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Section 1.
Clinical medicine

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RESYNCHRONIZING PHYSICAL THERAPY – A NEW DIRECTION IN MEDICINE

Abstract: To management the functional state of the organism and to treat a wide range of diseases, the company has developed a method of resynchronizing physiotherapy and a third-generation chronophysiology device.

Keywords: biorhythm, chronom, the principle of rhythmicity, chronomedicine, chronotherapy, pathological desynchronosis.

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РЕСИНХРОНИЗИРУЮЩАЯ ФИЗИОТЕРАПИЯ – НОВОЕ НАПРАВЛЕНИЕ В МЕДИЦИНЕ

Аннотация: Для управления функциональным состоянием организма и лечения широкого спектра заболеваний в компании разработан метод ресинхронизирующей физиотерапии и аппарат хронофизиотерапии третьего поколения.

Ключевые слова: биоритм, хроном, принцип ритмичности, хрономедицина, хронотерапия, патологический десинхроноз.

В последние годы биомедицинская наука преодолевает порог нового синтеза знаний, который ведет к формированию медицины нового поколения. Значительный прогресс наблюдается в области Хронобиологии и Хрономедицины, особенно в направлении исследования биоритмов организма. Они обнаружены на всех уровнях организации организма: молекулярном, клеточном, тканевом, органном и организменном. Установлена связь биоритмов организма с геофизическими

ритмами. В 2017 г. три учёных из США получили Нобелевскую премию в области биологии и медицины за открытие гена и белка period. Концентрация белка колеблется с периодичностью 24 часа и представляет собой биохимический осциллятор на молекулярном уровне, который синхронизирует биоритмы организма с циркадным (суточным) ритмом.

В результате анализа термодинамических процессов, происходящих в биологических системах, установлена природа биоритмов и раскрыт механизм химико-физического взаимодействия, лежащий в основе функционирования живых организмов. На основе полученных данных дано определение таких базовых понятий науки хронобиологии, как биоритм и хроном. Сформулированы принцип ритмичности биологических процессов и принцип взаимной когерентности химических и физических реакций, сопровождающих обмен веществ в клетках.

Всё это позволило разработать хронобиологический подход к управлению функциональным состоянием организма путём внешнего воздействия на его биоритмы, и сформулировать принцип хроноуправления в биологии. Принцип хроноуправления означает управление функциональным состоянием организма путём десинхронизации (нарушения) или ресинхронизации (восстановления) его биоритмов (принцип Де и Ре синхронизации). Рассмотрим возможности существующих методов лечения для реализации этого принципа.

Согласно принципу ритмичности живой материи все биопроцессы протекающие в организме имеют свои биоритмы. При заболевании в больной ткани происходит нарушение обмена веществ (биопроцессов) и возникает патологический процесс, который сопровождается отклонением биоритмов от нормы – десинхронозом. Согласно принципу взаимной когерентности в биологии, это означает возникновение в больной ткани взаимного патологического десинхроноза (ВПД), т.е. одновременного отклонения от нормы двух взаимосогласованных колебательных химико-физических процессов. Таким образом, с позиции хрономедицины патологический процесс в больной ткани представляет собой ВПД, и все заболевания можно лечить путём его устранения. При этом восстановить эти нарушенные колебательные процессы (биоритмы) можно путём воздействия на них, как химическими, так и физическими способами.

В настоящее время лечение заболеваний (устранения ВПД) происходит в основном методами фармакотерапии. В результате обычной медикаментозной терапии или хронотерапии (хронобиотики) в больной ткани восстанавливаются нарушенные обменные процессы, происходит нормализация биоритмов и устранение ВПД. Однако такой подход далеко не всегда гарантирует полное выздоровление из-за не достаточной эффективности и безопасности лечения лекарственными препаратами.

Известные на сегодняшний день методы и аппараты физиотерапии путём электромагнитного воздействия на больной организм условно можно разделить на следующие две группы.

1. Аппараты первого поколения. Большинство методов физиотерапии, такие как магнитотерапия, электротерапия и другие, разрабатывались «в слепую» без учёта роли биоритмов в организме, и поэтому положительная динамика лечения на этих аппаратах не превышает 70%. Это вспомогательные методы лечения, и аппараты с этими функциями в основном оказывают оздоравливающе воздействие на организм путём улучшения микроциркуляции крови, как в больной, так и здоровой ткани за счёт реологического эффекта. При этом отдельные случаи высокой эффективности лечения с позиции электро и магнитотерапи не нашли своего объяснения.

2. Аппараты второго поколения реализуют методы, так называемой биорезонансной и тому подобной терапии. Они разрабатываются на основе явления резонанса, путём эмпирического подбора резонансных частот для воздействия на биоритмы организма. Поэтому при хронотерапии ряда заболеваний на таких аппаратах действительно наблюдается высокая динамика лечения. Однако разработчики этих методов и аппаратов не могут с позиции явления резонанса объяснить механизм лечения, и как следствие этого, они не могут гарантировать безопасность терапии, что и наблюдается на практике. Этим объясняется критическое отношение к ним со стороны части научного и медицинского сообщества.

Таким образом, в настоящее время нет эффективных и безопасных методов лечения, которые бы позволили реализовать принцип хроноуправления функциональным состоянием организма. Решение этой проблемы связано с необходимостью разработки принципиально нового метода управления биопроцессами путём прямого воздействия на их биоритмы. Ключом к решению поставленной задачи послужило явление усвоения ритма живыми организмами, открытое академиком А. А. Ухтомским. Оно характеризует способность тканей, органов и организма в целом перестраивать свои биоритмы в соответствии с ритмами внешних раздражений и сохранять эти изменения.

Явление усвоения ритма положено в основу разработанного метода ресинхронизирующей физиотерапии (РФТ), в котором в качестве источника внешних ритмов используется частотная составляющая электромагнитного поля (ЭМП). В зависимости от поставленной цели: ресинхронизации или десинхронизации биоритмов и тем самым устранения или создания ВПД, используются частоты ЭМП из диапазонов биоритмов одной и той же здоровой или больной ткани соответственно. Исходя из этого, суть метода РФТ заключается в следующем. Если на больную ткань подействовать ЭМП частотой биоритмов этой же, но здоровой ткани, то, в результате явления усвоения ритма, в больной ткани установятся

колебания частотой биоритмов здоровой ткани. Согласно принципу взаимной когерентности произойдет восстановление нарушенных биологических процессов и наступит выздоровление больной ткани, т.е. произойдет устранение ВПД. При необходимости десинхронизации биоритмов с целью нарушения нормального функционирования организма, используется частота ЭМП из диапазона биоритмов соответствующей больной ткани.

С позиции явления усвоения ритма различная эффективность лечения заболеваний аппаратами физиотерапии, как первого, так и второго поколения объясняется следующим образом. Аппараты первого поколения работают на терапевтических частотах, которые подобраны произвольно. Поэтому, если эта частота случайно оказалась из диапазона биоритмов здоровой ткани, в которой возникла патология, то в больной ткани происходит усвоение ритма здоровой ткани и наблюдается положительная динамика лечения. Если эта частота оказалась из диапазона биоритмов больной ткани, то в здоровой ткани происходит усвоение ритма больной ткани и наблюдается отрицательная динамика лечения. Если частота ЭМП не попадает в эти диапазоны биоритмов, то происходит воздействие на ткань только магнитной или электрической составляющей ЭМП, которые не лечат, а оказывают оздоравливающе воздействие на организм.

Аппараты второго поколения работают на частотах вызывающих резонансный отклик в организме. Но в результате диагностики резонансный отклик могут вызвать частоты, как из диапазона биоритмов здоровой, так и больной ткани. В последнем случае, использование этой частоты при лечении вызовет в здоровой ткани, в результате усвоения ритма, возникнет десинхроноз или в больной ткани произойдёт обострение заболевания. Следовательно, методы биорезонансной терапии уже по определению не могут гарантировать получение только положительного терапевтического эффекта.

Для внедрения метода РФТ в медицинскую практику разработан хрономагнитотерапевтический аппаратно-программный комплекс ФизиоМаг – хронокорректор биоритмов организма. Это аппарат физиотерапии третьего поколения, основным лечебным фактором в котором является частотная составляющая ЭМП. ФизиоМаг работает в двух режимах: ресинхронизации и десинхронизации, и одновременно реализует две функции лечения: хронотерапию и магнитотерапию. В зависимости от решаемой задачи, для воздействия на организм используется соответствующая частота ЭМП из диапазона биоритмов здоровой или больной ткани. В результате этого в организме возникает явление усвоения ритма и запускается процесс ресинхронизации или десинхронизации биоритмов. Аппарат оказывает воздействие на все ткани и органы, биоритмы которых попадают в диапазон его рабочих частот. Эффективность лечения на аппарате различных заболеваний в режиме ресинхронизации, в зависимости от типа патологии, до-

стигает 95%. При этом употребление лекарственных препаратов снижается более чем на 50%.

