TGF-alpha, actively influencing angiogenesis and TGT –beta, stimulating chemotaxis of fibroblasts and their production of new collagen, elastin and fibronectin fibers;

Growth factors do not exist in the blood in a free form and act locally, being released during the organization of a blood clot (8).

In 1998, R. E. Marx et al. Developed a method for producing platelet-rich plasma (P.R.P.) by centrifuging the patient's blood and applied it in the clinic. P.R.P. effect. based on a high content of growth factors (approximately two orders of magnitude higher than in peripheral blood) and their powerful stimulating effect on the regeneration processes. In particular, in the conditions of the bone wound P.R.P. demonstrates pronounced osteoinductive properties, accelerating the formation and maturation of bone tissue, filling the defect, 1.5–2 times. Not less significantly the drug affects the healing of soft tissue wounds.

The aim of our study was to increase the efficiency of treatment of patients with odontogenic jaws by improving the quality of the examination and preparing the patient for surgery, clarifying the indications for choosing the optimal surgical method of treatment, improving the methods of individual stages of surgery, justifying the use of cystectomy in the surgical treatment of extensive jaw cysts filling the resulting bone defect platelet-rich plasma (PRP).

Material and methods

Despite the differences in the origin of cysts, the clinical manifestations are of the same type and have no symptoms for a long time: growth is slow, painless, functional impairment is not detected. Cosmetic changes occur only when a large tooth-sized cyst reaches, and in cases of keratocyst, which grows, as a rule, along the longitudinal jaw, they are absent, due to which the cyst is detected at a later date. Cysts are sometimes found accidentally when examining a patient for other diseases or if inflammation occurs in the cyst.

During the period 2013–2018, 80 patients with odontogenic cysts of the jaws were under our supervision, of which 35 were classified as extensive. Of the total number of patients with extensive jaw cysts, 15 were women and 20 men aged from 18 to 64 years. Radicular cysts were found in 21 cases, follicular in 9 patients, residual in 5 patients. Extensive cysts on the upper jaw were found in 18 patients, on the lower one in 17.

Complaints of patients with non-suppurative extensive cysts at admission were reduced to the presence of jaw deformities or fistulas on the alveolar process, and 6 patients noted numbness of the lower lip on the lower jaw. With suppuration of cysts, the general condition worsened, patients complained of pain and swelling.

During external examination of patients, deformation of the face was rarely observed. More often, asymmetry of the face was observed in the presence of cysts in the anterior part of the upper and lower jaws. In one patient, during germination of the cyst in the nasal cavity with rhinoscopy, a gerbera roll was observed. In case of non-suppurating cysts, when examined from the side of the oral cavity, in 19 patients the smoothness or protrusion of the rounded shape of the anterior wall of the jaw in the area of the transitional fold was determined. Palpation of the deformities was painless, the vybuchani boundaries are clear. Dupuytren's symptom was observed in 18 patients. In 5 patients with cysts in the region of the large molars of the upper jaw, no visible deformation of the jaw was observed due to the growth of the cyst towards the maxillary sinus. In the case of follicular cysts, the intraoral examination revealed the absence of one or two permanent teeth, and in some cases the presence of milk teeth in adult

patients. If there is a defect in the jaw bone under the mucous membrane, a bone window was palpated, in the center of which the fluctuation was determined.

Diagnosis of odontogenic extensive cysts was performed by puncture biopsy, x-ray examination (orthopantomogram and x-ray of the jaws) and, if necessary, computed tomography. During puncture, cysts obtained opalescent clear fluid. When suppurating a cyst in punctate, pus appeared. The X-ray picture of cysts was characterized by the presence of a site of bone thinning of a rounded shape with clear boundaries. In the case of follicular cysts, the crown of the impacted tooth or the entire tooth is projected into the cystic cavity.

All patients underwent surgery-cystectomy with the filling of the residual bone cavity of platelet-rich plasma (P.R.P). In 19 patients, the operation was performed under local anesthesia (Sol. Ubistesiniforte 4%, Sol.Supercaini 6.0 ml), in 11 under general endotracheal anesthesia.

Cystectomy for all patients was performed by the classical method. Removal of cysts in these cases was carried out according to the type of enucleation. The teeth, whose roots were in the cystic cavity and were of functional value, were preserved. They were previously depulped and endodontic treated. After complete removal of the cystic membrane, the resulting bone cavity was treated with antiseptics and filled with platelet-rich plasma (P.R.P). The wound was sutured tightly.

Results and discussion.

Dynamic observation of patients included, above all, a clinical examination, which was carried out according to the standard technique for 2–7, 14 days, 1,3,6 months later and a year after surgery. X-ray inspection included panoramic radiography of the jaws. On the first day, a pronounced infiltration of the wound edges was observed in 2 patients. Elimination of postoperative edema was observed for 6–7 days. Discrepancy of stitches in the postoperative period was not observed in any case.

With re-examination after 1 month and the follow-up follow-up period, the patients had no complaints, the mucosa in the surgical area was pale pink, without puffiness. On the 6th month, a complete repair of the defect was observed radiologically, however, homogeneity was not observed. Mature organotypical bone tissue was traced along the periphery of the defect. In the central areas, the bone pattern did not show signs of organotypicality: no formed gaversov channels, typical bone pattern, and bone mineralization were observed. In the control X-ray examination after one year, all patients showed complete recovery of the bone defect with an organotypic structure and mineralization. No decrease in the height of the bone tissue was observed in any case, which is very important for the further implantological rehabilitation of patients.

For illustration, we present clinical observation. Patient R., 20 years old, was admitted to the clinic on October 7, 2017. with complaints of swelling of the upper jaw, front and right. He considered himself a patient since May 2017, when he first came to the dental clinic, where a roentgenous maxillary cyst neoplasm was found on the roentgenogram on the right and right, about which the patient was sent to the maxillofacial department of the Bukhara regional multi-field medical center. Locally marked asymmetry of the face, due to swelling of the upper jaw to the right. Skin color has not been changed. On palpation, a tumor was determined, 3 × 4 cm in size, of dense consistency. Opening the mouth was free. There was a swelling in the alveolar process at the level of 11–35 teeth. The mucous membrane is edematous, slightly hyperemic. On a panoramic X-ray image, an enlightenment of the lower jaw bone of an oval shape was visualized, with clear contours, 3.5 × 6 cm in size, emanating from the root of the 13 teeth of the upper jaw.

A diagnosis was made: extensive radicular cyst of the upper jaw, anterior and right (Fig 1). October 8, 2017 under local anesthesia, cystectomy was performed with resection of the apex of the 13th root (Fig 1). After cystectomy, the defect was filled with platelet-rich plasma (P.R.P) (Fig 3, 4) in combination with hydroxyapol. The wound was sutured tightly. The antibiotic Ceftroxan was administered intramuscularly for 5 days in accordance with the accepted daily dosages. The wound healed by first intention (Figure 5).

Figure 1.

Figure 2.

Figure 3.

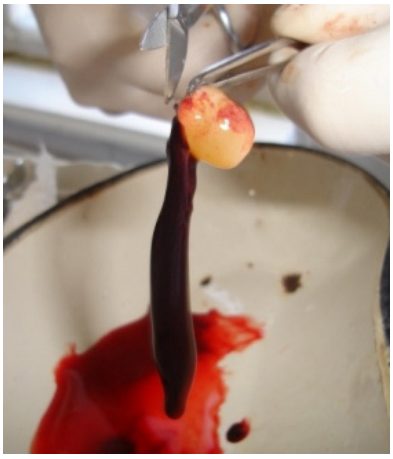

Figure 4.

Figure 5.

Thus, despite the existing contraindications to cystectomy, it can be concluded that extensive odontogenic cysts of the jaws with more than 2–3 intact teeth involved and with thinning of the lower bone wall of less than 1 cm are not a definite indication for cystotomy. The use of correctly selected osteoplastic materials (in our casebased plasma platelet (PRP) in combination with hydroxyapol) helps to restore large bone defects with the formation of organotypical bone, corresponding to the anatomy of this area, in optimal time, which shortens the postoperative rehabilitation period of patients and promotes early functional body load.

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TO THE QUESTION OF ORGAN-SPARING SURGICAL TREATMENT OF UTERINE FIBROIDS ON PREGNANCY

Abstract: As a result of conservative myomectomy, 24 out of 28 women managed to maintain the desired pregnancy. Pregnancy was terminated in 4 patients 12–22 days after the operation in the period of 11–25 weeks. There were no serious complications during the operation and in the postoperative period. All 24 women with retained carried her pregnancy to full-term period, among all, resulting in prompt delivery.

Keyword: uterus, pregnancy, myomectomy.

In choosing the tactics of surgical treatment of MM among pregnant women, perhaps the most important is the introduction of objective arguments on the most discussed issues: what is better, to terminate the pregnancy artificially, to carry out a conservative myomectomy after a while and then allow a woman to become pregnant; the second option may be a conservative myomectomy (CM) against the background of pregnancy with a clinical focus on its preservation; and finally, the third – to use one and the other tactics depending on the model of pathology [5; 6]. However, it requires the creation of comprehensively balanced models of pathology, coordination and consensus on their content among the leading domestic and foreign experts. Otherwise, the whole problem, as before, will be outside the Protocol clinical strategy, which is the basis for the formation of the medical state standard.

Purpose of research. The study of the feasibility, effectiveness, safety of CM in order to maintain the desired pregnancy.

Material and methods of examination. Under our supervision there were 779 patients with uterine myoma in the period from 2001 to 2007, of this number, 86 were women (11.0 per cent) of pregnant women in the period 4–32 weeks. In this group, special attention was drawn to 28(3.6%) pregnant women at gestation from 6 to 26 weeks. All pregnancy was desirable, and this criterion was the main factor in the formation of this sample. In 18 out of 28, pregnancy occurred after long-term treatment of primary infertility. The presence of uterine fibroids before pregnancy was known to 22 women out of 28, the rest she was first identified during this pregnancy. The age of pregnant women ranged from 24 to 32 years, the average-26.7 ± 2.1. All women were registered in the women's consultation, had no severe extragenital pathology. Primipara, including avtomobilnyj, was 21 out of 28 multiparous –7, nagaragawa was not. All 28 patients were admitted with the presence of intramural and intramural-submucous myomatous nodes. At the same time, their value ranged from 4.0 cm to 18.0 cm in diameter, and the number – from 1 to 4. Pregnant women with subserous nodes on the leg, small single asymptomatic myomas, as well as with small-nodular diffuse myometrial lesions, as well as those with irreversible forms of abortion, were not included in the development.

Research result. Among all 28 women, there was an increase in fibroids during the present pregnancy. However, in 11 out of 28, we described it as fast growth for the following reasons. Of these 11 women, 8 were aware of the presence of fibroids before pregnancy, and 3 it was detected for the first time during this pregnancy. The growth of fibroids, exceeding its initial (before pregnancy) size in 2 times was observed in 4 of 8 patients, 3–4 times – in 2, 5 times – in 2. In 3 women with newly diagnosed myoma during pregnancy, the tumor growth recorded in the women's consultation was: 2 times-in 2.3 times-in 1. At the same time, only 2 of 11 revealed growth of nodes with uterine cavity deformation. On the anterior wall and in the bottom of the body of the uterus, the nodes were located in 7 of 11, on the back wall – in 2, on the back and front wall of the body of the uterus – in 2 of 11.

