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Telefon: +998335157555
Email: nashruzjournals@gmail.com
Sayt: nashruz.uz
t.me: @nashruzjournals

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Andijan, st. Yu. Otabekova, house 1.
Phone: +998335157555
Email: nashruzjournals@gmail.com
Website: nashruz.uz
t.me: @nashruzjournals

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Телефон: +998335157555
Email: nashruzjournals@gmail.com
Сайт: nashruz.uz
t.me: @nashruzjournals

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ОПТИМИЗАЦИЯ ЛЕЧЕНИЯ БОЛЬНЫХ С РЕЦИДИВИРУЮЩИМИ МАТОЧНЫМИ КРОВОТЕЧЕНИЯМИ ПУБЕРТАТНОГО ПЕРИОДА.

С.А. Абдуллажанова, Д.М. Тиллабаева, А.С. Ходжаева
Центр развития профессиональной квалификации медицинских работников

Аннотация.

В статье рассматриваются вопросы оптимизации консервативной терапии маточных кровотечений у девочек-подростков, расширение возможностей противорецидивных исходов. Цель: оптимизация консервативной тактики ведения девочек-подростков с рецидивирующими маточными кровотечениями Материал и методы: Обследовано 90 пациенток – девочек-подростков(средний возраст 14.7±1.4г.) с рецидивирующими маточными кровотечениями. Результаты: Детально проанализирован преморбидный фон и определены факторы риска возникновения и рецидивирования маточных кровотечений пубертатного периода с акцентом на отягощенную репродуктивную наследственность с материнской стороны. Предложен патогенетический подход к лечению рецидивирующих маточных кровотечений у девочек-подростков. Выводы: необходим дифференцированный и поэтапный комплексный подход к консервативному лечению маточных кровотечений у девочек-подростков.

Ключевые слова: репродуктивное здоровье девочек-подростков, пубертат, отягощенная наследственность, маточные кровотечения пубертатного периода, рецидивы, вульвовагиниты, анемия, гиповитамимнозы.

PUBERTAT DAVRI BACHADON QAYTALANUVCHI QON KETISHI KUZATILGAN BEMORLARNI DAVOLASHNI OPTIMALLASHTIRISH.

S.A. Abdullajanova, D.M. Tillabayeva, A.S. Hodjaeva
Tibbiyot xodimlarining kasbiy malakasini oshirish markazi

Annotatsiya

Maqolada o'smir qizlarda bachadondan qon ketishini konservativ davolashni optimallashtirish, relapsga qarshi natijalar imkoniyatlarini kengaytirish masalalari muhokama qilinadi. Maqsad: takroriy bachadondan qon ketishi bilan og'rigan o'smir qizlarni davolashning konservativ taktikasini optimallashtirish.Material va usullar: Bachadondan takroriy qon ketishi bilan og'rigan 90 nafar bemor - o'smir qizlar (o'rtacha yoshi 14,7±1,4 yosh) tekshirildi. Natijalar: Premorbid fon batafsil tahlil qilindi va balog'at yoshidagi bachadondan qon ketishining paydo bo'lishi va takrorlanishi uchun xavf omillari aniqlandi, bunda ona tomondan yuklangan reproduktiv irsiyatga e'tibor qaratildi. O'smir qizlarda

takroriy bachadon qon ketishini davolash uchun patogenetik yondashuv taklif etiladi. Xulosa: o'smir qizlarda bachadondan qon ketishini konservativ davolashda tabaqalashtirilgan va bosqichma-bosqich kompleks yondashuv zarur.

Kalit so'zlar: o'smir qizlarning reproduktiv salomatligi, balog'at yoshi, og'ir irsiyat, balog'at yoshidagi bachadondan qon ketishi, relapslar, vulvovaginit, anemiya, gipovitaminoz.

OPTIMIZATION OF TREATMENT OF PATIENTS WITH RECURRENT UTERINE BLEEDING OF PUBERTY.

S.A. Abdullajanova, D.M. Tillabaeva, A.S. Khodjaeva

Center for the development of professional qualifications of medical workers

Abstract.