Использование частотной составляющей ЭМП из диапазона биоритмов здоровой ткани, в которой возникла патология, является необходимым и достаточным условием для возникновения явления усвоения ритма только в больной ткани и не оказывает побочного воздействия на другие ткани и органы. Таким образом, в результате прямого воздействия на биоритмы больной ткани лечение на аппарате гарантирует получение только положительного терапевтического эффекта.

По эффективности и безопасности метод РФТ является альтернативой методам фармакотерапии и открывает новое перспективное направление в медицине: лечение различных заболеваний, в т.ч. онкологических, путем управления биопроцессами в больной ткани. Устранение патологий происходит путём частотной коррекции отклонений, возникших в биоритмах больной ткани, и тем самым восстановления в ней нарушенных биопроцессов. На метод и аппарат получены патенты РФ.

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PECULIARITIES OF CLINICS IN CHILDREN WITH LEFT VENTRICULAR FALSE TENDONS AND MITRAL VALVE PROLAPSE

The paper presents the main clinical manifestations of small cardiac anomalies (SCA) in high school children. 106 adolescents with mitral valve prolapse (MVP) and 64 abnormal-located chords or false tendons (FT) in the left ventricle were examined. It was established that in these children, various complaints had a pronounced discretionary character. The tendency of the incidence of complications such as heart and headache, dizziness, palpitations and increased fatigue is more pronounced in children with MVP than with FT. Vegetative paroxysms were more characteristic of children with MVP than FT. Among crises dominated by weight-insular.

Keywords: false tendons, children, mitral valve prolapse.

Introduction. To date, dysplasia of the connective tissue forms the stroma of all organs and systems and tissues of the body. The uniqueness of connective tissue dysplasia structure and function creates conditions for the emergence of numerous numbers of its anomalies. One of the important visceral phenotypic manifestations of undifferentiated connective tissue dysplasia (UCTD) is mitral valve prolapse and other valves, abnormal ventricular chords, bivalvular aortic valve, and other changes that in fact attract the attention of researchers due to the high frequency of their occurrence and high risk of development complications and sudden death[1]. MVP – the most common manifestation of UCTD, especially among young people. Its frequency ranges from 5 to 10% in total[2]. The attention of the MVP is increased, due to the polymorphism and mosaic manifestations of its clinical picture. At the same time, children have complaints of cardial, somatic and psycho-emotional nature, however, 20–60% of them may be absent from any subjective symptoms[3].

The clinical picture of MVP and FT is often accompanied by a syndrome of autonomic dysfunction (AD). It remains to be seen whether there is an initial pathology of autonomic system, or this is an adaptation of the cardiovascular system to the presence of SCA. It is believed that AD has a constitutional and genetically determined character, mediated by the influence of the hypothalamus, which in fact plays a major role in the synthesis of collagen and neurohumoral regulation. AD syndrome includes pains in the left half of the chest (prickly, aching, without exercise, duration from a few seconds for prickly pains or several hours for those in need), hyperventilation syndrome (the central symptom is a feeling of lack of air, a desire to make a deep full breath)[4]. Complaints of heartbeat and heart failure as a manifestation of violations of autonomic regulation of cardiac rhythm may also occur[5].

Among other syndromes with MVP is characterized by syndrome of vascular disorders, hemorrhagic and psychopathological. The syndrome of vascular disorders includes syncope states – vasovagal (fainting in suffocating rooms, with a long vertical

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[5] Мартынов А. И., Акатова Е. В., Николин О. П., Урлаева И. В. Опыт длительного применения магния у пациентов с пролапсом митрального клапана.– Медицинский вестник Северного Кавказа,– 2016; 2(11): 298–302. – С. 4.

position, etc.) orthostatic, as well as pre-unconscious conditions under the same conditions[1], among other most striking phenomena in MVP is psycho-genetic paroxysms (crises), which in foreign literature are referred to as panic attacks[2], which may be the leading symptoms of MVP[3]. Consequently, the clinical picture with small cardiac anomalies is heterogeneous and needs further study.

The purpose of the study: To study the features of clinical manifestations of MVP and FT in high schoolchildren on the basis of analysis of their complaints.

Materials and methods of research. We examined 106 primary school children (62 boys and 44 girls) and 64 children with FT (40 boys and 24 girls) aged from 13 to 17 years. The examination was carried out on the basis of the Municipal Clinical Hospital "Mother and Child Center", which is the clinical base of the department. All children had a general clinical examination and ultrasound examination of the heart and internal organs. All children are advised by narrow specialists as needed. An analysis of the complaints of this category of children was conducted.

Research results. The analysis of complaints in children with PMK and FT has revealed a wide variety and a large number of them. So, most often among complaints in children with PMK was pain in the heart (63.55%). Other frequent complaints were: increased fatigue (60.6%), headache (52.4%), dizziness (38.8%) and palpitations (31.2%).

We have found a tendency for a greater frequency of occurrence of the main complaints in children with primary PMK than with FT. Thus, it was noted that pain in the heart area is significantly more common (74.5% and 45.3%, $p < 0.01$), dizziness (50.9% and 18.8%, $p < 0.01$), syncope (19.8% and 7.8%, $p < 0.01$). Somewhat more often, in comparison with the group of children with FT, MVP also met complaints of headache (64.2% and 32.8%, $p < 0.01$). The rapid fatigability of children in both groups was repeatedly noted (69.8% and 45.3%, respectively); on heartbeat – 35.8 and 34.3% respectively. Intolerance to transport was usually observed more with MVP. Abdominal pain has almost the same number of children in each subgroup, which was 19.4% in total. Shortness of breath was not common and also more common in children with MVP, while it was almost absent among children with FT (14.2 and 3.1%, respectively). Very rarely children of both groups worried about leg pain (Table 1).

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[2] Осовська Н. Ю. Клінічне значення аномальних хорд лівого шлуночка.– Експериментальна і клінічна медицина,– 2013; 3(60): 56–63.

[3] Остроумова О. Д., Степура О. Б., Мельник О. О. Пролапс митрального клапана – норма или патология? – Русский медицинский журнал,– 2002; 28: 1314–1317.

Table 1.– Frequency of main complaints in children with MVP and FT

Complaints	Frequency of occurrence				Total, n = 170	
	MVP, n = 106		FT, n = 64			
	Abs	%	Abs	%	Abs	%
Pain in the heart area	79	74.5	29	45.3*	108	63.5
Increased fatigue	74	69.8	29	45.3	103	60.6
Headache	68	64.2	21	32.8*	89	52.4
Giddiness	54	50.9	12	18.8*	66	38.8
Heartbeat	38	35.8	22	34.3	60	35.3
Abdominal pain	22	20.8	11	17.2	33	19.4
Syncope	21	19.8	5	7.8*	26	15.2
Shortness of breath	15	14.2	7	10.9	22	12.9
Intolerance to transport	12	11.3	3	4.7	15	8.8
Pain in legs	5	4.7	1	1.6	6	3.5

Note: the asterisk (*) indicates significant differences between the groups of children ($p < 0.01$)

As is known, the so-called vegetative paroxysms or "panic attacks" characterize the children with small cardiac anomalies. Among the studied group of children, there were two main types of vegetative crises: sympatho-adrenal (14.7%) and weight-insular (14.1%). They were provoked by emotional or physical overloading. Duration of paroxysms ranged from 5 minutes to 2 hours.

The simpatho-adrenal vegetative paroxysms were more common in children with MVP than with FT (in 17.9% of children with MVP and in 9.4% of children with FT) (Table 2). They were accompanied by headache, increased blood pressure, severe tachycardia, hyperthermia, polyuria, and anxiety.

Weight-insular paroxysms occurred more frequently than sympatho-adrenal in children with MVP, and less frequently in FT, They leaked with hypothermia, increased sweating, abdominal pain, nausea, and sometimes even vomiting. In addition, there was a pronounced headache, which was sometimes migraine-like, a decrease in blood pressure, a brady- or tachycardia.