Eating disorders of myomatous nodes, registered clinically in 6 of 28 patients, were verified by histological studies in all without exception episodes. In 5 of 6 patients myoma was monocular, large size (from 6 to 18 cm.), all lay deep, affecting the vascular layer of the myometrium. In 1 of 6 weeks of pregnancy, the size of the tumor in the uterine day reached 18 cm in diameter, exceeding the size originally established during pregnancy by 5 times. During the operation, the perimeter in the area of the outer pole of the tumor was inflammatory and covered with a thin fibrin coating, soldered to the lower pole of the greater omentum. In 5 others, on the background of pregnancy of 15–26 weeks, there was also a rapid growth of monocular tumor in 3 and 4 times compared to the established size in the early stages of this pregnancy. During the operation, the perimetry above the nodes in 3 of these 5 was

cyanotic, but without fibrin plaque, there were obvious foci of softening, areas of hemorrhage, swelling of the myomatous node. None of the 6 cases had purulent complications of eating disorders of myomatous nodes. In 4 of 6 episodes, myomatous nodes were located in the bottom and body along the anterior wall of the uterus, in 1 in the utero-tubal angle on the right, in 1 in the body of the uterus along the posterior wall. The examination in all cases showed moderate leukocytosis to 11.0×10^9 ml., noticeable irritation in the leukocyte formula, subfibrillitis, unevenness of echo density to echonegative foci in myomatous nodes in ultrasound. In 5 out of 6 cases, myomatous nodes were palpated, demonstrating the deformation of the surface of the pregnant uterus, and the most indicative was a symptom of local pain in the area of the myomatous node location.

As a result of surgical treatment, 24 out of 28 women managed to keep their pregnancy to full term, and 4(14.3%) patients (2 with eating disorders of fibroids and 2 with the symptom of rapid growth) had it spontaneously 12–22 days after CM in terms of 11–25 weeks. It should be noted that among these 4 women, the symptoms of threatened miscarriage gradually disappeared in the first 3–7 days after the operation, and they were discharged from the Department under outpatient control. Later, however, on the above date, for unknown to us reasons, once again developed the signs of threats of termination, which failed to stop. All 4 patients were admitted to our clinic again on the background of spontaneous abortion in the course. The miscarriage had no signs of violation of the integrity of the fresh stitches in the uterus (clinical and ultrasound monitoring). All underwent instrumental revision of the uterine cavity after spontaneous abortion under ultrasound control, in which all patients visualized the suture area on the uterus without doubt in its viability. Post-abortion period in all proceeded without significant complications.

In the remaining 24 patients, the dynamics of lysis of the symptoms of threatened abortion (in the near future after surgery) clinically did not differ from that observed among women with interrupted pregnancy. The level of blood loss, duration of intervention, the nature of anesthetic benefits (all women operated under endotracheal anesthesia), also did not differ significantly. At the same time, such factors as the size and number of myomatous nodes, the depth of tumor occurrence in the uterine wall, as well as its proximity to the placenta, significantly distinguished the group of operated pregnant women with interrupted pregnancy.

In 25 out of 28 women, the operation began with a pfanenstiel incision, in 3 – median laparotomy. Conservative myomectomy was done through the cross section of electrocautery of the myometrium in the projection of the greatest convexity of the tumor. In this case, not only the myometrium was dissected, but also the surface part of the tumor, which was captured by bullet forceps for external traction. Carefully, stupidly and acutely performed intracapsular enucleation of myomatous nodes using bipolar coagulation hemostasis. The void tried to take in in a single layer using only the nodal cooperhouse the seams such as peterbourgskaya, and its own method, depending on the depth of the niche and nature occur in a number of cases of "surplus" tissue of the myometrium. Resection of these "surpluses" never produced. Long-term absorbable suture material (vicryl, dexon) was used on atraumatic needles. Intraoperative protection of gestation was carried out by giving antispasmodics (baralgin, no-shpa), intravenous infusion of 25.0% –20.0 magnesia sulfate against the background of basic therapy with tocolytics (ginipral). At the initial stages of the operation, all intravenously administered 1.0 Gy without exception. Ceftriaxone, the appointment of which continued in the postoperative period. In one case out of 28 cases intraoperative plasma transfusion was performed, in none case blood transfusion was required. The level of intraoperative blood loss was dependent on the mass of removed myomatous nodes and the depth of their occurrence, ranged from 150,0 to 600,0 ml., on average 340.0 ± 25.0 ml.

As our sample clinical material shows, the threat of termination of pregnancy was the main symptom that patients received. The frequency of development of this syndrome among pregnant women with uterine myoma varies significantly from 30 to 75% [3; 4; 5; 6]. Probably, the localization, size and number of myomatous nodes in the pregnant uterus affect the frequency and severity of the threat of interruption. In our study, in a significant proportion of pregnant women (50%), the threat of interruption developed in the early stages of gestation. This is most clearly manifested in large (6–18 cm. in diameter) myomatous nodes with intramural localization.

As it was noted in the results of our studies, among 4 women whose pregnancy was terminated 12–22 days after the operation, the symptoms of the threat of interruption in the early postoperative period gradually disappeared, there were no visible complications, there were no blood secretions, ultrasound showed no signs of detachment of the child's place and expressed the threat of interruption. However, the pregnancy they broke off in the above terms. According to our observations, the unfavorable outcome of pregnancy was affected by the depth of occurrence, the number and size of myomatous nodes, as well as the rapid growth of the tumor with eating disorders. It should be noted that the operation in the above conditions in the early stages of gestation (up to 10 weeks), probably also had a negative impact on the outcome of pregnancy. Most researchers recommend CM closer to 16 weeks, because in this period, the placenta has already been formed and the level of progesterone significantly increases. However, in an urgent situ-

ation (eating disorders of fibroids), we were not always able to prolong the pregnancy to the optimum date.

However, in some cases, when removing large myomatous nodes, excessive flaps of the myometrium may form in the outer part of the uterus. Resect them in any case impossible. This consideration arose in the light of the recent fundamental studies of the morphology of myometrium, where the minimum proliferation of myocytes during pregnancy is established, and the growth of the pregnant uterus occurs in the majority of cases of hypertrophy of myometrial cells. Therefore, resection of the resulting excess myometrium can significantly reduce its total mass, which will adversely affect the further course of pregnancy [1]. This phenomenon was also noted in earlier studies, when, after resection of "excessive myometrium", in long-term terms, the uterus significantly decreased in size, resembling an infantile organ [2]. At the same time, in such conditions, the submerged method of niche restoration can significantly deform the uterine cavity, cause an increase in pressure in the cavity of the amnion, rupture of the membranes, detachment of the child's place. Therefore, we have proposed and implemented in their practice a way to restore the niche overlap. In this case, one part of the excess flap falls into the niche cavity, and the second on top of it. Both of the flap shall be attached to the underlying tissues independently for better fixation, hemostasis and reparation. Fears that one part of the flap lies on the perimeter of the contralateral flap were in vain, because the subsequent course of pregnancy and cesarean section showed quite normal retraction of the myometrium layers and repair of the organ without significant deformation of the uterine wall.

Conclusion. Thus, as shown by the practice of working with pregnant women against the background of uterine fibroids, there is a group of women, among whom the traditional conservative treatment to prolong the desired pregnancy is ineffective. Studies have shown that CM, in such conditions, quite effectively allows, in most cases, to maintain the desired pregnancy.

However, despite the very traumatic operation, there were no serious uncontrolled complications that could require urgent termination of pregnancy or hysterectomy. This is essential because otherwise the CM would lose all rational meaning during pregnancy.

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MODIFIED METHOD SURGICAL CORRECTION OF THE RECTOCELE IN WOMEN WITH DYSFUNCTION OF THE PELVIC FLOOR

Abstract: introduction of modified levatoroplasty allowed us to achieve appreciable positive results at surgical treatment of the rectocele in women with dysfunction of the pelvic floor. Also new method in the remote period authentically improves results of surgical treatment.

Keywords: pelvic prolapse, rectocele.

Introduction

The pelvic prolapse is an actual problem of health care and its frequency varies from 8 to 41% among parous women [1; 2] and there was the tendency to increase [3]. High indicators of a pelvic prolapse women contributes to manifestation various pathologies, as rectocele [5; 8]. Operations for a pelvic prolapse make 10–20% of all big gynecologic interventions [3; 6]. Thus a quarter of patients are exposed to repeated interventions in connection with recurrence. Rectocele is a form of a pelvic prolapse with involvement of back wall of a vagina and a forward wall of a rectum [4; 9].

In the past surgical treatment rectocele was directed mainly by elimination of omission of back wall of vagina. Because of insufficient understanding of communication of anatomic support and work of pelvic bodies functional results were not considered in details [5; 9]. Thanks to growth of the elderly population and increase of its activity the measure of productivity of operations extended from exclusively anatomic restoration before improvement of sexual functions and the related quality of life [7].

Traditional way of elimination of rectocele is restoration of a rectovaginal partition by levatoroplasty of various accesses. Operation gives good anatomic effect [2; 6]. However, connected with rectocele the complicated defecation can remain or even to worsen irrespective of existence or absence of recurrence [8].

One of the possible reasons of adverse functional results can be the accompanying syndrome of puborectal muscles at which the superfluous contractility of these muscles interferes with smoothing of an anorectal corner at a defecation, there by complicating it [4]. In that case the lobby of levatoroplasty aggravates functional obstruction of rectum and can lead to the adverse remote results concerning the quality of defecation.

The aim of our research was to study the results of surgical correction of the rectocele in women with dysfunction of the pelvic floor.

Materials and methods: In the 1-republican clinical hospital in the department of Coloproctology were treated 64 women with rectocele. The age of patients fluctuated from 24 to 62 years (average 44.6 ± 5.8 years).

Depending on the way of perineal levatoroplasty the patients were divided into 2 groups: control group with 31 patients passed front levatoroplasty by perineal access by means of two sets of seams, and the main group of 33 women passed levatoroplasty by the modified way offered by us (an improvement suggestion No. 639).

Updating of the way consists in the following (fig. 1): the cross-section of 4 cm dissects skin in the middle to border between mucous vaginas and crotch skin (stage I). The hydraulic dissection of a rectovaginal partition is made by a well-known technique. The sharp way makes mobilization of a forward wall of rectum, back wall of vagina and forward portions of levator on the right and at the left. Beginning from proximal edge of levator 3 seams (maxon, vikril, polysorb 2/0.0) not in the perpendicular direction, and in parallel, i.e. on a course of muscles lifting back pass and 2 seams on an anal sphincter accordingly (by stage II, III) are imposed. An additional number of goffering seams on a forward wall of rectum is not imposed. The perineal wound is restored in the longitudinal direction by central seams, then the increase in distance between vagina and an anus (stage IV) is reached. After that, at rectocele surplus of mucous rectum on a forward semi-circle will be mobilized and reduced to the anal canal (stage V). Excision is made by the mucous surgery of Milligan-Morgan, and edges of the mucous hem to skin of the crotch «П» – figurative seams (stage VI).