The article deals with the optimization of conservative therapy of uterine bleeding in adolescent girls, the expansion of the possibilities of anti-relapse outcomes. Objective: optimization of conservative tactics of management of adolescent girls with recurrent uterine bleeding Material and methods: 90 adolescent girls (mean age 14.7±1.4) with recurrent uterine bleeding were examined. Results: The premorbid background was analyzed in detail and risk factors for the occurrence and recurrence of uterine bleeding of puberty were determined, with an emphasis on burdened reproductive heredity on the maternal side. A pathogenetic approach to the treatment of recurrent uterine bleeding in adolescent girls is proposed. Conclusions: a differentiated and step-by-step integrated approach to the conservative treatment of uterine bleeding in adolescent girls is needed.

Keywords: reproductive health of adolescent girls, puberty, burdened heredity, uterine bleeding of puberty, relapses, vulvovaginitis, anemia, hypovitaminosis

Гинекологические заболевания периода полового созревания, в частности аномальные маточные кровотечения пубертатного периода (АМКПП), в дальнейшем оказывают существенное влияние на репродуктивное здоровье женщины фертильного возраста. По данным исследователей, частота АМКПП колеблется от 19% до 39%, рецидивы-до 45% и не имеют тенденции к снижению. Основной причиной их возникновения является незрелость репродуктивной системы девочки-подростка. Отягощенный преморбидный фон в сочетании с лабильностью нейроэндокринной регуляции менструальной функции являются пусковым моментом в патогенезе АМКПП (2, 5, 6).

Этиологические факторы, способствующие возникновению АМКПП, разнообразны. Большинство исследователей подчеркивают значимую роль в генезе МКПП бактериально-вирусной инфекции, гиповитаминозов,

нарушений в системе гемостаза. Воздействуя на организм девочки-подростка в период гормональной перестройки, эти факторы (отдельно взятые или совместно) в итоге приводят к нарушению метаболизма эстрогенов, появлению состояния относительной и/или абсолютной гиперэстрогенемии(1, 3, 4).

В связи с вышеизложенным, целесообразен патогенетически оправданный комплексный мультисистемный подход к лечению АМКПП. Вместе с тем, имеющиеся сегодня многочисленные методы лечения девочек-подростков с АМКПП несовершенны, о чем свидетельствует высокая частота их рецидивов (до 46%). Поэтому поиск клиницистами оптимальных методов лечения девочек-подростков, страдающих АМК, продолжается.

Целью нашего исследования явилась оптимизация тактики ведения девочек-подростков с РАМКПП.

Материал и методы исследования. Нами были обследованы 90 девочек- подростков с АМКПП в возрасте 13-16 лет, не живущих половой жизнью, за период 2022-2023 гг.(средний возраст 14.7±1.4). Впервые заболевание (АМКПП) возникло у 62% обследованных девочек-подростков, в 38% случаях отмечены рецидивы. В соответствии с намеченной целью исследования, обследованные девочки-подростки были разделены на две сравнительные группы: 1-я группа – первичные АМКПП (п=30), 2-я группа – рецидивы РАМКПП (п=60). Контрольную группу составили девочки-подростки с нормальным менструальным циклом (п=20). Критерии включения в исследование и исключения из него соответствовали общепринятым в гинекологической практике при пубертатных маточных кровотечениях. Все исследования проводились с учетом требований Хельсинской декларации Всемирной Ассоциации «Этические принципы проведения научных и медицинских исследований с участием человека», нормативных документов МЗРУзб, согласно принципам доказательной медицины.

Для выявления факторов риска возникновения АМКПП, способствующих возникновению РАМКПП, нами был проведен детальный сравнительный анализ преморбидного фона (ПФ) обследованных пациенток, поскольку соматическое здоровье ребенка влияет на становление репродуктивной системы в дальнейшем. Наибольшее отягощение преморбидного фона заболеваниями ЖКТ отмечено у 74% обследованных пациенток П группы, анемией 1-2- степени (59%), патологией щито-

видной железы (56%) , хроническими тонзиллитами и частыми ОРЗ (47%), гиповитаминозами (особенно витаминами группы В) – 45%. У пациенток 1-й группы ПФ оказался менее отягощенным вышеперечисленными соматическими заболеваниями (до 32%).

Изучение гинекологической заболеваемости среди обследованных пациенток выявило воспалительные заболевания гениталий (вульвовагиниты, аднекситы) в 69% у пациенток 2й группы, 34% - у пациенток 1й группы. Бактериологическое изучение влагалищных выделений выявило моновозбудитель лишь в 13% , в остальных 87% случаях обнаружена ассоциация микроорганизмов с преобладанием хламидийно-грибково-кокковой (аэробной-анаэробной) флоры. Биохимия крови выявила анемию 1-2 степени у 58% обследованных больных.