Table 2.– Frequency of occurrence of vegetative paroxysms in children with MVP and FT

Type of paroxysmal	MVP, n =106		FT, n = 64		Total, n = 170	
	Abs	%	Abs	%	Abs	%
Sympatho-adrenal kerrisis	19	17.9	6	9.4	25	14.7
Weight-insular crises	22	20.7	2	3.1	24	14.1
Total	41	38.7	8	12.5	49	28.8

Conclusions. Thus, in the study group of children with MVP and FT revealed a variety of complaints that have a pronounced dissecting nature. A greater tendency to meet the main complaints (pain in the area of the heart, headache, dizziness, palpitations, increased fatigue) was found among children with MVP than with FT. Vegetative paroxysms were more characteristic of children with MVP than FT. Among crises dominated by weight-insular. Detected in children with MVP and FT, various cardiovascular complaints such as heart pain, palpitations, shortness of breath, which disturb children not only due to heart disease, require a more in-depth study of the state of the heart in the study group of patients. All children with small cardiac abnormalities need careful monitoring by family doctors and nursing specialists to prevent the deterioration and progression of their clinical symptoms.

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CONGENITAL PARVOVIRUS INFECTION

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ВРОЖДЕННАЯ ПАРВОВИРУСНАЯ ИНФЕКЦИЯ

Инфекции во время беременности являются одной из основных причин фетальной и неонатальной заболеваемости и смертности. Врожденные аномалии, хотя и встречаются редко при внутриутробных инфекциях, могут привести к смерти

плода. Асимптоматические инфекции при рождении могут иметь поздние клинические проявления, которые становятся очевидными только позднее, в основном, в первые годы жизни[1]. Первичные инфекции во время беременности существенно более разрушительные, чем повторные инфекции или реактивации инфекционного заболевания. Аналогично, инфекции, приобретенные в более ранний гестационный возраст, как правило, приводят к более серьезным инфекциям[2].

Среди 30–50% беременных, не имеющих иммунитета к ПВ B19V, сероконверсия по специфическому IgG выявляется в 1,5–13,5% случаев, частота заражения значительно повышается в случае постоянного контакта беременной с детьми дошкольного возраста.

Профилактика. Систематический скрининг

Материнские инфекции, которые могут повлиять на плод, могут быть диагностированы когда имеются доступные ресурсы. Потому что во многих случаях, даже при первичном заражении инфекции протекают бессимптомно и диагноз зависит от эффективных методов скрининга. Для некоторых инфекций стоимость льготного объема рутинного скрининга во время беременности отсутствует.

Во многих областях наиболее специфичные и чувствительные тесты нелегко бывают доступны. Если подтверждается материнская инфекция, то внутриутробную передачу часто трудно подтвердить. Поэтому в ранней диагностике и своевременном лечении важную роль играет наличие предварительных и антенатальных скринингов матерей и неонатальных скринингов младенца.

Профилактика материнской первичной инфекции путем изменения образа жизни, а именно избегания привычек, которые могут привести к увеличению контакта с инфекционными агентами является актуальным. Кроме того, просвещение матерей о проведении антенатальных скринингов и профилактики инфекци имеет решающее значение для избежания упущенных возможностой профилактики.

В данной статье мы представим довольно редко диагностируемую парвовирусную инфекцию.

Парвовирус B19 (также известный как эритровирус B19) представляет собой небольшой вирус, который вызывает инфекционную эритему (пятая болезнь) среди детей, артропатию у взрослых и переходные апластические анемии у пациентов с повышенным эритропоэзом, например, серповидноклеточную анемию

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[1] Courtier J., Schauer G. M., Parer J. T., Regenstein A. C., Callen P. W., Glenn O. A. Parvovirus B19 infection during pregnancy and risks to the fetus // Ultrasound Obstet Gynecol. – 2012. – No. 40 (5). – P. 604–6; Nadimpalli S. S., Miller R. S., Kamath V. M., et al. Congenital Parvovirus B19 Infection: Persistent Viremia and Red Blood Cell Aplasia. Open Forum Infectious Diseases. –2015. 2(2): ofv 049. doi:10.1093/ofid/ofv049.

[2] Ornoy A., Ergaz Z. Parvovirus B19 infection during pregnancy and risks to the fetus // Birth Defects Res. – 2017. – Mar 15. – 109(5). – P. 311–323.

у детей. Парвовирус В 19 может вызывать водянку (hydrops) плода и врожденную анемию. Эритроцитарный Р антиген является клеточным рецептором для эритровируса В 19. Вирус является мощным ингибитором дифференцировки эритроидных клеток, цитотоксических для клеток-предшественников эритроидов и может вызывать эритроцитарную аплазию[1]. Вирус во время беременности распространяется воздушно-капельно и трансплацентарно и заражает только людей.

После перенесенной инфекции сохраняется длительный иммунитет, однако описаны случаи повторного заражения и персистенции инфекции у лиц с ослабленным иммунитетом. По статистике около 25%-80% женщин до беременности уже бывают невосприимчивы к вирусу. Годовая доля женщин детородного возраста, у которых сероконверт составляет 1,5%. Трансплацентарный путь заражения В19 встречается при 30–50% острой парвовирусной инфекции матерей, однако большинство новорожденных рождаются нормально.

Клинический особенности

У детей заболевание состоит из легкой сыпи – «пятая болезнь». Еще в прошлом веке экзантемы у детей были разбиты на пять групп. Инфекционная эритема получила название пятой болезни, корь – первой, скарлатина – второй, краснуха – третьей, болезнь Дьюка – четвертой; в настоящее время четвертая болезнь не признается отдельным заболеванием[2]. Впоследствии была описана младенческая розеола (roseola infantum).

Инфекционная эритема – наиболее распространенная клиническая форма парвовирусной инфекции В 19 у детей. Начинается с неспецифических симптомов – лихорадка, недомогание, озноб, миалгии, которые продолжаются в течение 2–5 суток. Затем присоединяется патогномоничный симптом «отшлепанных» щек – яркая эритема кожи в области щек, а также пятнисто-папулезная «кружевная» сыпь (сетчатый рисунок) на туловище и конечностях, зуд не беспокоит. Иногда сыпь может чесаться. Ребенок обычно не очень беспокоен, и сыпь разрешается через 7–10 дней.

Неиммунная водянка плода может развиваться при поражении парвовирусом В19 плода с гестационным возрастом 13–20 недель. Сопровождается анемией, гипоксией, гепатитом (непосредственное повреждение гепатоцитов вирусом и опосредованное – за счет отложения гемосидерина), кардитом, с формированием печеночной и сердечной недостаточности. При проведении ультразвукового исследования плода выявляется: кардиомегалия, отек грудной клетки, асцит, выпот жидкости в плевральные полости и перикард, отек плаценты. При

[1] Bihari Ch., Rastogi A., Saxena P. et al. Parvovirus B19 associated hepatitis // Hindawi Publishing Corporation // Hepatitis Research and Treatment.– 2013; Article ID472027: 1–9.

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своевременной диагностике и проведении гемотрансфузии плоду внутриутробно, благоприятный исход возможен в 83% случаев[1].

У большинства взрослых с острой инфекцией не отмечается каких-либо симптомов. Только у немногих взрослых развиваются типичные сыпи пятой болезни, но бывают распространены боль и/или опухоль в суставах. Обычно, повреждаются больше, чем один сустав, наиболее часто затрагиваются суставы руки, запястья и коленей. Боль и отек в суставах обычно разрешаются через неделю или две, но могут сохраняться несколько месяцев.

Человек, инфицированный парвовирусом B19, заразен от 4 до 7 дней до начала и до 2 недель после сыпи. Интервал между острой материнской инфекцией и диагнозом заболевания плода колеблется от 2 до 6 недель. Риск неблагоприятного исхода плода очень низкий, но выше, если инфекция возникает во время 1 и 2 триместров, особенно между 9 и 16 неделями беременности.

Диагностика парвовирусной инфекции B 19

Иммуноферментный анализ (ИФА) – IgM в сыворотке крови пациента обнаруживаются одновременно с появлением симптомов заболевания (на 12–14 день после заражения), их уровень достигает максимума на 30-й день, затем снижается в течение 2–3 месяцев. Через 5–7 дней от момента клинических проявлений парвовирусной инфекции появляются IgG, которые сохраняются в течение нескольких лет.

В случае, если у беременной женщины регистрируются симптомы парвовирусной инфекции B19 (инфекционная эритема, артропатии) или она была в контакте с больным данной инфекцией, рекомендовано проведение ПЦР и/или ИФА сыворотки крови.