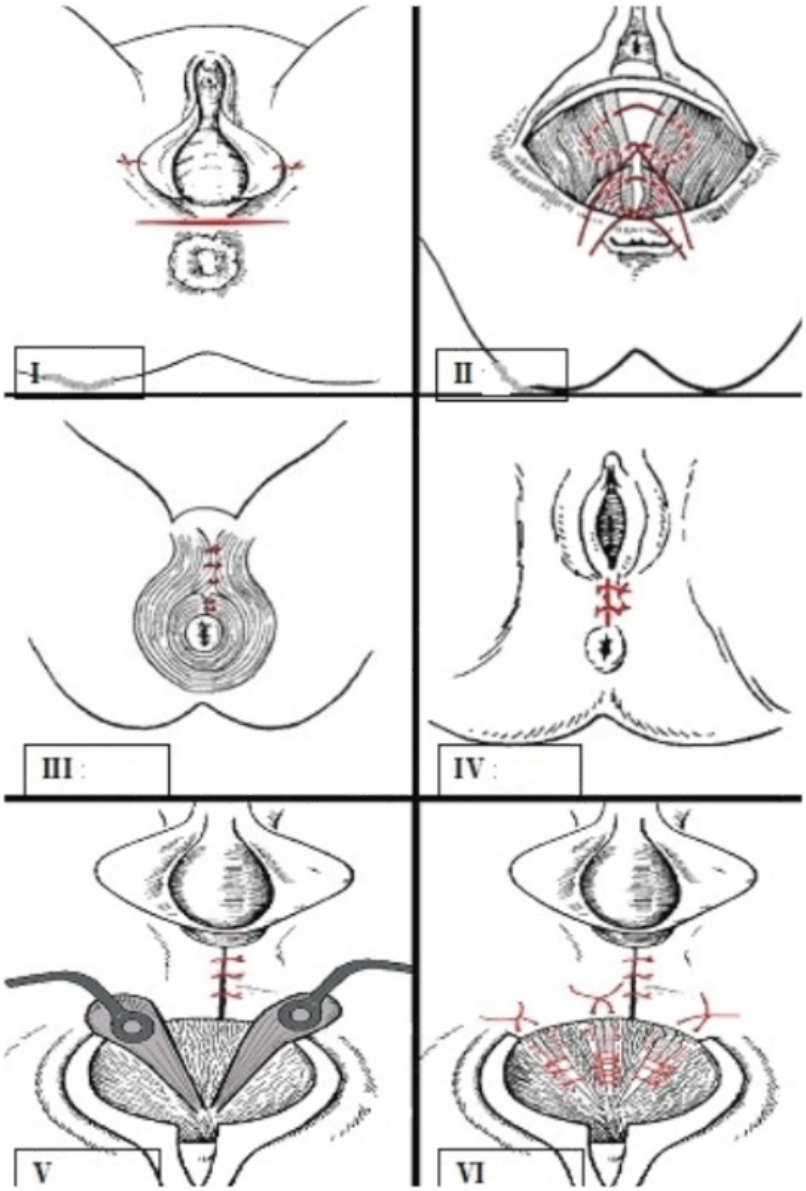

Figure 1. Stages of surgery by the modified way of levatoroplasty

The standard classification of rectocele was used. At rectocele of degree I (there were no such patients) the prolapse of back wall of a vagina does not reach the threshold, at degree II (control group of 19 patients, main group of 21 patients) a prolapse to vagina threshold is available, at degree III (control group of 12 patients, main-12) it falls outside the limits of vagina threshold. Compared groups were represented by age (to t = = 0.304; p > 0,05) and disease stages ($\chi 2 = 1.75$; p > 0.05).

Results of the carried-out inspection were estimated in a complex by the following criteria: good, satisfactory, unsatisfactory: the good – absence of complaints, clinical, radiological and ultrasonic symptoms of rectocele; the satisfactory – a free evacuation of rectum at corrective diet without application of a manual grant, existence of a outpouching of a gut in vagina at the rate to 2 cm according to tool inspections; the unsatisfactory – preservation of the complicated evacuation, use of a manual grant at a defecation, absence of reduction of the sizes of rectocele.

Statistical data processing was carried out on the computer by means of the Excel 7.0 programs. For each series of results calculated arithmetic-mean (M), a standard deviation (σ) and an error of an average (m). Besides, for indicators with the wrong distribution calculated a median. In tables and schedules results are presented in the form of M ± m. For comparison of average sizes used t-criterion Student. For level of reliability of statistics $p < 0.05$ is accepted.

Results and discussions: After surgical intervention at 55(85.9%) patients were not observed earlier revealed outpouching of a wall of rectum in a vagina, at 9(14.1%) the

patients who earlier had the rectocele in the size more than 4 cm, remained outpouching to 2.0 cm, thus at all these anastomosis patients settled down highly (higher than 4–5 cm of the gear line), but violations of an out pouching of a rectum against observance of corrective high-slag diet in the postoperative period was not observed at anybody. Back rectocele and a superfluous crinkle of a mucous membrane of rectum are noted in one case in comparison with indicators before operation.

Results of comparison on duration of operation showed that in control group duration of operation averaged 80.3 ± 5.7 minutes, and this indicator in the main group made 58.3 ± 6.2 minutes ($t = 2.61$; $p > 0.05$). Reduction of duration of operation speaks that at performance modified levetoroplasty is applied single-row seams and without additional goffering seams on a forward wall of a rectum.

Also in the postoperative period duration of days in hospital decreased (7.5 ± 0.5 days in control group and 5.4 ± 0.4 days – the main group; $t = 3.28$; $p < 0.05$) at the expense of reduction of postoperative complications (16.1% in control group and 6.1% – control; $\chi^2 = 1.66$; $p > 0.05$).

Violations of the act of a defecation in all groups of patients were estimated by a locking scale and a control defecography. The moderate locking semiology before operation is revealed at patients of all groups. In control group there was no essential change of an indicator (before operation – 11.2 ± 2.6, after – 13.0 ± 3.1; $t = 0.44$; $p = 0.66$). Essential changes took place in the main group of patients – well-founded from the anatomic point of view levatoroplasty led to sharp decrease in an obstructive defecation that was shown by increase of points on scale of locks (before operation – 10.5 ± 2.8, after – 16.0 ± 3.2; $t = 1.29$; $p = 0.2$). We did not see authentic improvement of quality of a defecation in control group.

As a whole quite good results are received: in control group at 67.7% of patients good results are received, satisfactory – at 22.6% and recurrence is revealed – at 9.7%, and in the main group good results are noted at 90.9% of patients, satisfactory – at 9.1% and recurrence of a disease is noted at one patient ($\chi^2 = 6.13$; $p < 0.05$).

Undoubtedly, in most cases rectocele is operated as anatomic defect, at not expressed functional frustration. Therefore, there is a need in effective anatomic and safe for anorectal function a method of intervention as which we consider modified levatoroplasty.

Thus, introduction of modified levatoroplasty allowed us to achieve appreciable positive results at surgical treatment of the rectocele in women with dysfunction of the pelvic floor. Also new method in the remote period authentically improves results of surgical treatment.

Conclusions

1. The technique offered by us in comparison with traditional methods authentically reduces days in hospital (7.5 ± 0.5 days in control group and 5.4 ± 0.4 days – the main group; $t = 3.28$; $p < 0.05$) and postoperative complications (16.1% in control group and 6.1% – control; $\chi^2 = 1.66$; $p > 0.05$).

2. The new method in the remote period authentically increases good results (in control group – 67.7% and basically – 90.9%) and sharply reduces disease recurrence.

3. This way is universal and can be offered for operative treatment of the disease, in particular rectocele and a postnatal rupture of a rectovaginal partition with insufficiency of an anal sphincter.

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REASONS OF FUNCTIONAL DISTURBANCES AFTER RHINOPLASTIC DEPENDENCE ON SURGICAL ACCESS, TECHNOLOGY AND VOLUME OF OPERATION

Abstract: The aim of this research was to study the reasons of functional disturbances after rhinoplastic dependence on surgical access, technology and volume of operation. We were operated 54 patients with deformity of the skeleton of the external nose in the period from 2015 to 2017. Open osteotomy was applied in 38 patients who needed correction of both the bone and cartilage sections of the external nose. In closed osteotomy (16 patients), we used lateral vestibular access. The study showed that to achieve a good result after endonasal intervention on the intranasal structures in combination with rhinoplasty, an important fact is the adequate management of patients in the postoperative period, with careful carrying out the necessary therapeutic and preventive measures.

Keywords: rhinoplasty, surgical access, septoplasty, closed osteotomy, mucous membrane.

Recently, many have shown interest in rhinoplastic operations, while at the same time trying to eliminate the deformity of the external nose and do not pay attention to the preservation or restoration of the functions of the nasal cavity and paranasal sinuses. It must be borne in mind that when performing rhinoplasty, in addition to cosmetic tasks, it is also necessary to solve more complicated task – restoration of the functions of the nasal cavity. Therefore, aesthetic operations in the area of the external nose should be performed by otorhinolaryngologists, who also have endonasal surgical procedures [1; 3; 6].

Abroad in many countries, this situation has been corrected, and now, for example, in the United States, about 85% of rhinoplasty is performed by otorhinolaryngologists, who simultaneously perform intranasal operations to restore respiratory function and restore the shape of the nose [2].

Starting to master rhinoseptoplasty, the surgeon should master the skills of several related specialties: plastic surgery, maxillofacial surgery, thoroughly study the anatomy of both the bone and cartilage sections of the pyramid of the nose, know the features of reparative processes in the bone, cartilage tissue, skin and subcutaneous tissue. It is simply impossible to do rhinoseptoplasty badly, since repeated operations will be much more complicated [4].

Under our supervision there were 68 patients who underwent rhinoplasty. When comparing the results of the examination of patients operated on with various surgical approaches, it turned out that nasal breathing disorders were significantly more frequent after the "endonasal" technique (65%) than after the "open" rhinoplasty (48%) [5].

We have found the connection of functional disorders after rhinoplasty with the volume of the operation. In order to assess the dynamics of the disease after the operation, we used the method of visual assessment of symptoms. To do this, patients before the operation were offered to fill in special cards in which they noted the severity of the main symptoms (nasal breathing, nasal discharge, headache) on a 10-point scale.

When comparing patients in whom one-stage with rhinoplasty was performed various intranasal interventions (conchoplasty, septoplasty) and patients who had exclusively rhinoplasty, the functional result of the intervention was significantly better in the first group (5.3 ± 1.5 points and 9.2 ± ± 1.3 according to the subjective assessment of patients, respectively).

A significant proportion of patients (71%) who have undergone aesthetic rhinoplasty have a significant impairment of nasal breathing. The main causes of postoperative nasal obstruction are insufficiency of the nasal valve (65%), curvature of the nasal septum (61%), hypertrophy of the lower nasal concha (35%), synechia of the nasal cavity (8%), bulls of the middle nasal conchae (4%).

Unlike the function of nasal breathing, the state of mucociliary transport in patients undergoing rhinoplasty does not significantly suffer (the time of mucociliary transport is 17 ± 2.8 versus 16 ± 2.9 ($p > 0.05$). Signs of impaired sense of smell have been detected in some patients only early postoperative period.

In 60% of patients undergoing aesthetic rhinoplasty, is detected a violation of local innervation in the form of hypoesthesia. With the course of the postoperative period, the severity of neuralgic disorders decreases, but in 3% it persists with long-term follow-up. The most significant changes are observed in patients after open access, resection of the base of the wings and lateral endonasal osteotomy.