Наследственность оказалась отягощенной различными гинекологическими заболеваниями матерей (миомы, кисты, ДМК, бесплодие) также преимущественно у пациенток 2-й группы (68%), в то время, как у пациенток 1-й этот показатель составил 19%.

Преморбидный фон у обследованных пациенток оказался полиморбидным, в связи с чем нами был выбран дифференциальный подход к лечению.

Результаты: Общее состояние тематических больных оценивалось как удовлетворительное с учетом обьективного статуса и показателей гемодинамики. Пациентки 1-й группы (п=30) получали гемостатическую терапию традиционно половыми стероидными гормонами (КОК) первоначально с целью остановки кровотечения, затем с целью нормализации менструального цикла в циклическом режиме 3-6 мес (этинилэстрадиол 30мкг+дезогестрел 0.75мкг). Стартовая доза гемостаза зависела от обильности и длительности кровотечения, веса пациентки, составив от 2 до 4 таблеток, с последующим переходом в циклический режим. Полиморбидность фона диктовала необходимость консультации смежных специалистов (невролога, эндокринолога), чьи рекомендации учитывались при выборе адекватной тактики ведения, одновременно проводилась коррекция выявленных нарушений. Положительная динамика наблюдалась на 3-4месяце лечения, стойкий положительный эффект – 6-8 мес.

Пациентки П группы (п=60), получали лекарственные препараты с гемостатической целью, корригирующие фибринолиз, т.е. обладающие антифибринолитической активностью, а также оказывающие противо-

воспалительный эффект, поскольку воспалительные заболевания гениталий имели высокий удельный вес (до 69%). Для достижения поставленной цели предотвращения повторных кровотечений (рецидивов), а также для репрезентативности выбора лечебной тактики П группа пациенток была разделена на две подгруппы ПА (п=30) и ПБ (п=30). Пациентки ПА группы в комплексном лечении получали лекарственные препараты, активным компонентом которых являлась транексамовая кислота, обладающая антифибринолитическим, противовоспалительным действием, в дозе 250-500 мг 2-4 раза в день. Доза препарата подбиралась индивидуально в зависимости от редукции силы кровотечения. Выраженный положительный эффект отмечен уже со следующей нормальной менструацией у 15 пациенток, стойкий положительный эффект – к 3 месяцу лечения. Пациентки ПБ группы наряду с транексамовой кислотой получали Витаминно-минеральный комплекс (ВМК), представленный смесью 5-ти биологически активных компонентов (витаминов, минералов), взаимодействие которых является синергическим и кофакторным. Обоснованием назначения данного ВМК явилось то, что репродуктивная система тесно связана с микроэкологией питания, а также высокая частота (45%) выявления гиповитаминоза у обследованных нами пациенток. Доза препарата также подбиралась индивидуально в зависимости от редукции силы кровотечения (по 1-2 порошку 2раза ежедневно в течение 5-7 дней). Остановка кровотечения наблюдалась с 4-5 го дня от начала лечения с незначительной «мазней» 1-2 дня). Стойкий положительный эффект отмечен уже со следующей нормальной менструацией. Период реабилитации у пациенток ПА группы длился 2-3 мес без рецидивов, в то время, как у пациенток 1-й группы отмечена длительная реабилитация 6-8мес.

Клиническое течение коррелировало с лабораторными показателями. Исходный уровень тропных гормонов аденогипофиза контрольной и основных группах до начала лечения соответствовал референсным нормативным значениям (ФСГ 3,8± 0,16 МЕ/л; ЛГ 2.96±0.12 МЕ/л) (p<.001). Однако в основных группах была повышена концентрация эстрадиола 189.6± 7.1 нмоль/л, 188.9± 4.1 нмоль/л, соответственно по сравнению с контролем 179.2±7.30 нмоль/л. Величина АМГ в контрольной группе составила 2.6±0.5нг/мл, в основных группах 1.88± 0.3 нг/мл, 1.86± 0.2нг/мл, соответственно (p< 0.001). Концентрация тестостерона в сравниваемых группах была выше 1.22± 0.06 нмоль/л, чем в группе контроля 0.83± 0.04

нмоль/л. Полученные лабораторные данные указывали на наличие яичниковой недостаточности у обследованных пациенток основных групп .