Лечение

В настоящее время специфической этиотропной терапии парвовирусной инфекции не существует. В зависимости от клинической формы парвовирусной инфекции B 19 проводится посиндромная терапия (нестероидные противовоспалительные препараты, глюкокортикостероидные препараты, трансфузия эритромассы и т.д.).

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ANEMIA AND THROMBOCYTOPENIA IN HIV–INFECTED CHILDREN DEPENDING ON GENDER

HIV remains a major global public health challenge[1]. In 2015, there were 36.7 million people living with HIV worldwide (34.0–39.8 million) (Global AIDS Update, Unaids, 2016).

In HIV – infected children, hematological pathology is one of the most common disorders[2]. In recent years there have been many studies on a single integrated cellular-humoral system of protection which form adoptive immunity, hemostasis and innate mechanisms of the body immunoresistance (Kuznik B. I., 2004–2006; Tsybikov N. N. etc., 2004, Vitkovski Y. A. and others, 1997–2005). The interconnection of hemostasis and immunogenesis systems is known[3], (Vitkovski Y. A. et al., 2005). In addition, foreign researchers have proved that HIV affects bone marrow hematopoiesis, so all the elements – red blood cells, platelets, etc[4]. are affected. According to some authors it is

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known that a number of infections[1], for example, parvovirus in 19, CMV, Epstein-Barr virus, etc., as well as a number of diseases (thalassemia, hemoglobinopathies, etc.) can lead to a decrease in blood counts in HIV-infected children.

The decrease in production of red blood cells may be a result of suppression factors such as inflammatory cytokines or HIV itself[2]. Also in anematized HIV-infected patients the reduced production of erythropoietin can be documented[3]. Another obvious cause of hypoproliferative anemia in HIV-infected patients is the large number of drugs[4], many of which (Zidovudine, Ganciclovir) can suppress the bone marrow and/or red blood cells[5].

The cause of thrombocytopenia may be a decrease in platelet production, their accelerated destruction, platelet deposition and a combination of these factors[6]. There is reason to believe that in HIV infection, thrombocytopenia is caused by a decrease in platelet production, and their accelerated destruction. Structural disorders of megakaryocytes were found in HIV-infected patients[7], in addition, HIV-1 RNA was

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detected in megakaryocytes[1]. The cause of thrombocytopenia can also be tumor infiltration of the bone marrow and infection. Drugs, except for antitumor agents, rarely inhibit the production of platelets.

Achievements in the sphere of diagnosis and treatment of hematological disorders shall improve the quality of life of HIV-infected people, but there are many "white spots" in the impact of comorbidities, opportunistic infections and the gender of the patient on the frequency of hematological abnormalities in this group of sick children.

The aim of the study was to study blood counts in HIV-infected children who received different regimens of antiretroviral therapy depending on the gender of the child.

Materials and methods of research. We examined 60 children with HIV receiving antiretroviral therapy (ARVT). The children were under medical surveillance in the Republican Center on combat against AIDS. The diagnosis was established on the basis of clinical and laboratory data in accordance with the order of the Ministry of Health of the Republic of Uzbekistan No.81 dated 5.03.2015. Of the children included in the study, 61.6% were boys (37 children) and 38.3% were girls (23 children). The mean age of patients was 12.2 ± 1.9 (years median). Transmission pathway: perinatal-35% (n – 21), parenteral – 31.6% (n – 19), unknown source of infection – 33.3% (n – 20).

According to WHO classification (2012), the patients were distributed as follows: clinic stage II – 16 children, stage III – 38 children and stage IV – 6 children. Before the start of treatment, all children were examined for the presence of secondary diseases that cause the stage of the disease. For example, lymphadenopathy was observed in 35% of cases, tuberculosis in 10%, herpetic infections in 11.6% of children, fungal infections – 21.6%, recurrent upper respiratory tract diseases – 35%, chronic hepatitis in 10%, lymphoma was diagnosed in 5% and fibrous leukoplakia of the tongue in 1.6% of cases.

The degree of immunodeficiency was determined by the level of CD4 + lymphocytes (according to the WHO classification dated 2012.) and also the level of HIV RNA was determined. Prior to the treatment, the average number of CD4 + lymphocytes was 345.3 ± 135.4 cells/ μl, the average level of RNA HIV – 5.55 IG copies / ml.

Changes on the part of red blood cells were evaluated on the international scale based on the dynamics of hemoglobin levels, the number of red blood cells, white blood cells and platelets before treatment and 24 and 48 weeks after initiation of therapy. According to the international scale, 1 degree eritropenia – from 3 to 3.6; 2 degree – from 2.5 to 2.9; and the 3 – below 2.5 × 10^{12}/L. 1 degree anemia –Hb-100–120 g/l, 2 degree-90–100 g/l, 3 degree – 70–90 g/l, 4 degrees – below 70 g/l. Platelet count

Megakariocytes of human immunodeficiency virus-infected individuals express viral RNA. Proc. Natl. Acad. Sci. USA 86.– 1989.– 5595 p.

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100 – 150 × 10^9/l corresponds to the 1 degree of thrombocytopenia, 2 degree – from 50 to 100, 3 degree – 25–50 and 4 degree – at least 25 × 10^9/L.

Therapy of children with HIV infection was prescribed in accordance with the national Protocol of treatment (order No. 81 dated 5.03.2015). These children were divided into five groups, depending on the treatment regimen. Group 1 consisted of 19 children receiving zidovudine, lamivudine and efavirenz. Group 2 (n – 14) received zidovudine, lamivudine and nevirapine, the group 3 (n – 11) – abacavir, lamivudine, efavirenz. Group 4 (n – 5) received zidovudine, lamivudine and kaletra (later it was replaced with aluvia). Group 5 (n – 11) received a combination drug duovit (virocomb) and efavirenz.

Results. In order to clarify the impact of antiretroviral therapy, especially given that almost all of the regimens included the drug zidovudine (as it is known from the literature, the drug has the effect on the blood system), we have carefully studied children before therapy. The results of the study showed that before treatment, 30 children (50%) had 1 degree anemia, 2 (3.3%) – 2 degree, and only 1 child (1.6%) had 3 degree.

When analyzing the data of hematological parameters studies depending on the gender, we found that initially more often in girls in 65.2% of cases, there was a decrease in the level of hemoglobin. While in boys this figure was 48.6% ($P < 0.05$). After initiation of therapy with ARV drugs (each regimen included zidovudine), after 24 weeks, there was a positive dynamics of increasing the level of hemoglobin in girls to 78.2% and in boys to 59.4%, respectively. However, in 48 weeks after the start of therapy in 8.1% (3) boys and in 43.4% (10) girls again there was the decrease in hemoglobin ($p < 0.05$).

Given the impact of drugs on the performance of red blood cells, we surveyed the children prior to beginning therapy. Eritropenia was identified in 8.1% of cases in boys and 26% in girls, respectively. In 48 weeks of therapy, the number of red blood cells decreased in 10.8% (4) of boys and 43.4% (10) of girls ($p < 0.05$).

It should be noted that thrombocytopenia was registered equally often among boys and girls: 24.3% and 21.7% respectively before the start of therapy. After 24 weeks of therapy there were no significant differences, only after 48 weeks of treatment there was a significant difference: 21.6% in boys and 13% in girls ($p < 0.01$).

Conclusion. Deviation of hematological parameters from the values of healthy persons was registered in 55% of HIV-infected patients before therapy. In the process of antiretroviral therapy in girls anemia and erythropenia were revealed more often, and thrombocytopenia less often than in boys.

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APPROBATION OF PREDICTIVE MODELING TECHNIQUE FOR IMPROVEMENT OF CARDIOLOGICAL MEDICAL SUPPORT ORGANIZATION FOR COMBATANTS WITH COMBAT TRAUMA

Introduction

Four-year follow-up for the injured combatants with combat trauma in Ukraine showed significant incidence of secondary cardiovascular pathology after combat trauma[1]. In patients with severe combat trauma, such incidence may even reach 95%[2]. Secondary cardiovascular pathology has often moderate-to-severe intensity and, in some cases, can result in dilated cardiomyopathy or other severe and life-threatening complications[3]. Hence, it is critically important to identify as early as possible injured combatants with high risk of secondary cardiovascular pathology and refer them to the prophylaxis/treatment. It is also essential that predictors proposed should be available on the first and second levels of the medical assistance for the injured combatants. Recently, results of research addressed the prediction of the secondary internal pathology in injured combatants were published[4], but the model proposed included multiple

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measures and was not able to predict selected diseases, e.g., cardiovascular pathology, which is among most common secondary internal pathology[1].