Nasal breathing disorders are significantly more common after endo-nasal surgical access (55%) than after open rhinoplasty (48%). In a one-step rhinoplasty and intranasal intervention (conchoplasty, septoplasty), the functional result of the intervention is significantly better (5.8 ± 1.5 points versus 8.9 ± 1.3 by subjective assessment.

Functional impairment after rhinoplasty is usually associated with the size of the operation. When comparing patients in whom one-stage with rhinoplasty was performed various intranasal interventions (conchoplasty, septoplasty) and patients who had exclusively rhinoplasty, the functional result of the intervention was significantly better in the first group (6.2 ± 1.5 points versus 8.9 ± 1.3 by subjective assessment.

The main types of osteotomy are: lateral, medial, and paramedial. Depending on the tasks of the operation and the features of the structure of the bone pyramid of the nose, we use all these types of osteotomies, often combined. For better mobilization of the nasal bones before performing the lateral we carry out a medial oblique or paramedial osteotomy. We do not connect the lines of the medial and lateral osteotomies, trying to break the bone bridge in the "green line" type.

In principle, there are two methods for performing osteotomy – open and closed. We were operated 54 patients with deformity of the skeleton of the external nose in the period from 2015 to 2017. Open osteotomy was applied by us in 38 patients who needed correction of both the bone and cartilage sections of the external nose. The advantages of the open technique are that the access to the structures of the nasal dorsum is maximal and the manipulations are performed under visual control. Another distinctive feature of open osteotomy is the possibility of controlled displacement of the bones of the nose with respect to the nasal septum and the correction of the latter, if necessary, without additional incisions.

In closed osteotomy (16 patients), we used lateral vestibular access. Traditionally, we performed an osteotomy with special chisels (2 mm) with stops, starting from the edge of the pear-shaped hole below the anterior end of the lower turbinate. In this case, the likelihood of damage to the nasal mucosa along the osteotomy line is minimal. When using 4 mm bits, the risk of intraoperative complications is markedly increased. So, 2 patients had damage to the nasal mucosa (which led to a slight narrowing of the anterior valve of the nose in one of them), in 1 – a step-like deformation of the nasal pyramid.

A good cosmetic result was achieved in 50 patients. We believe that in patients with distortions of the osseous part of the external nose, closed osteotomy should be dominated by lateral vestibular access, open osteotomies are indicated with combined pyramid deformations.

The main stages of the postoperative period. The final stage of rhinocorrection is the closure of the operative wound, immobilization and fixation of the intra- and extranasal structures. Stitching the wound was performed with frequent and accurate absorbable sutures, with careful adaptation of the edges. After precise suturing, there remains a thin scar that does not deform the skin and mucous membrane, the external valve structure of the nose in the postoperative period. After suturing, intranasal structures were fixed. Fixation of the nasal septum in a strictly medial position and hemostasis were achieved by installing plastic tubes of appropriate diameter and length along the bottom of the nasal cavity with a nonlengthening tamponade with special hydrophilic spongy tampons made from self-expanding oxycellulose. Such a tamponade is more easily tolerated by patients, protects the wound from infection, contributes, due to light pressure exerted from the nasal cavity, gluing tissues, reduces the possibility of hemorrhages and hematomas, keeps the reconstructed structures in the right position. The presence of plastic tubes, in addition to fixation, provides air through the nose, protecting the oropharynx from excessive drying. After all corrective manipulations, a plastering bandage is applied to fix the skin on the reconstructed pyramid of the nose. Immobilization of extranasal structures was carried out by applying a plaster cast, modeling it so that it covered the entire nose from its root to the tip and wings, and it should be smooth from the inside and exert a uniform slight pressure on the nose. Analysis of the data of the observed patients and clinical experience revealed that the postoperative course after single-stage rhinoplasty and endonasal correction of the intranasal structures has important criteria and features that need to be discussed in more detail. Immediately after surgery, the period of recovery of the epithelium of the nasal cavity begins. This stage is crucial for the complete healing of defects of the mucous membrane, affects the results of endonasal intervention, and therefore requires close attention in the postoperative period. Inadequate management of patients in the postoperative period can cause new pathological changes in the nasal cavity, which can cause relapses that are worse to treat than the primary disease. As noted, immediately after the operation, a tampon of self-expanding cellulose is inserted into the middle nasal passage. At the same time, it is necessary, if possible, to separate all contiguous de-epithelized wounded surfaces – the septum and the middle shell, or the middle shell and the lateral wall of the nose. Minor bleeding in the postoperative period, especially after removal of tampons on the third or fourth day after the operation, leads to the formation of blood clots in the nasal cavity, which then dry out, forming massive scabs. Due to the lack of mucociliary clearance, mucous secretions from the open sinus dry out and form yellow-brown crusts that adhere to existing defects of the mucous membrane. Then, in the following days, granulations are formed at the

sites of these defects. Most of the sero-mucous wound discharge accumulates at the bottom of the nasal cavity and in the paranasal sinuses. On the mucous membrane of the nasal concha, fibrinous deposits are often formed, significantly complicating nasal breathing. Until the mucociliary system begins to function adequately, the secretions of the respiratory epithelium will dry out and form crusts. Even small damage to the epithelium can lead to bleeding with the formation in the postoperative period of adhesions between the mucous membranes. After a few days there are sometimes quite extensive swelling. They are due to impaired lymphatic drainage and can last up to 4 weeks after the intervention. The edema of the mucous membrane, to a greater degree, is expressed in the region of the lower and anterior edges of the newly formed or expanded anastomosis in the middle nasal passage, may be similar to small polyps. In narrow places, edema can even cause occlusion of the anastomosis, accompanied by pain. X-ray examination to determine the tactics of further treatment, at this stage of the postoperative period, is impractical, since the inflamed edematous mucosa of the paranasal sinuses will darken the X-ray, and can lead to incorrect hyperdiagnostic conclusions. According to many authors, and based on clinical experience, the final results and the effectiveness of endonasal intervention should be more correctly based on the CT data of the study, moreover, carried out not earlier than 2–3 months after the intervention. Within a week after the intervention should be performed a thorough toilet of the nasal cavity; only lumps and mucus from the vestibule, the bottom of the nose and the middle nasal passage should be carefully removed. For this purpose, a straight metal suction is used, allowing the finger to precisely control the force of aspiration. Damage to the mucosa should be avoided by coarse insertion of the suction tip or aspiration from areas of the loose mucosa. To remove exudates dried in the form of crusts, scabs or fibrinous plaque, cranked or bayonet-shaped tweezers are suitable. Already at this stage, it is recommended to carry out postoperative therapy under endoscopic control. The use of endoscopy helps prevent injury to the regenerating parietal mucosa, effective cleaning is provided by gentle aspiration, and a small retractor or exciting forceps are suitable for removing large patches of crusts and crusts. Care should be taken to avoid additional damage to the epithelium, since bleeding from the mucous membrane is the result of too rough manipulation. During the first week after surgery, the restoration of the epithelium is just beginning. During this period, all emerging cicatricial adhesions in the nasal cavity should be removed, sucking the contents and removing crusts and deposits. Particular attention should be paid to the formation of adhesions between the de-epithelized areas of the mucous membrane, namely, the middle turbinate and the nasal septum, the middle turbinate, and the lateral wall of the nose. It is here that the contiguous wound surfaces are often glued to each other by fibrin bridges, which within 10–12 days turn into fibrin cicatricial synechia. In many cases, these synechias lead to obstruction of even, sufficient in size, fistula of the maxillary sinus and, ultimately, to a violation of the outflow from the frontal and ethmoid sinuses. This leads to accumulation of secretions in these cavities. In addition, a pronounced narrowing of the labyrinth of the ethmoid bone leads to partial or complete cicatricial obliteration, fibrin bridges from these areas should be carefully removed by suction or cross them. After gentle removal of crusts and blobs and suction of secretions, to accelerate the recovery of the epithelium, and in order to facilitate the cleaning process, it is recommended that the nasal cavity be moistened with saline or isotonic saline. In special cases, it is recommended to use low viscosity ointments, gels or drops containing antibiotics and corticosteroids. All this helps cleanse and heal the wound, destroying the fibrin layer and clotted blood, and also has an anti-inflammatory effect on the edematous mucosa. Instilling a saline solution into the nose or using a nasal spray from an isotonic sea salt solution prevents the secretions from drying out and dissolves adhesions between the surfaces covered with mucous membrane, increases the level of secretion in the goblet cells, thus stimulating mucociliary clearance. After the early postoperative stage, which lasts approximately two weeks, there is a late postoperative period. Hyperplasia and granulation of the mucous membrane gradually begin to decrease, but the swelling may persist for several weeks or months. Mucociliary clearance, which is known to be a criterion for restoring the function of the mucous membrane of the nasal cavity and paranasal sinuses, usually returns to normal only 2–4 months after surgery. In the late postoperative period, granulations, tissue proliferation and sometimes small polyps can occur. In addition, again may increase mucosal edema. Regular implementation of the endonasal examination and the toilet allows you to timely detect such changes and monitor the condition of the nasal cavity and lumen of fistulas. One of the main late complications is the formation of cicatricial adhesions between the middle shell and the lateral wall of the nose. To prevent the formation of pronounced synechia on the front of the middle turbinate, it is necessary to clean the fibrin strands, and when synechia are formed, it is enough to excise the scars with a nasal scissors or an appropriate scalpel. In order to avoid recurrence of the formation of synechiae, it is necessary to periodically insert within 8–10 days small fragments of tampons from self-expanding hydroxycellulose between the contacting wounded surfaces. In the late postoperative period, you need to continue drug therapy. To moisten the mucous membrane, the patient is recommended to

regularly instill into the nose a saline solution, an isotonic solution of sea water. In addition to the moisturizing effect, this type of irrigation allows you to effectively clean the mucous membrane. According to the authors, the ionic concentrations of sea salt solutions enhance the function of cilia, which improves mucociliary clearance. At this stage of treatment, as an adjuvant therapy, you can regularly irrigate the nasal mucosa with oil drops, olive or sesame oil. After endonasal interventions, swelling of the mucous membrane can last for several weeks. The epithelium covering the wound sites is initially thickened and has an uneven, undulating surface. The epithelium is very easily damaged during the recovery phase, so any unnecessary manipulations should be avoided. A staged endoscopic examination of the nasal cavity, as well as through the extended fistula, and the operated sinus, revealed that only a few months after the intervention, the wound surfaces completely epithelialized, and the nasal mucosa and paranasal sinuses acquire a smooth surface. The ciliated epithelium, however, is not represented everywhere, since some areas are covered by stratified squamous epithelium. However, in this period, there is no longer any risk of restenosis of fistulae or the formation of synechias and obliterations. Maintaining patients after single-stage rhinoplasty and correction of the intranasal structures in relation to the pyramid of the external nose, also has important steps and features. The plaster cast is removed on the 7th day after the intervention. Then a re-bandage was applied, if necessary, also a plaster bandage. Postoperative puffiness and thickening of the nasal tissues decrease and disappear by the end of 2–3 weeks and depend on the volume of surgical intervention and rehabilitation capabilities of the body. Hypersensitivity and soreness to pressure decreased by the 4th week after the operation, the tightening of the nasal tissues was observed within 2–3 months. After the disappearance of pain, if necessary, in order to restore the mobility of the skin and the prevention of coarse subcutaneous scarring, a gentle massage, often performed by the patient himself, was recommended.