Результаты УЗИ в контрольной группе соответствовали возрастной норме. Однако у всех пациенток основных групп на фоне нормативных размеров матки М-эхо на 2-3 день цикла визуализировалось в виде гиперплазированной линии (гиперплазия эндометрия).15.3± 0.09 мм, несколько единичных фолликулов (1-2) диаметром 2-3 мм и мелкие точечные фолликулы в количестве 6 -8 диаметром 1-2 мм. Признаки овуляции отсутствовали. Эти данные свидетельствуют о яичниковой и маточной несостоятельности у пациенток основных групп.

Показатели гормонального профиля по окончании лечения показали положительную динамику в уровнях половых гормонов: снижение концентрации андрогенов у пациенток основных групп до 0.86± 0.03 нмоль/л, снижение уровня эстрадиола до референсных значений 181.5± 7.2 нмоль/л, 181.3± 4.2 нмоль/л, соответственно по сравнению с контролем 179.2±73.1нмоль/л. Также наблюдалось выравнивание показателей АМГ до нормативных данных.2,4± 0.3 нг/мл и 2.31± 0.21 нг/мл (p< 0001) соответственно.

УЗИ результаты после лечения у всех пациенток основных групп и подгруппах выявил позитивные изменения в виде уменьшения величины гиперплазированного эндометрия -тонкую линию эндометрия 5.1± 0.02 мм, повышенную эхогенность эндометрия матки, что свидетельствовало о появлении полноценной секреции; в яичниках появились здоровые ранние антральные фолликулы в количестве 4-5, исчезла мелкозернистость. Визуально налицо признаки уменьшения яичниковой и маточной недостаточности, появившейся яичниковой состоятельности.

Анализ показателей красной крови выявил компенсаторно повышенные значения гемоглобина на фоне умеренного кровотечения (не профузного), что характерно для пубертатного возраста: гемоглобин до лечения составил в среднем 130 г/л, после лечения – 129,07 г/л; гематокрит до лечения -38.3, после лечения – 38.2.

Показатели гемостазиограммы статистически значимых различий в сравниваемых группах не выявили: время свертывания крови до лечения начало 2.58 с. /конец 3.46 с. после лечения время свертывания крови начало 2.44 с./конец 3.26с.

Параллельно с положительной динамикой в лабораторно-инструментальных методах исследования, наблюдалось улучшение клинической

симптоматики, остановка маточного кровотечения – восстановился ритм менструаций, появилась двухфазность менструального цикла (66%). Побочных эффектов у в ходе применения витаминно-минерального комплекса в сочетании с КОК не наблюдалось.

Вывод. Предлагаемое нами комплексное лечение пациенток с РАМКПП является эффективной альтернативой традиционным методам лечения, поскольку затрагивает патогенетические звенья механизма возникновения АМКПП. Данный метод лечения оправдан, поскольку гемостатический эффект достигается без гормональной нагрузки на незрелую ГГЯС, а также способствует профилактике рецидивов. Клинические исследования показали, что эффективность предлагаемого нами лечения МКПП составила 84%, рецидивы отсутствуют, остановка кровотечения наблюдалась к концу 1й недели лечения, нормализация менструального цикла и стойкий положительный эффект – к началу следующей менструации, что сократило длительность лечения в три раза.

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ROLE OF ACIDOSIS IN THE MECHANISMS OF FORMATION OF MULTIPLE ORGAN FAILURE

S.M. Musakhonov[1], O.B. Najmiddinov[2], A.B. Mamadaliev[2]
Republican scientific and practical center for emergency medical care
Andijan State Medical Institute

Abstract.

The authors carry out the analysis of review of literature about the influence of lactate acidosis in the development of multiple organ failure at the patients being in critical state. Hyperlactatemia is one of the most wide-spread metabolic disturbances at patients in critical state. It accompanies the most difficult phase of systemic inflammatory response, i.e. multiple organ failure (MOF). During emergency state at patients the precursors of multiple organ failure (MOF) are often aggravating metabolic disturbances in organs, systems and tissues with the development of syndrome hypermetabolic hypoxemia. In these conditions mitochondria becomes more sensitive to acidosis, incompletely oxidized metabolic products launch the mechanism of "mitochondrial dysfunction" and close the vicious circle of metabolic disturbances by increasing hypoxemia. Such changes occur in the myocardial metabolism and they lead it to structural changes. Myocardial infarction (MI) is the corollary of them. Because of it, the working of theoretical principles of the development of multiple organ failure (MOF) and its pathogenetically proved prophylaxis and treatment are at the centre of attention of scientists.