The problem of cardiovascular pathology in combatants including those with combat trauma is based on the data of up-to-date military conflicts, particularly anti-terrorist operation (based on experience of operation in the period 2014–2017), which is underway on the East of Ukraine. It is known that foreign school of the military physicians considers development of secondary cardiovascular pathology as a consequence of posttraumatic stress disorder[2], while Russian and Ukrainian therapeutic school mainly tends towards traumatic disease theory, namely, complex of pathological conditions appearing after trauma[3]. However, to date, there is no final understanding of pathophysiologic mechanisms of secondary cardiovascular pathology in wounded with combat trauma, thus arrangements for its prognosis and effective prophylaxis were not developed.

Recently, we proposed a new concept of secondary cardiovascular pathology development based on examination of more than 600 combatants with combat trauma using math modeling for the better understanding of the character cardiomyopathy in such patients. It was surprisingly shown that pattern of intracardiac hemodynamics in injured combatants with secondary cardiovascular pathology is much similar to such in patients with hypothyroidism (model of metabolic cardiomyopathy in our research)[4].

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[1] Казмирчук А. П., Мясников Г. В., Сидорова Н. М., и соавт. Патология внутренних органов при боевой травме. Реестр пострадавших в зоне проведения антитеррористической операции // Сучасні аспекти військової медицини: збірник наукових праць Головного військово-медичного клінічного центру «ГВКГ» МО України.– Вип. 21.– К.,– 2014.– С. 44–49.

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There is a strong need to identify among combatants with combat trauma those with high risk of secondary cardiovascular pathology as early as possible, which provides an opportunity to improve organization of specialized health care for such patients. Thus, we tested the possibility of usage of routine laboratory measures obtained within the first days after trauma for determination of patients with high risk of secondary cardiovascular pathology development. Based on such results, it is possible to develop options for diagnostic technical assistance improving in military hospitals for better cardiovascular pathology diagnostics especially among combatants.

The purpose of our study was to develop easy-to-make predictors of secondary cardiovascular diseases that can be used on the first and second levels of the medical assistance for the injured combatants.

Methods

Based on the data collected from Registry of injured combatants[1] from National Military Medical Clinical Center (Kyiv, Ukraine), we created two models with main laboratory indicators that are usually determined on the first and second levels of the medical assistance for the injured combatants. The model 1 was calculated on the base of laboratory indicators measured within the first 3 days, and the model 2 – for the period 10–14 days after combat trauma. We used binary logistic regression for the model creating. For the model quality assessment, we analyzed adequacy (Fisher test), informativeness (the multiplier correlation coefficient R and the determination coefficient R^2, Fisher test), sustainability (correlation coefficient 0.3–0.4), and reliability of our models.

For the model 1, we used data of 103 injured combatants (52 of them with signs of secondary cardiovascular pathology), for the model 2–210 injured combatants (103 of them with signs of secondary cardiovascular pathology), male 100%, mean age 37.77 ± 1.98 years). For the measure of the secondary cardiovascular pathology risk (Ri) < 0.5 we suggest that injured combatant has no secondary cardiovascular risk, for Ri < 0.5 – presence of such risk. Control sample included 85 injured combatants with combat trauma (52 of them with signs of secondary cardiovascular pathology, male 100%, mean age 37.31 ± 1.76 years).

Results

The final predictive model 1 (for the measures done within the first 3 days after trauma) for risk of secondary cardiovascular pathology in injured combatants appears as follows:

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[1] Казмирчук А. П., Мясников Г. В., Сидорова, Н.М., и соавт. Патология внутренних органов при боевой травме. Реестр пострадавших в зоне проведения антитеррористической операции // Сучасні аспекти військової медицини: збірник наукових праць Головного військово-медичного клінічного центру «ГВКГ» МО України.– Вип. 21.– К.,– 2014.– С. 44–49.

Ri = 0.71 – 0.013TP + 0.099G, where Ri = risk measure, dependent dichotomous variable that can be expressed as 0 or 1 (presence or absence of the event), TP = total protein level, g/L, G = glucose, mmol/L. This model indicates that patients with lower total protein blood levels and higher blood levels of glucose, as measured within the first 3 days, have greater risk of cardiovascular pathology. This model is statistically significant (F – calculated = 10.6048 > F – critical = 3.0870 for significance level α = 0.05), but explains only 45.91% of the general distribution.

The final predictive model 2 (for the measures determined within interval 10–14 days after trauma) for the risk of secondary cardiovascular pathology in injured combatants appears as follows:

R = 0.610 – 0.009TP + 0.085G, where R = risk measure, TP = total protein level, g/L, G = glucose, mmol/L.

Both regressors in this model were significant (t – calculated > t – critical; p = 0.0227 and 0.0094, respectively). This model 2 is adequate and reliable (F – calculated = =6.9040 > F – critical = 3.0415 for significance level α = 0.05, p = 0.0013).

The values of the main operational characteristics of the model 1 (sensitivity and specificity) are 57.58% and 84.62%, respectively. The accuracy of the method for the model 1 is 74.12%

Conclusion

Both predictive models 1 and 2 are similar and include the same laboratory parameters (regressors). This underlines importance of protein and carbohydrate disturbances in development of secondary cardiovascular pathology in the injured combatants with combat trauma. However, model 2 by R-testing explains only 25.01% of the general distribution. Therefore, it is reasonable to use laboratory indicators assessed within the first 3 days after combat trauma for prediction of risk of secondary cardiovascular pathology in the injured combatants (model 1) and only if those data are missed – model 2. This information as well as technique of predictive modelling can be useful for improvement in organization of medical assistance for combatants with combat trauma.

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INVESTIGATION OF THE GENES THE HEMOSTATIC SYSTEM IN PREGNANT WOMEN IN VARIOUS REGIONS OF RUSSIAN FEDERATION

The miscarriage of pregnancy is one of the most urgent problems of obstetrics in its social significance According to the summary data of the literature, the frequency of this obstetrical problem ranges from 16 to 20%[1]. One of the reasons for the loss of pregnancy in the early stages are hereditary conditions associated with gene mutations.

Physiological pregnancy itself is a thrombophilic condition from the earliest date, in which the risk of venous thrombosis rises by 5–6 times[2] due to compression of the inferior vena cava and iliac veins, the increase in blood volume during pregnancy, and the inadequacy of venous valves. Predisposing factors may be a tendency to stasis as a result of hormonal changes, the state of physiological hypercoagulation, inhibition of fibrinolysis, a decrease in the content[3] and activity of natural blood anticoagulants, an increase in the functional activity of thrombocytes[4].

In recent years, issues of the influence of hereditary hemostasis defects in the form of gene mutation / polymorphism on the realization of the generative function of women

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with a habitual miscarriage of a pregnancy in anamnesis have been actively studied[1]. The issues related to the deficit of antithrombin III, as well as proteins C and S[2] are described in sufficient detail. At the same time, issues related to the possible influence of other gene polymorphisms of the hemostasis system remain insufficiently studied.

According to modern terminology, the mutation refers to gene polymorphism, which consists of alternative variants of the gene (usually normal and mutant). With respect to the notion of "gene polymorphism", neutral mutations that do not lead to noticeable violations of the function of the gene are usually considered, whereas "mutations" are usually called changes that lead to a pronounced disruption of the gene. It is customary to call polymorphism of the MTHFR C677T, FV (Leiden), and FII G20210A gene mutations, which is probably due to well-known data on their high risk of possible thromboembolic and other complications. It is known that hereditary hemostasis defects exacerbate physiological hypercoagulation during pregnancy and often activate intravascular thrombogenesis processes with subsequent adverse events for the pregnant and fetus. Given the rapid development of assisted reproductive technologies, one can't fail to note the failure in IVF in the presence of polymorphisms of genes associated with thrombophilia.

According to the study of Makatsariya A. D. and Bitsadze V. O., conducted from 1997 to 2008, the incidence of hereditary forms of thrombophilia was 90% in patients with a history of IVF failure[3]. According to Qublan H. S., in patients with 3 or more unsuccessful IVF attempts, the incidence of hemostasis mutations is higher in the anamnesis[4]. Research Coulam C. B. show the negative effect of congenital thrombophilia on the frequency of implantation after embryo transfer in in vitro fertilization programs[5]. A consecutive study by Azem F. states that congenital thrombophilia can play a role in the etiology of recurring implant failures in IVF programs – especially in

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patients with infertility of an unknown genesis[1]. But, according to Vaquero E., there is no evidence of a relationship between the carriage of hematopoietic mutations in hemostasis systems and failures in IVF program[2]. In determining the effect of Leyden mutations, prothrombin and the mutation of methylene tetrahydrofolate reductase (MTHFR) on the incidence of failed IVF outcomes in Simur A. It was shown that the data of thrombophilia form do not play an important role in the absence of implantation after embryo transfer into the uterine cavity[3].