Thus, to achieve a good result after endonasal intervention on the intranasal structures in combination with rhinoplasty, an important fact is the adequate management of patients in the postoperative period, with careful carrying out the necessary therapeutic and preventive measures. It should be noted that in the preoperative period, at the planning stage of the intervention and discussion with the patient of the plan and algorithm of surgical treatment, it is necessary to inform the patient in detail about the main stages of the postoperative period, the phases of postoperative wound healing, and his health during this period. Full mutual understanding and agreement between the patient and the operating surgeon will make it possible to successfully complete the difficult stage of the postoperative period and overcome all the difficulties of rehabilitation.

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STUDYING THE CONDITION OF ACOUSTIC STEM POSSIBLE POTENTIALS IN PATIENTS WITH OTOSCLEROSIS

Abstract: The aim of this research was to study the characteristic changes in acoustic brainstem waves caused by potentials in patients suffering from otosclerosis in order to assess the functional state of the auditory analyzer pathways. 100 patients suffering from otosclerosis were studied. The age of patients ranged from 30 to 50 years. Depending on the side of the lesion involved in the otosclerotic process, the patients were divided into 2 groups: group 1 was 65 patients with bilateral otosclerosis, group 2 was 25 patients with unilateral otosclerosis. The study showed that the patients with otosclerosis have abnormalities in the conductive component of the auditory analyzer, which is confirmed by the results of the study of acoustic brainstem evoked potentials. In a two-sided process, changes are observed at the latency amplitude of all acoustic brainstem evoked potential waves. Whereas with a one-way process, changes in the latency and amplitude of the IV and V waves were not observed.

Key words: otosclerosis, acoustic brainstem evoked potentials, otoacoustic emission, auditory analyzer pathways.

The problems of complex diagnostics and treatment of patients with otosclerosis do not lose their relevance [2; 3; 4]. For many years, the state of various parts of the auditory analyzer in patients with otosclerosis has not lost its relevance. There are suggestions that otosclerosis is a degenerative process that affects the entire organ of hearing. But this question requires more detailed research and evidence. In the literature, science-based work in this direction is not enough.

In this regard, it was of interest to study the functional state of the auditory analyzer pathways in patients with otosclerosis.

The study of the functional state of the conducting pathways of the auditory analyzer in patients with otosclerosis will clarify its pathogenesis, which contributes to the improvement of diagnostic methods and complex treatment of this pathology.

To date, the existing arsenal of modern medical equipment, provides an opportunity to study the functional state of the auditory system throughout its length. Acoustic brainstem evoked potentials [1, 6, 12] have proven themselves to objectively assess the functional state of the auditory analyzer pathways. The study of acoustic brainstem evoked potentials shows the state of the longest portion of the auditory analyzer. In particular, acoustic brainstem evoked potentials are far-field potentials and reflect the state of the auditory stem nuclei of different levels and the state of the auditory nerve [5].

Acoustic brainstem evoked potentials, being the earliest response potentials for the auditory stimulus, have a typical morphology. Peaks or waves appear in the responses. Each wave corresponds to an excited neuron in specific nuclei of the auditory path. Peak I and II come from the auditory nerve, peak III comes from the cochlear nuclei. Peak IV is produced in the olive complex and V- in the lateral lemniske [10]. Waves appear at a certain latency of the corresponding stimulus intensity. The lower the intensity, the longer the latency. When high intensity neurons are excited faster, it means that synaptic transmission is faster. This leads to a shortening of latency. Thresholds of acoustic brainstem evoked potentials correlate well with subjective tonal audiometry, which has been proven by many studies [13; 14].

Changes in acoustic brainstem evoked potentials are more specific than other modalities. Using the study of acoustic brainstem evoked potentials, it is possible to identify a lesion of the peripheral link of the auditory analyzer, the auditory nerve, stem structures, regardless of the age and degree of contact of the patient.

Thus, the study of the functional state of the auditory analyzer pathways in patients with otosclerosis will reveal new aspects of the pathogenesis of this disease.

Purpose of the study. To study the characteristic changes in acoustic brainstem waves caused by potentials in patients suffering from otosclerosis in order to assess the functional state of the auditory analyzer pathways.

Materials and methods. 100 patients suffering from otosclerosis were studied. The age of patients ranged from 30 to 50 years. The average age of 39.2 ± 8.6 years.

Depending on the side of the lesion involved in the otosclerotic process, the patients were divided into 2 groups: group 1 – patients with bilateral otosclerosis – 65 patients, group 2 – patients with unilateral otosclerosis – 25 patients. At

the same time, patients with a tympanic form of otosclerosis were selected to exclude the influence of the inner ear, which occurs when its form is mixed.

The control group consisted of 20 volunteers between the ages of 30–45 years old, with normal hearing (according to tonal threshold audiometry), who did not show any pathological changes during otoscopy, tympanometry – type "A" from two sides, delayed induced otoacoustic emission is recorded with both sides. An individual analysis of wave parameters of acoustic brainstem evoked potentials in patients was performed under the condition of counting the intensity of the stimulating signal from the hearing threshold of each patient (dB SL). In the control group, acoustic brainstem evoked potentials were estimated by sending tone bursts 40 dB SL above the threshold. For a given above-threshold volume of a stimulus, all waves of acoustic brainstem evoked potentials are distinguished.

The registration of the auditory evoked potentials was carried out on the Neuro-Audio apparatus (Neurosoft, Russia), in conditions of the patient's calm wakefulness. Patients in the study were in a reclining position.

The analysis of acoustic brainstem evoked potentials was performed at the end of the test using the function of marking the peaks of acoustic brainstem evoked potentials, measuring the amplitude of the selected peaks, fixing the FMP (Feature Modeling Plug-in) parameters, fixing the number of runs required to achieve 99% probability of signal reliability.

According to the results of the study, the smallest number of runs to obtain a reliable response is required when using the Chirp-stimulus with a frequency of 1000 Hz (Samkova).

Monaural acoustic stimulation was performed using 1000-Hz Cirp-stimulus headphones. The intensity of the stimulus was chosen individually at the rate of 40 dB above the subjective threshold and ranged from 100 to 120 dB. The frequency band is from 0.5 to 100 Hz, the number of averagings is 2000, the epoch of analysis is 10 ms. The response of acoustic brainstem evoked potentials was recorded during ipsilateral monaural stimulation. Allocation was carried out according to a single-channel scheme, with the location of the active electrodes at the ipsi-M1 point (mastoid of the side under study), the reference electrode – at the contra-M2 point (contralateral mastoid), grounding – Fpz. The study was carried out according to the parameters recommended by the manufacturer (N. Y. Shubina et al., 2013). The absolute latencies of peaks I, II, III, IV, V, peak intervals I – III, III – V, I – V, amplitudes of peaks I – Ia, III – IIIa, V – Va were analyzed.

Patients were enrolled after receiving informed consent for this procedure.

Results of research. The study revealed that in patients with otosclerosis, there is a general shift in the curve of acoustic brainstem evoked potentials to the right.

In the first group, an increase in the absolute latency of all the waves was observed, as well as an increase in the interpeak intervals between all the waves of the acoustic brainstem evoked potentials. In the second group, the absolute latency of all waves was also increased compared with the control group. The peak interval, unlike the first group, increased in the interval I – II and II–III, and the peak interval III–IV and IV – V did not differ from the indicators of the control group (Table 1).

Table 1. – The latency parameters of acoustic brainstem evoked potentials in patients with otosclerosis (M±σ)

Parameters		Control group	1-group	2 – group
Peak latency, ms	I	1.83 ± 0.14	2.48 ± 0.15*	2.38 ± 0.14*
	II	2.81 ± 0.1	3.63 ± 0.19*	3.56 ± 0.17*
	III	3.97 ± 0.16	4.91 ± 0.13*	4.9 ± 0.13*
	IV	5.12 ± 0.12	6.26 ± 0.21*	6.02 ± 0.18*.**
	V	5.83 ± 0.17	7.39 ± 0.17*	6.76 ± 0.16*.**
Inter-peak interval, ms	I–II	0.98 ± 0.12	1.15 ± 0.06*	1.18 ± 0.06*
	II–III	1.16	1.28*	1.34*
	III–IV	1.15	1.35*	1.12**
	IV–V	0.71	1.13*	0.74**
	I–V	4.0	4.91*	4.38*.**
	I–III	2.14 ± 0.13	2.43 ± 0.11*	2.52 ± 0.11*
	III–V	1.86 ± 0.17	2.48 ± 0.11*	1.79 ± 0.13**

**– statistically significant changes compared with the control group ($p < 0.05$);*

*** – statistically significant changes compared with the 1 – group ($p < 0.05$)*

So, if in the control group the latency of the I, III and V waves was 1.83 ± 0.14, 3.97 ± 0.1 and 5.83 ± 0.16 ms, among patients of the 1st group, these figures were 2.48 ± 0.15, 4.91 ± 0.19 and 7.39 ± 0.13 ms, and among patients of the 2nd group 2.38 ± 0.14, 4.9 ± 0.17 and 6.76 ± 0.13, respectively.

In this case, the peak intervals I–II and II–III, in the control group were 0.98 ms and 1.16 ms. In the first group, these figures significantly increased to 1.15 ms and 1.28 ms, while in the second group, a significant increase was also observed to 1.18 ms and 1.34 ms, respectively. Inter-peak intervals III–IV and IV–V differed in the two examined groups. So, if in the control group these figures were 1.15 and 0.71 ms, in the first group there was an increase to 1.35 and 1.13 ms, whereas in the second group these figures did not differ from the control group, amounting to 1.12 and 0.74 ms, respectively.

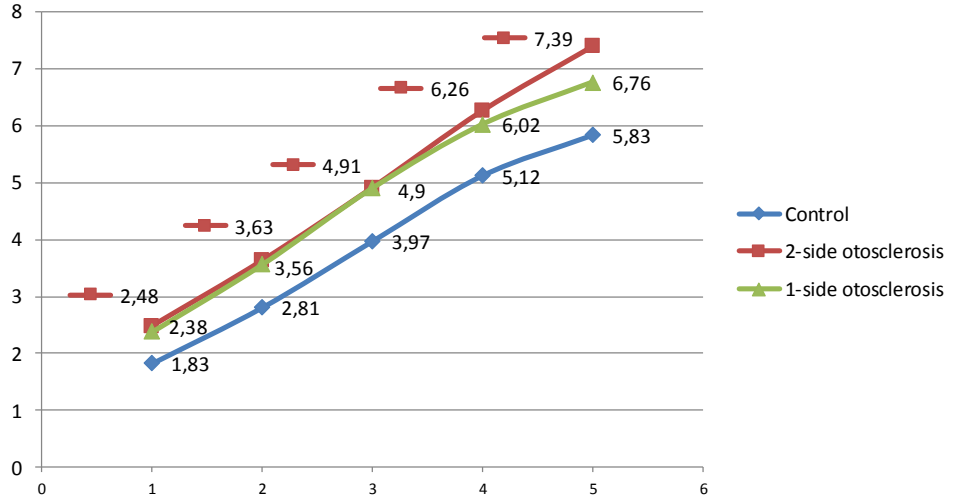

Figure 1.