Keywords: lactate acidosis, mitochondrial dysfunction, multiple organ failure (MOF), critical states, hypoxemia, systemic inflammatory response (SIRS).

POLIORGAN YETISHMOVCHILIKNI SHAKLLANTIRISH MEXANIZMLARIDA ATSIDOZNING O'RNI

S.M. Musaxonov[1], O.B. Najmiddinov[2], A.B. Mamadaliyev[2]
Respublika shoshilinch tibbiy yordam ilmiy markazi
Andijon davlat tibbiyot instituti

Annotatsiya

Maqolada og'ir holatdagi bemorlarda poliorgan yetishmovchiligining rivojlanishida laktat atsidozning roli bo'yicha adabiyotlar tahlil qilinadi. Giperlaktatemiya og'ir holatdagi bemorlarda eng ko'p uchraydigan metabolik kasalliklardan biridir. Bu tizimli yallig'lanish reaktsiyasining eng og'ir bosqichi - poliorgan yetishmovchilik bilan birga keladi. Bemorlarda favqulodda vaziyatlarda POYe (poliorgan yetishmovchilik) ning prediktorlari ko'pincha organlar, tizimlar va to'qimalarda ularning

gipermetabolik gipoksiya sindromi rivojlanishi bilan progressiv metabolik kasalliklar ekanligi ko'rsatilgan. Ta'riflanishicha, bunday sharoitlarda mitoxondriyalar atsidozga eng sezgir bo'lib qoladilar, kam oksidlangan metabolik mahsulotlar "mitoxondriyal disfunktsiya" mexanizmini ishga tushiradi, bu esa gipoksiyani kuchaytiradi va metabolik kasalliklarning ayanchli doirasini yopadi. Xuddi shunday o'zgarishlar miyokard metabolizmida sodir bo'ladi va uning tarkibiy o'zgarishlariga olib keladi, bu esa miokard infarktiga olib keladi. Shuning uchun ham POYe rivojlanishining nazariy asoslarini ishlab chiqish va uning patogenetik jihatdan asoslangan oldini olish va davolash tadqiqotchilarning diqqat markazida bo'lib qolmoqda.

Kalit so'zlar: laktat atsidoz, mitoxondrial disfunktsiya, POYe (poliorgan yetishmovchilik)*, kritik holatlar, gipoksiya, tizimli yallig'lanish reaktsiyasi.*

РОЛЬ АЦИДОЗА В МЕХАНИЗМАХ ФОРМИРОВАНИЯ ПОЛИОРГАННОЙ НЕДОСТАТОЧНОСТИ

С.М. Мусахонов[1], О.Б. Нажмиддинов[2], А.Б. Мамадалиев[2]

Республиканский научный центр экстренной медицинской помощи

Андижанский государственный медицинский институт

Аннотация.

В статье проведён анализ литературы о роли лактат-ацидоза в развитии полиорганной недостаточности у больных, находящихся в критических состояниях. Гиперлактатемия - одно из самых распространённых метаболических нарушений у больных, находящихся в критическом состоянии. Она сопровождает наиболее тяжёлую фазу системной воспалительной реакции - полиорганную недостаточность. Показано, что при неотложных состояниях у больных нередко предшественниками ПОН (полиорганной недостаточности) являются прогрессирующие нарушения метаболизма в органах, системах и тканях с развитием синдрома их гиперметаболической гипоксии. Описано, что в этих условиях митохондрии становятся наиболее чувствительны к ацидозу, недоокисленные продукты обмена запускают механизм «митохондриальной дисфункции», усиливающей гипоксию, и замыкают порочный круг метаболических нарушений. Подобные изменения происходят в метаболизме миокарда и приводят к его структурным изменениям, следствием которых является инфаркт миокарда. Именно поэтому разработка теоретических основ развития ПОН и патогенетически оправданной её профилактики и лечения остаётся в центре внимания исследователей.