Thrombophilic conditions are one of the most common causes of obstetric complications, such as the syndrome of habitual fetal loss, intrauterine growth retardation, placental insufficiency. A separate group of thrombophilia is caused by hereditary conditions associated with gene mutations[4]. According to the literature, about 40% of thromboembolism and 30% of obstetric complications are associated with hereditary maladaptation of hemostasis[5].

Since full placental blood circulation depends on a balanced ratio of procoagulant and anticoagulant mechanisms, hereditary thrombophilia can lead not only to the development of thrombosis during pregnancy and the postpartum period, but also to various placental vascular complications, which may result in impaired implantation or development of the embryo[6]. The risk of venous thrombosis and thromboembolism is further increased in women with AFS-associated thrombophilic conditions[7].

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Nevertheless, the risk of thrombotic and gestational complications with various hereditary thrombophilia appears to be different and requires detailed study.

Congenital causes of increased thrombosis may be a deficiency in the blood stream of natural anticoagulants and a lack of fibrinolytic factors, as well as an excess of procoagulant factors[1].

In view of the foregoing, the study of the role of hereditary thrombophilia, the most common in the habitual miscarriage of pregnancy, their influence on the formation and course of pregnancy, the postpartum period, the development of various, primarily, thrombotic complications, and the quality of life in general, is one of their most urgent and requiring the study of obstetrics and gynecology[2].

We studied the works devoted to the issues of miscarriage related to the carriage of polymorphisms of genes associated with thrombophilia in the subjects of the Russian Federation (Kursk and Kirov regions) and compared with the data obtained in the course of research on this issue in the Kaliningrad region.

An analysis was made of an article that examined the prevalence of polymorphisms in the genes of the hemostasis system in women with a history of reproductive loss living in the Kursk region. In this article, a genetic analysis of 50 case histories of women suffering from thrombophilia, in whose history there were recurrent reproductive losses. The study was conducted on the basis of the regional perinatal center of the city of Kursk[3].

Among the 25 (50%) women who had a history of 1 loss of pregnancy, 20 (40%) women with 2 cases of recurrent fetal loss, 5 women (10%) who had suffered 4 pregnancies. A study for the presence of thrombophilic polymorphisms included PCR diagnostics of thrombophilia: methylenetetrahydrofolate reductase (C677T MTHFR), Leiden (FV: 1691 G/A), prothrombin (FII: 20210 G/A), plasminogen activator inhibitor (PAI-1: 675 5G/4G), platelet receptor fibrinogen (GPIIIa la/lb Leu33Pro), fibrinogen (FGB455 G/A). After obtaining the detected thrombophilic polymorphisms of the hemostasis gene, statistical processing of the data[4].

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The results of the study were as follows: the average age of all the examined women with recurrent history loss was 33 years (from 24 to 41). Hereditary form of thrombophilia was established in 100% of women, in whose anamnesis reproductive losses were noted. A high incidence of heterozygous forms of mutations in the MTHFR, PAI-1 genes was found, and the absence of defects in the FV and FII genes was found. The ratio of the frequency of distribution of the heterozygous mutation to homozygous form was 4: 1 ($p < 0.001$). According to studies of frequency distribution of genotypes of polymorphism rs1801133 of the MTHFR gene, the heterozygous mutation form of the gene coding for MTHFR synthesis is the most frequently observed and is observed in 45 (90%) patients. The homozygous mutation variant of the MTHFR gene was not found in the women under study. In the study of the frequency distribution of the genotypes of the polymorphism rs1799768 of the PAI-1 gene, the following results were found: gene mutation occurs in 44 (88%) of women out of 50. At the same time, the heterozygous variant of the mutation occurs almost 2 times more often homozygous (58% and 30% < 0.001). All women whose genotype was marked with the PAI-1 mutation, at least one mutation of the folate cycle was identified with it. In this study, the combination of heterozygous forms of mutations in genes encoding the synthesis of MTHFR and PAI-1 is more likely. This pair of mutations occurs in half of women suffering from hereditary thrombophilia, with a history of reproductive loss[1].

It was also determined that the genes encoding V and II coagulation factors were normal homozygotes in all the patients studied. Mutations in the study of polymorphisms of the F2 and F5 genes were not met in any patient[2].

In the study of the polymorphism rs1800790 of the FGB gene, it was established that the heterozygous mutation form of the gene coding for fibrinogen synthesis was found in 9 patients (4.5%). A homozygous variant of the mutation was not detected by any woman.In the study of rs 5918 polymorphism of the GPIIIa gene, a mutation of the gene coding for the platelet receptor for fibrinogen was found to occur at a frequency of 16%. The heterozygous form of the mutation was more frequent than the homozygous form in 1.67 times ($p < 0.05$)[3].

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[2] Ibid.

[3] Ibid.

This study informs us that mutations in the PAI-1 gene (88%) are most common in women with reproductive loss in the Kursk region. The combination of mutations in the genes MTHFR and PAI-1 is found in 78% of women[1].

In 2015, an article was published that voiced the problem of the prevalence of polymorphism of genes associated with thrombophilia in female residents of the Kirov region. 47 women were examined, who applied for help to the "For Birth" medical center. All patients had a history of habitual miscarriage (2 or more miscarriages). The average age of the subjects was 32 years. In 6 patients IVF was performed, in two of them the procedure was repeated, due to failure[2].

It was found that the heterozygous mutation in the PAI-1 gene (38.2%), rs1126643 polymorphism in the ITGA2 gene (23.4% heterozygous variant and 12.8% homozygous variant), polymorphism rs1800790 gene FGB – 19.1% and 4.3%, respectively. Heterozygous polymorphisms in folate metabolism genes MTRR66 and MTHFR677 occurred in 31.9% and 19.1% of cases, and homozygous in 8.5 and 6.4% of cases. A very high risk of thrombosis (thrombophilia) was noted in 12.8% of patients (polymorphism of the genes F2: 20210 G/A, MTHFR: 677 T/T), high – 21.3% (PAI-1: 675 4g/4g, FGB: 455A/A), the average – 65.9%. Interruption of pregnancy was mainly for 6–8 weeks of gestation. The Leiden mutation was not detected in any case[3].

We are studying this issue in the Kaliningrad region. In 2016, we examined 72 women, among whom were pregnant women planning pregnancy and patients before preparing for IVF. All women in the study group had at least 1 loss of pregnancy in their history. The average age of the patients was 32 years. The research was conducted on the basis of the State Autonomous Institution of the Kaliningrad Region "Regional Perinatal Center" and the Laboratory of Genomic and Proteomic Research of the Immanuel Kant Baltic Federal University. Genetic polymorphisms of blood coagulation genes, fibrinolysis system genes, folate metabolism genes, and

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[3] Ibid.

platelet glycoprotein genes were detected by pyrosequencing using the PyroMark genetic analysis system.

According to preliminary data obtained during the study, the prevalence of the homozygous minor allele 4g/4g polymorphism rs1799786 of the PAI-1 gene in the Slavic population of the Kaliningrad Region. Genetic polymorphisms associated with a development risk of 36%, and heterozygous 5g/4g – 38%. The frequency distribution of the genotypes of the F16 and F20210A polymorphisms of the F2 gene regulating the blood coagulation activity was as follows: GG – 95.5%, GA – 1%, AA – 3.5% and GG – 98.1%, GA – 1.9%, AA – 0%, respectively, which indicates their small variability. The polymorphism rs1126643 in the ITGA2 gene and the polymorphism rs1800790 of the FGB-T/T gene – 18% and A/A – 5%, were observed with the greatest frequency, respectively. In contrast, the polymorphism (A1/A2) in the GP1b gene and polymorphism rs5918 of the GPIIIa gene are less often A2/A2–1.8% and T/T – 1.5%. The polymorphisms A1296C and C677T of the MTHFR gene of the folate cycle are more common – 10% and 16%, respectively. In this case polymorphism A2756G in the MTR gene was detected only in 3.5% of cases. Polymorphism of the gene prothrombin G20210A in the heterozygous state is rare (2%), but the combination with the mutation FV–Leiden G1691A is unfavorable, since the risk of thrombosis increases almost 80 times.