Wave latency curves of acoustic brainstem evoked potentials in the control group and patients with otosclerosis.

Figure 1 shows how there is a shift in the curve of the acoustic brainstem evoked potentials to the right, and the differences in its IV and V waves.

Thus, the peak interval I–II and II–III were equally extended in both groups compared to the control, whereas intervals III–IV and IV–V were significantly increased compared to the control only in patients of the first group, and in the second group these indicators did not differ from control. Intervals III–IV and IV–V in the first and second groups differed significantly among themselves.

When assessing the amplitude of the waves, we paid attention to the detection threshold of the V wave in the control group and in the examination groups. It was revealed that in the control group the threshold of detection of the V wave corresponded to the threshold of hearing, which was detected during a tone audiogram. In patients with otosclerosis, the threshold for detection of the V wave acoustic brainstem evoked potentials was increased by 20–25 dB, i.e. All waves of acoustic brainstem evoked potentials in the control group were distinguished when the threshold was increased by 20 dB above the threshold of the audiogram, and in patients with otosclerosis only with an increase of 40 dB above the patient's hearing threshold. This indicates a sharp decrease in wave amplitude. A comparative analysis of wave amplitudes was carried out with an increase in the stimulus of 40 dB above the patient's hearing threshold.

In the first group, a statistically significant decrease in the amplitude of all waves was observed. Thus, the amplitude of waves I–Ia and III–IIIa in the control group was 0.13 μV and 0.36 μV, in the first and second groups these figures were reduced, and in the first group they were 0.056 and 0.18 μV and in the second group 0.059 and 0.18 μV, respectively. The amplitude of the V–Va wave in the control group was 0.47 μV, while there was a difference in the groups, i.e. if in the first group the amplitude of the V–Va wave was 0.34 μV and was significantly different from the control group, in the second group this indicator was 0.45 μV and did not differ from the control group (table 2).

Table 2. – Wave amplitude parameters of acoustic brainstem evoked potentials in patients with otosclerosis (M ± σ)

Parameters		Control group	1-group	2-group
Peak amplitude, μV	I–Ia	0.13 ± 0.02	0.056 ± 0.02*	0.059 ± 0.01*
	III–IIIa	0.36 ± 0.05	0.18 ± 0.04*	0.18 ± 0.04*
	V–Va	0.47 ± 0.03	0.34 ± 0.05*	0.45 ± 0.05**

** – statistically significant changes compared with the control group ($p < 0.05$);*

*** – statistically significant changes compared with the 1-group ($p < 0.05$)*

Discussion. The main changes identified in the study of acoustic brainstem evoked potentials in otosclerosis was to increase the latency and decrease the amplitude of the peaks.

An increase in acoustic brainstem evoked thresholds indicates that the number of functioning axons and neurons is decreasing. When comparing the amplitudes of the waves, a significantly smaller amplitude of all the waves of acoustic brainstem evoked potentials in patients with otosclerosis was also revealed.

The decrease in activation of the auditory nuclei caused by otosclerosis can be interpreted as a reduced stimulation of the activation of neurons.

There was interest in changes in acoustic brainstem evoked potentials in a one-way process, since it is known that the auditory pathway has a cross. Most of the axons II of the neuron, which, on the curve of acoustic brainstem evoked potentials, constitutes the third wave, switches to the opposite side, switching in the upper olive and the nuclei of the trapezoid body. Another, smaller part of the fibers ends on its own side. The axons of the nucleus of the upper olive and trapezoid body (III neuron) are involved in the formation of the lateral loop, in which there are fibers of the II and III neurons.

The main differences in the two groups were observed on the latency of the IV and V waves, as well as on the inter-peak intervals I–V and III–V.

With conductive hearing loss, the time required to transmit sound along the middle ear and activate the cochlea increases. The total amount of sound energy reaching the cochlea decreases. Consequently, the latency of wave I is inhibited, and the curve of the intensity of the latency of wave V shifts to the right by an amount equivalent to hearing loss, without any change in the slope of the curve. Since the latency of wave I is extended longer than the latency of wave V, the interval between intervals V–I is reduced [9]. But according to the results of our study in patients with bilateral otosclerosis, we observed an increase in both absolute and relative latency of all waves.

The data from the study show that a decrease in peripheral auditory stimulation in itself is detrimental to the efferent and afferent innervation of the hair cells in ways similar to that observed with age-related and noise-induced hearing loss. The mechanisms underlying cochlear deefferentation, according to the authors, indicate a decrease in cholinergic stimulation in the auditory nerve to the level of the olycochlear complex, which is confirmed by experimental studies [8].

The reasons for these changes can be explained by experimental studies. In the study of the metabolic activity of the auditory nuclei through the measurement of the absorption of 2-deoxyglucose, experimental conductive hearing loss led to a marked decrease in its absorption [15]. In another study, there was a significant decrease in the activity of cytochrome oxidase in conductive hearing loss in the ipsilateral anteroventral cochlear nuclei [16].

In addition, according to other authors, with experimentally induced conductive hearing loss, a decrease in vGluT1 expression in the presynaptic terminal, a decrease in the size of synaptic vesicles, and an increase in the thickness of the postsynaptic membrane in the cochlear nucleus were found [7]. Conductive hearing loss also led to a decrease in the number of synchses of the cochlear nerve in the cochlear nuclei [11].

Thus, the resulting changes in the waves of acoustic brainstem evoked potentials in our study indicate the presence of functional changes in the conductive segment of the auditory system in patients with otosclerosis.

All these changes result from a lower rate of activation of distribution in afferent pathways and a delayed reaction to cortical and subcortical levels. It is possible that the decrease in the amplitude of the acoustic stem waves evoked potentials is a consequence of prolonged deafferentation, which leads to a decrease in the nuclei in the stem structures of the auditory tract [12].

Findings:

1. Patients with otosclerosis have abnormalities in the conductive component of the auditory analyzer, which is confirmed by the results of the study of acoustic brainstem evoked potentials.

2. In a two-sided process, changes are observed at the latency amplitude of all acoustic brainstem evoked potential waves. Whereas with a one-way process, changes in the latency and amplitude of the IV and V waves were not observed.

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CASE OF BLEEDING FROM THE INTERNAL CAROTID ARTERY WITH A LETHAL OUTCOME

Abstract: The aim of this research was to present a clinical case of profuse nasal bleeding associated with a complication of invasive fungal sinusitis, leading to arrosive bleeding from the internal carotid artery. The study showed that the observation confirms once again the need to provide close attention and conduct an in-depth examination in the first episode of nasal bleeding, especially when it is not revealed its source and the presence of destruction of the bony walls of the nasal cavity and paranasal sinuses to consider as a potential potential cause of profuse bleeding.

Keywords: nasal bleeding, internal carotid artery, fungal sinusitis, nasal cavity and paranasal sinuses.

Nasal bleeding (NB) ranks first in frequency among spontaneous bleeding and is one of the most common indications for emergency hospitalization (up to 20.5% of all urgent conditions) [1]. Bleeding of this localization is controlled with difficulty and in 7–10% of observations lead to fatal outcomes. The causes of NB are not always obvious. As a rule, these bleedings are single, but in 4% of cases they are persistent and recurrent, representing a real threat to the life of the patient [2]. This group includes profuse bleeding from the internal carotid artery (ICA) [3–6]. Bleeding from the ICA is rarely observed. Special difficulties are caused by the diagnosis of rare diseases and pathological conditions for which nosebleeds are uncharacteristic [7].

We present a clinical case of profuse nasal bleeding associated with a complication of invasive fungal sinusitis, leading to arrosive bleeding from the internal carotid artery.

Patient N. K., born in 1986, resident of Takhtakupyr district of the Republic of Karakalpakstan, arrived at 15:30 hours on 7 July 2016 as a matter of urgency in the ENT department of the first clinical hospital in Tashkent.

Complaints on admission to pain in the left half of the face, left orbit, headache, difficulty in nasal breathing on the left and the presence of purulent discharge with an unpleasant smell on the same side, reduced left vision, swelling of the eyelids and protrusion of the left orbit, severe weakness.

From the anamnesis, it was found out that 5 months ago, with complaints of nasal congestion on the left, difficulty in breathing and the presence of purulent discharge from this side, the discharge towards the nasopharynx received conservative treatment in the clinic in the community. After treatment, some clinical improvement was noted. In June, congestion and difficulty breathing from the left half of the nose, as well as discharge into the nasopharynx, increased. The patient began to notice the discharge of purulent discharge with an unpleasant odor on this side. For several days in the clinic at the place of residence was conducted conservative therapy, but due to the lack of effect from the activities, as well as due to the appearance of edema of the eyelids, exophthalmos on the left, the patient was sent for in-depth examination and treatment in Tashkent.

According to the patient's brother in history in May 2016, acute renal failure occurred as a complication of the nephrotic form of chronic diffuse glomerulonephritis, which previously had no manifest clinical manifestations. In this regard, started conservative therapy, and held 5 sessions of hemodialysis. After the end of the hemodialysis sessions as prescribed by the doctor, the patient received systemic glucocorticoid therapy with prednisone for one month, and subsequently arbitrarily sharply reduced the recommended dose and mode of prednisolone. At the time of treatment, medical documents, specifying the above pathology are not presented.

It was also found that 29 June 2016 and 3 July 2016, nose bleeds from the left half of the nose were noted with an approximate volume of 200–250 ml, which were stopped by anterior tamponade of the nose and hemostatic therapy.

Within 9 days prior to hospitalization in the ENT department of the first clinical hospital in Tashkent, a survey was conducted in various clinics, including a MSCT of paranasal

sinuses, a histological examination of biopsy material taken from the nasal cavity.

Conclusion MSCT of the nose and paranasal sinuses of 30 June 2016 – complete homogeneous darkening of all the paranasal sinuses with a density of 35–80 HU. In the main sinus on the left against the background of homogeneous darkening, the presence of single dense small foci with a density of 95–130 HU is determined. Marked bone destruction in the lateral wall of the main sinus on the left.

The conclusion of the oncologist from 06 July 2016: Thrombosis of the cavernous sinus. Syndrome of the upper eye gap. Based on clinical, radiological, morphological studies, a tumor of the nose and paranasal sinuses is excluded.

The conclusion of the ophthalmologist: exophthalmos. Subperiosteal abscess of the orbit. Defeat n.abducens, n.oculomotorius.

Objective status at the time of going to the clinic: the general state of moderate severity, conscious, sluggish, the skin and visible mucous membranes are pale. Blood pressure is 90/60 mm Hg. Pulse 89 beats per minute, weak filling. There is an exophthalmos on the left with the displacement of the eyeball to the outside, ptosis of the upper eyelid, chemosis, injection of the conjunctival vessels, restriction of the mobility of the eyeball to the left outwards.

Anterior rhinoscopy: on the left, the mucous membrane of the nasal cavity is hyperemic, the lower and middle nasal conchae are swollen, are reduced after anemization; Signs of nasal bleeding are not available. Other ENT organs without pathology.

The patient was hospitalized as a matter of urgency in the ENT department. It was decided to conduct surgery on the same day in an urgent manner after further examination and preparation of the patient.

In 16:10 of 07 July 2016, that is, in the process of preoperative preparation (in the 40th minute of being in the ward), a spontaneous massive bleeding from the left half of the nose appeared in the patient's ward bed. Developed acute hemorrhagic shock. The doctors on duty attempted to impose a rear tampon. In parallel, appropriate resuscitation measures were performed in the ward – a closed heart massage, artificial mouth-to-mouth breathing. In spite of the measures taken, in 16:15 the resuscitating physician who arrived at the department stated biological death.

Final diagnosis:

Primary: Exacerbation of chronic purulent pansinusta. Complications: Subperiosteal abscess of the orbit. Defeat n.abducens, n.oculomotorius. Profuse arrosive nasal bleeding due to the destruction of the lateral wall of the left main sinus. Acute hemorrhagic shock IV degree. Aspiration syndrome. Acute post-hemorrhagic anemia severe.

Companion: Chronic diffuse glomerulonephritis. Nephrotic form.

Conclusion morphological studies: In the lumen of the main sinus on the left and posterior cells of the ethmoid bone on the same side, isolated dull, dense consistency, gray-brown pieces (formations) ranging in size from 0.4 cm to 4 cm with a rough surface, thick purulent discharge were found. In the lumen of all other paranasal sinuses there is a thick purulent discharge. The mucous membrane of the paranasal sinuses is thickened due to their hyperplasia.

Histological examination of the mucous membrane of the main sinus of the posterior group of ethmoid cells revealed areas with polypoid growths and signs of chronic inflammation, extensive areas of necrotic masses, including mycotic druses from interwoven mycelium strains, invading into the deep layers of the mucous membrane and underlying tissues, lesion of the vascular walls with pronounced tissue necrosis.

The pathoanatomical diagnosis of 07 July 2016:

Primary: Chronic suppurative hyperplastic sphenoiditis, frontal sinusitis, ethmoiditis, antritis on both sides. Subperiosteal abscess of the orbit.

Complications: Exophthalmos. Partial destruction of the side wall of the left main sinus and the Turkish saddle. Arrosive bleeding from the internal carotid artery. Destruction of the left cavernous sinus. Post-hemorrhagic anemia. Purulent fusion of the pituitary gland.

Companion: Chronic glomerulonephritis. Pyelonephritis.

The results of cultural mycological research revealed mold fungi of the genus Aspergillus flavus.

Thus, on the basis of an assessment of the clinical course of the disease, the results of instrumental and histological studies, the patient had an acute (fulminant) form of invasive fungal sinusitis. This is consistent with the data of literary sources [8].

This observation once again confirms the invasive course of fungal lesions of paranasal sinuses with the destruction of their bone walls. The peculiarity of this observation is that the relatively massive lateral bony wall of the main sinus was subjected to destruction, which created the conditions for unimpeded arrosion of the internal carotid artery wall. In the literature available to us, we did not find a description with a similar mechanism for the development of bleeding from the internal carotid artery.

Our observation confirms once again:

– the need to provide close attention and conduct an in-depth examination in the first episode of nasal bleeding, especially when it is not revealed its source;

– the presence of destruction of the bony walls of the nasal cavity and paranasal sinuses to consider as a potential potential cause of profuse bleeding.

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SELECTION OF SURGICAL TACTICS IN THE PATHOLOGICAL IZVITOSTI OF CAROTON ARTERIES

Abstract: To study role of color duplex scanning in the diagnosis and choice of surgical technique in pathological tortuosity of the carotid arteries.

Keywords: Carotid artery, tortuosity, color duplex scanning, surgery.

Introduction

The introduction into clinical practice of modern ultrasound methods for diagnosing diseases of the internal carotid arteries (ICA) in many ways positively determine the results of surgical treatment of their pathological tortuosity (PI) [11].

Pathological studies of F. Koskas et. all. [3] found that convoluted carotid arteries are observed in 10–43%, in patients with impaired cerebral circulation. As a cause of impaired cerebral circulation in adults, pathological tortuosity (PI) of the internal carotid arteries (ICA) is second only to atherosclerotic lesions in prevalence.

According to WHO, at least 15 million strokes are recorded every year in the world. Of the 15 million patients who suffer a stroke, 38% die from primary cerebrovascular accident, 28% after a second stroke. The incidence of ischemic stroke recorded in Uzbekistan was 60.000 cases per year for 29 million people.

According to the data of various authors in the USA and Europe, from 62% to 85% of Pokrovsky AV are subjected to surgical treatment [2]. However, unlike atherosclerotic lesions, which have been the subject of extensive multicenter studies, and as a result of which clear generally accepted conclusions and recommendations were obtained, no such studies have been conducted on the problem of PI branches of the aortic arch, and the indications for surgical treatment largely continue to depend on the personal opinion of the surgeon and neuropathologist on this issue Bockeria L. A. et al., [1].

The most difficult for this category of patients is the determination of indications for surgical treatment, the hemodynamic significance of the PI of the carotid arteries, which ensures the effectiveness of the performed operation [4–10].

Material and methods

For the period from 2006 to 2014 in the Department of Vascular Surgery RSCH them. Acad. V. Vakhidov examined 223 patients with PI CA, of whom 115 according to duplex scanning revealed hemodynamically insignificant pathological deformations of the ICA, and the remaining 108 patients underwent 138 surgical interventions. The patients' age ranged from 29 to 74 years. There were 56 women (51.8%) men – 52(48.1%). In 112(81.1%) cases, bilateral ICA deformity was detected, in 26(18.8%) cases on the one hand. In 1 case, the PI BCA was accompanied by an aneurysmal expansion at the site of bending (Figure 1). In (2%) patients, the pathological deformation of the ICA was combined with the pathological tortuosity of the common carotid artery (OCA), in 34(31.4%) cases, the PI ICA and the vertebral arteries were diagnosed. In 62 cases, PI was combined with ICA stenosis in various percentages, of which 33(30.5%) patients had hemodynamically significant stenosis: (more than 70%). In the overwhelming number of cases of the disease, arterial hypertension was accompanied in 124 patients.

Table 1.

Crimp Distribution		
The form	**Number of cases**	**Percent**
S- and C-shaped (tortuosity)	52	37.6%
Kinks	59	42.7%
Double kinks	23	16.6%
Looping (coiling)	4	2.1%
Total	138	100%

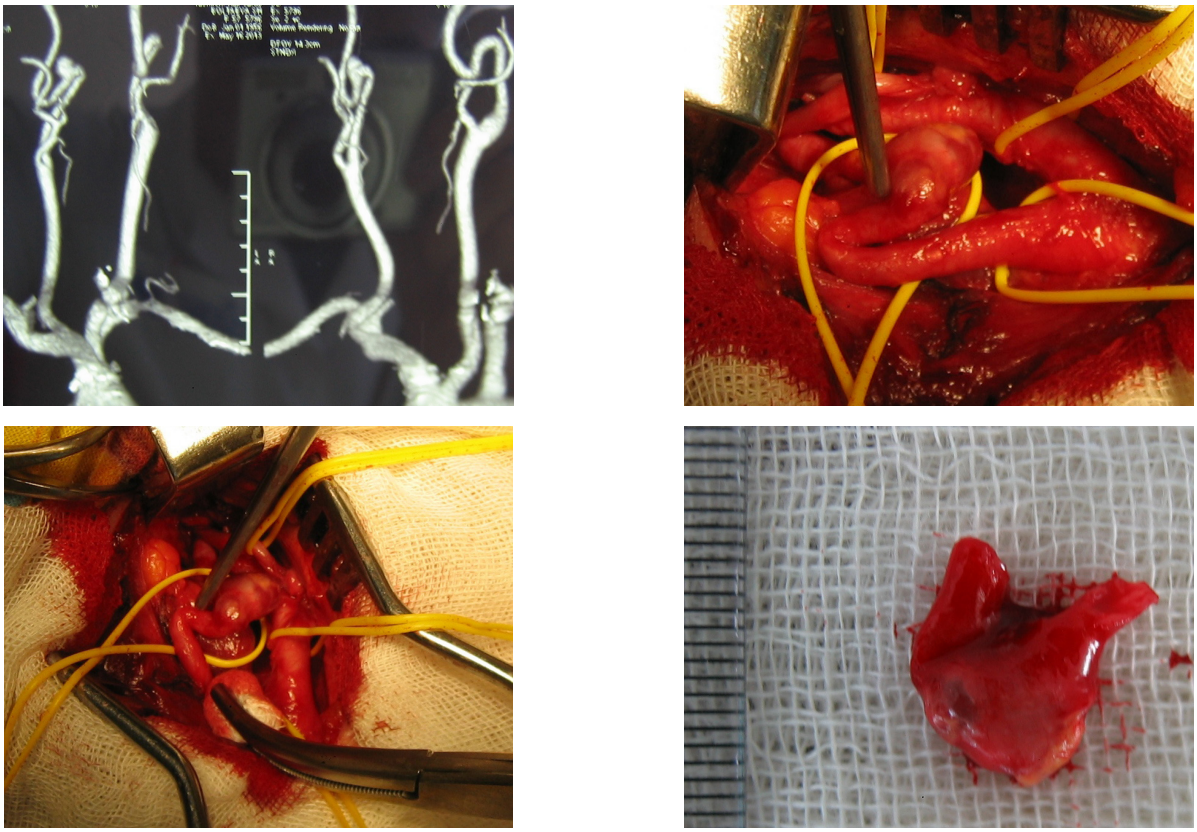

Figure 1. Aneurysm of the ICA at the site of bending. MDCT angiography and intraoperative imaging

In determining the stage of cerebrovascular insufficiency, we were guided by the classification of A. V. Pokrovsky (1979).

I st. HNMK (Asymptomatic Current) – 14 (12.9%);

II st. HNMK (Transient ischemic attacks) – 79 (54.6%);

III Art. HNMK (Dyscirculatory encephalopathy) – 41 (28.7%);

IV art. HNMK (Stroke) – 4 (3.8%).

Asymptomatic PI was observed in 14(12.9%) patients, and 124 (89.8%) had symptoms of cerebral circulation of various degrees: transient ischemic attacks (TIA) occurred in 79(57.2%) patients, dyscirculatory encephalopathy (DE) – in 41(29.7%), ischemic stroke (IS) history was observed in 4(2.8%) patients. It is necessary to emphasize that diseases with C- (8 patients) and S-shaped (4 patients) tortuosities, 2 patients with kinks of the ICA, asymptomatically proceeded.

Table 1. – Clinical manifestations of cerebral ischemia

Clinical manifestations of the media	**S-shaped crimp**	**Coiling**	**Atherosclerosis Kink**
1	***2***	***3***	***4***
Asymptomatic	12	0	2
Tia	24	2	53
Dyscirculatory encephalopathy	14	2	25

1	*2*	*3*	*4*
Ischemic stroke in history	2	0	2
Total	52	4	82

As already noted, out of 52(37.6%) cases with C and S-shaped tortuosity, neurological deficit was observed in 40(76.9%) patients: TIA – in 24, DE – in 14. In 2 cases, the clinical picture of SMN accompanied It was produced by the spiral-shaped tortuosity of the ICA in combination with the atherosclerotic lesion of the OSA bifurcation, in these patients there was an AI in history.

Of 82(59.4%) cases of excesses, 23 were observed to have double, 80(97.2%) had the following events: TIA – in 51, DE- in 27.