Probably, the pattern of polymorphism of genes associated with thrombophilia in the Kaliningrad region and similarities with the results of studies in the Kursk and Kirov regions can be explained by the peculiarities of the geographic location of the region's economic development and the demographic situation in the country.

Section 2. Mediobescience

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FEATURES OF THE METABOLISM HISTIDINE OF NEWBORNS

Introduction

Protein metabolism in adult and children has many similarities but also some major differences. The literature over free amino acid concentrations in organism of children under the 1–3 years old age sparse. Adult and children have different nutritional needs regarding amino acid intake in order to promote a normal protein homeostasis and in children growth[1]. In addition to the amino acids that are essential for adults, also histidine, arginine, cysteine, tyrosine and taurine are considered to be semi-essential amino acids in children for a normal development. Changes of amino acid concentration are seen in different clinical and physiological conditions both in adults and in infants adapting to the amino acid metabolism to the metabolic and nutritional needs[2]. Children show a faster recovery and are more easily attaining equilibrium of nitrogen balance following a protein catabolic event such as trauma, operation and infection[3]. The amino acid need for the infants has earlier been derived from levels of amino acids in plasma, which in some respects differ from the levels seen in adults[4].

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Histidine, an essential amino acid, has as a positively charged imidazole functional group[1]. As an essential amino acid, histidine is not synthesized de nova in humans and other animals, who must ingest histidine or histidine-containing proteins. The amino acid is a precursor for histamine and carnosine biosynthesis[2], also histidine ligands include Zn2+and haem, tropomyosin, heparin and heparan sulphate, plasminogen, plasmin, fibrinogen, thrombospondin, IgG, Fcγ R and complement.

This review outlines the molecular, structural, biological and clinical properties of the histidine as well as describing the role of the histidine in various physiological processes.

Changes amino acids Age-related changes of muscle and plasma in healthy children earlier been described, showing mainly lower values in younger children, but no data exist regarding the change of levels histidine pattern in growing children.

The aim of the study was to explore if histidine in plasma changed during growth and differed compared to values obtained in an adult reference group. In the present study plasma histidine were determined in plasma obtained in otherwise healthy children between the ages of 1–3 years. The correlation between age and concentration was calculated.

Materials and methods

Metabolically healthy children (n = 69) aged 1–3 years. All the children were well-nourished and within the normal range with regard to length and weight and considered otherwise healthy.whom we received blood samples and who, after careful revision of their medical charts, showed no evidence of metabolic, renal, hepatic, cardiac, or muscular disorders. The study was conducted by the Hospital Ataturk University.

The children were grouped as follows: group 1 (age 1–3 years, females, n = 34), group 2 (age 1–3 years, male, n = 35) and group 3(age 10–15, n = 27).

The possible risks and the study design were explained to the parents of the children and to the healthy volunteers putting emphasis on the fact that participation was (frivillig) before approval and inclusion in the study.

Histidine analyses

A determination of the concentrations of histidine in both plasma was Liquid chromatography–mass spectrometry (LC–MS/MS). In brief, plasma was mixed Zivak and Amino Asit commercial kit. The homogenate was centrifuged and the histidine in the supernatant were determined using an automatic analyser (Zivak Tandem Gold LC–MS/MS, Seri number: ZV1MS1011W002, Zivak Technologies, Turkey.) as described previously. The concentration of the histidine in plasma was expressed as mmol/L respectively.

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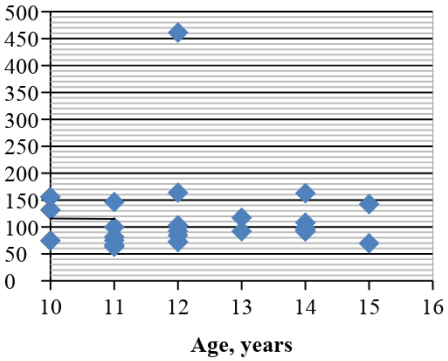

Figure 2. Correlation (R = 0.01) between age and the histidine concentration on age grop 10–15, female/male

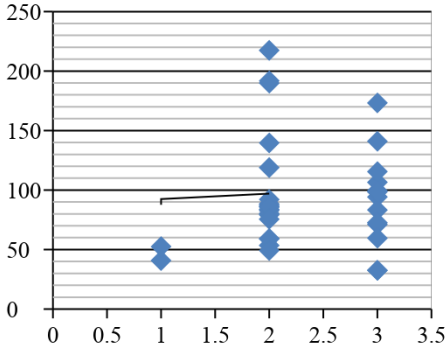

Figure 2. Correlation (R = 0.06 the 1) between age and the histidine concentration on the female

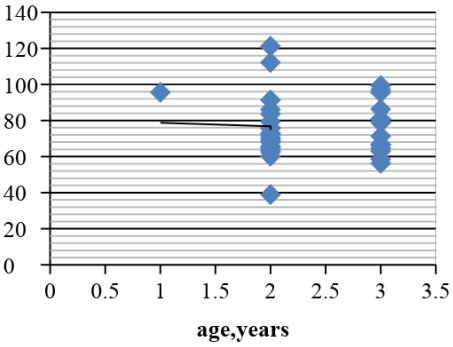

Figure 2. Correlation (R = 0.063) between age and the histidine concentration on age grop 1–3, male

Statistics

All values are given as mean ± SD except from the plasma values in group 1–3 and 10–15 years which was presented as range. Analysis of variance was performed for histidine for all the groups and concentration gradient. Scheffe's test was used as a post hoc test. A P-value less than 0.05 were considered as statistically significant. The values of the reference group are presented as mean and 95% confidence interval for observations. Calculations of correlation were performed using regression analysis[1].

Table1.– Plasma amino acid mmol/l and correlation

Groups	Histidine levels	Correlation (R) with age within the study group (1–3)	Correlation (R) with age within all the groups
Group 1 n = 34	93.92059	0.061	0.014
Group 2 n = 35	76.12	0.063	
Group 3 n = 27	115.5111	0.01	

Results

In plasma higher concentrations were seen in group 10–15 years as compared with group 1–3 year for histidine. When comparing the histidine concentrations of the 1 and 2 group with the study groups the mean values were higher whereas (Table 1). Figures are showing the correlation between the concentrations of histidine and age (P\0.05).

Discussion

In this study the concentrations of histidine in plasma pattern changed in relation to age among children. The most pronounced difference was between males 1–3 years and the older children (10–15 years) with females (1–3 years) in between. The general pattern was an increase in concentrations in plasma during growth. Moreover, in comparison group 3, there were also clear differences in the hıstıdıne of the children (1–3 years). In adults characteristic changes in the plasma pattern has been described during catabolic conditions[2]. The total sum of histidine in plasma increased in relation to age in children, and exhibited correlation to age. The skeletal muscle of the newborn amounts to 25% of the body weight, while it represents a larger proportion in adults, 30–40%[3]. This corresponds to a water-free protein proportion of 12.5% in the full

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term baby compared to 18% in the adult, an increase that mainly is explained by the increase in skeletal muscle mass[1].

Changes in muscle and plasma amino acid concentrations during growth may be explained by changes in protein synthesis, in tissue composition as well as to metabolic alterations. The amino acid concentration in the intracellular space is the net-effect of the combination of protein synthesis, breakdown, deamination, amination and transmembrane transportation[2]. In the growing individual substrate availability, the influences of growth factors and the activity of amino acid transportation are of importance. The differences in amino acid and protein metabolism between children and adults following trauma is reflected by unchanged body protein flux, protein synthesis, amino acid oxidation and protein degradation, measured with isotope technique, in children as compared to adults[3].

In critically ill neonates undergoing operation for necrotising enterocolitis increased levels of BCAA, histidine were shown, the extent of which correlated with the severity of the disease which in turn mirrored the degree of liver dysfunction and deranged amino acid metabolism in the tissue[4].

The present study shows that plasma histidine change during growth. This may be explained by a combination of increase in protein stores, an increased uptake of amino acids for protein synthesis, maturation of amino acid transport system, at least in low age differences in tissue hydration state. It is probably important to take age dependent differences into account when nutritional therapies are designed in growing individuals.

Many analyses, including plasma amino acid, show an age-related distribution of their concentrations. This underlines the importance of using appropriate reference values when working with a paediatric population.

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VARIANT ANATOMY OF THE HUMAN PANCREAS BY ULTRASOUND

Introduction. The pancreas is a mixed organ. Today, there is a growing number of various pancreatic diseases caused by the spread of such etiological factors as alcoholism, obesity, eating disorders, etc. The ultrasonic method of examination of the pancreas is generally considered safe and minimally invasive on the one hand, and relatively difficult in terms of visualisation, on the other.

Purpose: to reveal the morphological and morphometric parameters of the adult pancreas based on the data obtained in the course of ultrasonic examination.

Materials and methodology. The study material was comprised of data obtained in the course of ultrasonic examinations of the abdominal cavity of 35 patients (20 men and 15 women) aged 16 to 75 years without pancreatic pathology. The study was carried out using the ultrasonic diagnosis device Acuson s1000 manufactured by Siemens (Germany), in accordance with the standard procedure.

Results and discussion. The study showed that topographically, the pancreas is closely connected to a number of vessels and organs of the abdominal region and retroperitoneal space. The head of the pancreas is circled and partially covered on the front by the duodenal loop and is adjacent to the large intestine, the liver, the lower genital vein, and the aorta. The body is adjacent to the posterior wall of the stomach, the transverse colon, the jejunum, mesenteric and splenic vessels. The tail, located in the depths of the left hypochondrium, is adjacent to the spleen, the gastric fundus, the splenic vessels.

In an ultrasonic examination, the pancreas is detected in the epigastric region anterior to the main vessels (inferior vena cava, aorta) and the vertebral spine. In the area of the anterior surface of its head, the gastroduodenal artery is clearly visible. Several large arterial and venous vessels are detected in the body area of the gland as well. In the tail area, splenic vessels are clearly visible, spreading along the pancreas into the splenic hilum.

The analysis of morphometric parameters showed that the human pancreas is characterised by individual features of morphometric parameters. The average head width is 26.0 ± 2.0 mm, the average body width is 17.7 ± 2.2 mm; the average tail width is 21.2 ± 2.0 mm.

The study of the width of the pancreas in different age periods showed that the minimum dimensions are characteristic for the organ during the period of adoles-

cence (head – 24 ± 0.8 mm, body – 18 ± 1.1 mm, tail – 25 ± 0.9 mm). These parameters further increase in the age group of 34 – 55 years (head – 28.1 ± 0.7 mm, body – 19.8 ± 1.2 mm, tail – 21.3 ± 0.7 mm). With time, as the patient grows older, the morphometric parameters of the pancreas gradually decrease. The study including patients of the 2nd period of adulthood (35–55 years) and elder patients showed that there is a tendency to a uniform increase in echogenicity, smoothing of parenchymal granulosity of up to an almost homogeneous hyperechogenic structure in patients of 75–89 years of age.

Morphometric parameters of all parts of the pancreas in men (head – 26.6 ± 2.1 mm, body – 18.2 ± 2.0 mm, tail – 23.8 ± 2.1 mm) were significantly larger than in women (head – 24.8 ± 2.1 mm, body – 17.1 ± 2.2 mm, tail –18.9 ± 2.2 mm).

Conclusion

The pancreas is characterised by age- and gender-specific features of morphometric parameters. The average head width is 26.0 ± 2.0 mm, the average body width is 17.7 ± 2.2 mm; the average tail width is 21.2 ± 2.0 mm, respectively. The transverse dimensions of all parts of the pancreas in men exceed the equivalent dimensions in women.

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THE OPEN WOUNDS AND PLANTS USING FOR THEIR TREATMENT IN GEORGIA (REVIEW)

A wound is a mechanical abnormality, which is associated withthe break of the skin and mucous membrane integrity. During the break of the integrity ofa healthy human body, the body's healing system is switched on automatically. Different diseases inhibit the healing process (reduction in blood circulation, diabetes mellitus) and the open wounds or ulcers appear on the human body.

Since ancient times, the treatment of the open wounds has received much attention in China, India, Greece and many other countries[1]. This disease is still problematic and studying and developing the methods of its treatment are still relevant. It is known

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that the fight against this disease is a long and time-consuming process. This papers wells on a review of methods for the treatment of the open wounds, as well as medical books and manuscripts on the the open wounds.

Wound healing is a dynamic process that involves the process from the timethe injury was occureduntilthe complete recovery. The recovery processes may occur simultaneously or successively[1]. In the healing process, depending on the type of injury, the different mechanisms are switched on. Knowledge of the recovery mechanisms, maintaining the impact on them and their optimal regimes helps the clinician to effectively treat the disease[2].

There is no uniform definition of a "chronic wound", we often find the termsa "problematic" or "complexwound", "trophic ulcer", "lasting injury". Besides, tropical ulcerin lower extremities, depending on etiological factors, may be venous, arterial, in the setting ofdiabetic neuropathy and angiopathy, hypertonic and caused by systemic diseases and so on[3].

The conditions for detecting the open wounds are secondary injuries, ischemia, enhancement of protease synthesis in the wound, decreased activity of the tissue growth factor, and so on[4].

The open wounds create a man's discomfort, and they break the rhythm of his life. During research, we studied the impact of disease on the quality of human life, affecting the physical, social, emotional and functional characteristics of the patient. Scientists consider that these features are necessary to increase the effectiveness of the patient's treatment in the clinic[5].

Treatment of the chronic wounds is a complex issue and requires elimination of the impact ofinjury factor, and improving venous and arterial blood circulation. Unless injury factors are eliminated, the duration of treatment is prolonged and is progressed

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to the chronic phase[1] and this issue is still relevant today. In the treatment, the wound is washed with a large stream of disinfectants, and antibiotic and anti-inflammatory therapy is also being used[2].

For the purpose of stimulating reparative processes, there are used many methods and means, for example, ultraviolet and infrared irradiation, oxygenation, cryogenic stimulation and so on. Studies have shown that the use of bioactive rays based on soya protein increases the re epithelization[3].

Diabetic foot ulcers, as is well-known, are the difficult-to-heal wounds. Often, after achieving the positive results, the ulcer is still detected again. Scientists conduct randomized trials on various chemical compounds[4]. There are also being carried out studies of bandages[5].

For the treatment of the open wounds, together with synthetic chemical compounds, there are also used natural compounds (plant and animal). Using old manuscripts existingin different countries, scientists have studied the the impact of these compounds on regeneration of the damaged tissues. It turned out that natural compounds heal the wounds andaccelerate the regeneration events[6].

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Georgian manuscripts and medicalbooks contain much information on the use of plant raw materials for treating the wounds[1]. In different regions of Georgia, the young plants have been used for the treatment of the open wounds: licorice, chamomile, plantain, acacia, lilac, vine leaves, calendula, eucalyptus, sea buckthorn, etc. There have also been widely used bee products: propolis, pollen, royal jelly.

Flora of Georgia is rich in plants containing phenolic compounds. Phenolic compounds are characterized by antioxidant, anti-inflammatory, antibacterial and tissue-regenerative capacity.

Researchers from the Akaki Tsereteli State University (Al. Tsulukidze Kutaisi Pedagogical Institute) have done a quite extensive and exhaustive work on habitats of plants. There have been studied the Imeretian limestone flora[2].

During the expedition from spring to early autumn (2017), we explored some of the areas of Imereti: Zestafoni, Tkibuli, Terjola, Chiatura, Sachkhere, Baghdati, and Samtredia districts, Kutaisi surroundings, the banks of the rivers of Kvirila and Tskaltsitela. Plants containing phenolic compounds are found in almost every district. We have studied habitat, chemical compositions and drying conditionsof some of them. For example, licorice *Glyceriza glabra* is rich in flavonoids, the content of which in the roots reaches 3–4% andis drying in theairor at 50 °C; chamomile*Chamomilla recutita*flowers contain 0.2% flavonoids andare drying in the air or at 40 °C; plantain-*Plantago major* leaves contain 2% of flavonoids andare drying in the air; calendula *Chamomilla recutita* flowers contain 1% of flavonoids andare drying in the air or at 45 °C; eucalyptus *Eucaliptus globulus* – the leaf contains phenolic compounds and is drying in the air or at 40 °C; sea buckthorn *Hippophae rhamnoides* fruit contains phenolic compounds andis drying in the air; lilac *Siringa culgaris* flower contains phenolic compounds andis drying in the air. However, the less studied false acacia contains the flavonoid-robinin.

As a result of studying the manuscripts and scientists papers, it has been found that the nature of Georgia is rich in plants containing phenolic compounds, the study of which is an interesting material for further development of the new drug dosage forms.

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