The leading role in the study of blood flow in case of pathological tortuosity is assigned to color duplex scanning, the information content of which exceeds 90% (Zanneti P.P. et al., 1997; Del Corso L. et.all. 1998; Kazanchyan P. O., 2001; Valikov Ye. A. ., 2003; Pokrovsky A. B., 2010. etc.).

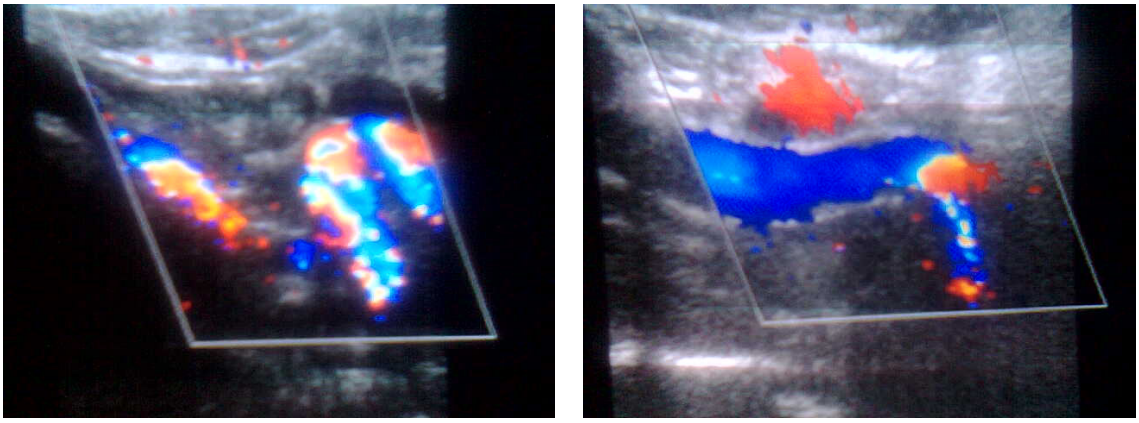

Figure 2. S-shaped crimp. C-shaped crimp

The picture of color duplex mapping (kink) is shown in (Figure 2).

All patients underwent color duplex scanning (Logic PQ-6, USA) and transcranial Doppler sonography (Angiodin-PC) using standard techniques. In case of insufficient informativeness of U3I – methods, if there is a suspicion on the pathology of the intracranial segments of the brachiocephalic arteries, we perform multislice computer tomography with contrast (GE, OPTIMA 660 USA).

A picture of multislice computed tomography with contrast (kink) is presented in (Figure 3).

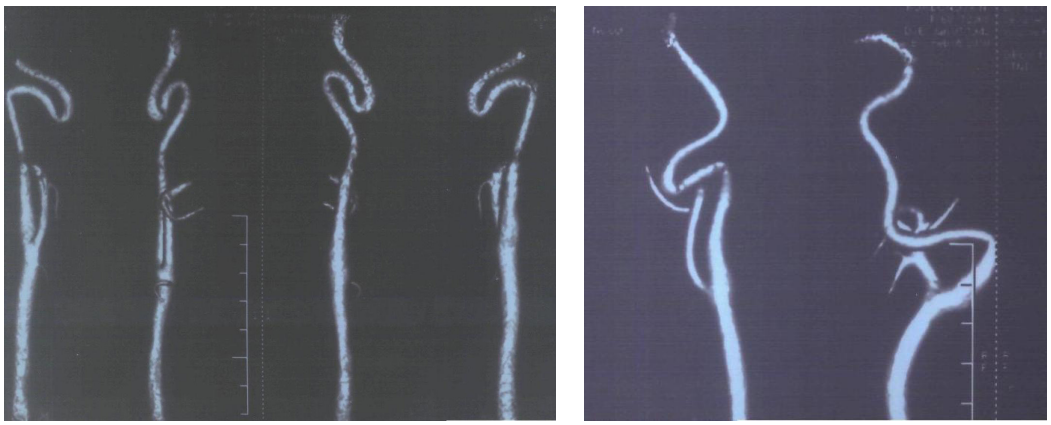

Figure 3.

We used the classification of J. Weibel and W. Fields (1965). Under tortuosity (tortuosity) should be presented S- or C-shaped deformation of the ICA without acute angles and visible blood flow disorders. This type of deformity is hemodynamically controversial. Looping (coiling) is characterized by circular deformation with the formation of a loop. Under the bending (kinking) refers to hemodynamically significant angulation of the ICA with stenosis of its lumen.

S-or C-shaped deformation of the ICA without acute angles and visible impairment of blood flow was detected in 115(51.5%) patients. These patients received conservative treatment and are under observation.

These patients received conservative treatment and are under observation. The tortuosity of the ICA with an acute angle and hemodynamic blood flow disorders was detected in 52(37.6%) patients. Looping (coiling) was detected in 4(3.2%) patients. Kinking – in 59(42.7%) patients and double kinking in 23(16.6%) patients.

Evaluation of hemodynamic changes in blood flow in the ICA due to pathological deformity was carried out according to the duplex scanning standard and the significance of the deformities:

– change in the form of blood flow proximal to the deformity with elevated indices of peripheral resistance – turbulence;

– an increase in the linear blood flow velocity (BFV) in the deformation zone by more than 2 times the initial one;

– reduction recorded by the VSA LSK after deformation, compared LSK before bending.

Changes in the blood flow parameters in the region of the deformity of the carotid arteries and segments distal to the deformity of the artery are presented in (table 2).

Results

The need for surgery in patients with pathological deformity requires clear indications for surgical treatment, primarily based on the determination of the hemodynamic significance of tortuosity.

Table 2. – Linear rotary speed on duplex scaning

Crimpiness	LSK to the zone of deformation m/s	LSK deformation zone m/s	LSK after deformation zone m/s	Number of patients
S-shaped tortuosity (tortuosity)	0.60–0.70	0.9–1.0	0.30–0.40	52(37.6%)
Kink (kink)	0.55–0.70	0.8–1.0	0.25–0.30	82(59.4%)
Looping (coiling)	0.40–0.60	0.7–1.0	0.30–0.50	4(2.8%)

Norm: 0.40–0.50 from 40 years and up

Regarding the pathological tortuosity of the carotid arteries, 138 operations were performed in 108 patients. The nature of the operations performed is presented in (Table 3).

Table 3.

Operation name	Number of patients
Resection of the ICA with redressing and reimplantation into the old mouth	101(70.7%)
Resection of the ICA and redressing with reimplantation into the old mouth after eversion carotid endarterectomy	31(24.3%)
Resection of the ICA with anastomosis (end-end)	4(3.3%)
Prosthetics of the ICA (with a modified wall)	2(1.7%)
Total:	138(100%)

We have experience in surgical correction of 138 crimps in 108 patients. In case of correction of PI VSA, we prefer the operation of resection of an abnormal artery segment with redressing and implanting it into the old mouth. This operation was performed in 101 cases, and in 31 cases it was combined with eversion carotid endarterectomy. In the case of a small length of the process, with fibrous transformation and aneurism outside the tortuosity zone, a resection with anastomosis from end to end (6 C and S figurative tortuosity and coiling operations) was carried out when the ICA was bent.

Discussion

The observations show high sensitivity and informative duplex scanning and spiral computed tomography in determining the type of PI, identifying the combined atherosclerotic lesions of the carotid arteries, including the study of the morphological characteristics of plaque and its surface structure. Intraoperative data on the character of PI coincided with the information obtained during the examination in 80% of cases.

The method of CDS allows to characterize in detail the form of tortuosity, its localization and to reveal the nature of the blood flow. The criteria for local hemodynamic significance of PI VSA are:

1. gradient peak systolic blood flow velocity between the proximal and distal parts of the vessel in relation to the place of tortuosity with a decrease in speed in the distal direction by 20% or more:

2. the increase in peak velocity at the site of angulation compared to the proximal site of the ICA by 30% or more: disorganization of blood flow in the tortuosity zone, manifested by an increase in spectral expansion and violation of the blood

flow pattern in the color mapping mode: compared with the same area unchanged contralateral ICA.

Thus, it has been established that one of the links in the pathogenesis of cerebral circulatory disorders in PI ICA is a local hemodynamic disorder in the tortuous zone with a decrease in blood flow in the distal direction.

The use of duplex scanning as a non-invasive method for studying the vessels of the brain, combining the advantages of visualization and quantitative assessment of blood flow, has expanded the understanding of this pathology. In adults, changes in the length and shape of the carotid arteries are most often seen in the sixth decade of life. The ratio of men and women at the same time is 4: 1, respectively.

Currently, the PI VSA may be the cause of transient and persistent violation of cerebral circulation. In the presence of modern ultrasound equipment, the CDS diagnostics of the PI VSA does not represent technical complexity.

When deciding on the treatment tactics, it is necessary to proceed from the hemodynamic significance of the lesion. In the case of concomitant atherosclerotic stenosis of the carotid arteries, the morphology of the plaque is important. The indication for surgery is the presence of a hemodynamically significant lesion of the vessel with a change in blood flow velocity at the site of stenosis, that is, an increase in the linear blood flow rate by 2 times.

In case of correction of PI ICA, we prefer the operation of resection of an excess artery segment with redressing and implanting it into the old mouth. This operation performed in 101 cases, and in 31 cases combined with eversion carotid endarterectomy.

Analysis of the clinical results of operations showed a positive dynamics of neurological status. Repeated TIA and AI in the pool of the operated SA was not observed. The symptoms of DE were completely eliminated in 23 of 41 patients, 15 patients showed partial regression of neurological symptoms, in 3 patients the neurological status remained unchanged, due to a lesion in the contralateral carotid artery. In 4 patients with a history of AI who underwent repeat stroke was not observed. Long-term results of the operation (at follow-up periods of up to 3 years) were followed up in 58 patients.

The absence of neurological symptoms, TIA, ONMK during the observation period. The surgical effect of the performed reconstructions was evaluated using ultrasound diagnostics, the state of the anastomosis, the straightness of the vessel stroke, and hemodynamic disorders were studied. Good and satisfactory results were obtained in 92.3% of cases.

Findings:

1. Ultrasound duplex scanning is a highly informative method for the diagnosis of pathological tortuosity of the ICA. The method makes it possible in 90.2% to diagnose not only the anatomical structure of the pathological tortuosity of the carotid arteries, but also to determine the hemodynamic significance of the lesion, which is important in determining the indications for surgical intervention.

2. Hemodynamically significant pathological tortuosity of the carotid arteries is an indication for the surgical treatment of this disease, pathology as prevention of acute cerebrovascular accident.

3. When determining the indications for reconstructive surgeries at the SAI, it is necessary to clearly assess the clinical manifestations of the disease, thoroughly study the anatomical structure, that is, determine the place and degree of artery bend, determine the hemodynamic significance of vessel damage blood flow and resistance index of the affected artery, the type of tortuosity and the presence of concomitant stenotic lesions.

4. Surgical intervention in pathological tortuosity is shown when the linear flow velocity in the deformation zone is accelerated by 2 times. Characteristic for the inflection of the internal carotid artery should be considered the asymmetry of the reaction with an increase in BFV.

5. Surgical correction of the pathological tortuosity of blood vessels is a more effective method of treating and preventing the progression of chronic cerebrovascular insufficiency in the carotid pool compared with conservative therapy.

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