Ключевые слова: лактат-ацидоз, митохондриальная дисфункция, ПОН (полиорганная недостаточность), критические состояния, гипоксия, системный воспалительный ответ.

In modern medicine of critical states, anesthesiology and intensive therapy occupy the main place, since, directly interfering in the activity of the body, most significant affects various functions, and, consequently, on the state of homeostasis [9]. A critical state is an extreme degree of any, including a phenomenon of pathology, which requires support for the vital functions of the

body. The concept of insufficiency of the function of vital organs - multiple - organized insufficiency (PON) - is based on the unperture of the mechanisms of its occurrence and a close relationship with the severity of the injury, the period and quality of specialized assistance. That is why the development of the theoretical foundations of the development of pathogenetically justified its prevention and treatment remains at the center of attention of researchers.

Polyorgan failure is the most severe phase of the development of a systemic inflammatory reaction and is the consequences of a non-specific stress of the body of a high degree of severity. These phenomena are due to progressive metabolic disorders in organs, systems and tissues with the development of their hypermetabolic hypoxia syndrome [11]. One of the most common metabolic disorders in patients in critical condition is hyperlactamia. The level of lactate in the blood and/or lactate clearance is a diagnostic, therapeutic and projection marker of tissue hypoxia for circulatory shock [18]. For the pathogenic compensation of acute blood loss, it is necessary to take into account not only the state of hemodynamics, but also the parameters characterizing the tissue metabolism using transport and oxygen consumption indicators, the acid-main state of the venous blood and a number of metabolites, including lactate and pyruvate [12]. According to V. X. Timirbaev, E. S. Vladimirov [2], lactate monitoring is required in patients in a state of shock. A direct dependence between the nature of the dynamics of blood lactate against the background of the on -shock therapy and death was revealed. At the same time, the pieron coefficient is 0.68, and the probability of a fatal outcome is higher in the victims, in which the lactate level at the end of the operation, despite the intensive tenders, increases.

The occurrence of multiple organ failure syndrome after adopted mass blood loss, which is a common cause of death of patients, is also associated with the development of lactate ancidosis. Violation of microcirculation, tissue hypoxia and acidosis, which compose the basis of the development of Pont, lead to vicious activation of the immune system, which defends further progression of the pathological state. Oxygen deficiency on the periphery of 3 to 24 hours leads to the appearance of a systemic inflammatory pollutant characterized by hyperproduction of endogenous vasoactive mediators. The cascading reactions of the acute phase of inflammation lead to a sharp increase in oxygen deficiency, an increase in lactate, acidosis and the progression of PON [19]. Hyperlactacidemia and lactate -acidosis is an important feature of cardiogenic and other types of shock. An increase in lactate concentration from 2.1 to 8.0

Meq % reduces the possibility of survival from 90 % to 10 %. The value of lactate, exceeding 7-8 Meq %, is always critical [9].

In states such as peritonitis, political trauma, sepsis, pancreatic, shocks of prize etiology, an extensive complex of pathological syndromes is observed, which, if not corrected, ultimately lead to death [8, 15]. These syndromes include metabolic disorders, and the leading pathogenetic factors are: hypoxia, hypoergosis, endotoxemia, metabolic acidosis, and out of the processes of lipid peroxidation, pronounced disorders in the hemostasis system [16].

The state of prolonged hypoxia of organs becomes a factor in the progressive trafficking of all energy -dependent processes responsible for the structural support of intracellular reactions. Forming tissue hypoxia leads to an increase in them of lactic acid content, which instantly decomposes into hydrogen ions and lactate and thereby leads to the development of lactate ancidosis [14]. An increase in lactate can be due to both enhanced products and a reduced consumption. Normally, the lactate is mainly utilized in the liver, kidneys and heart muscle, where it is used for energy purposes and glucose synthesis (gluconeogenesis), only is only excreted in the urine. Against the background of oxygen deficiency and consistently developing polyorgana, the role of these organs in reducing the concentration of lactate is significantly weakened and in some cases does not manifest itself at all. In particular, in the late stages of shock, there is insufficient use of lactic acid by the liver (due to reduced perfusion), and the measles cycle becomes invalid [9].

The situation is also aggravated by the fact that the carbohydrate metabolism is suffering first of all, as a result of which hyperglycemia develops as one of the components of hypermetabolic syndrome. However, the supply of carbohydrates is small, if not replenished, they are enough for only 6 hours, and fats are 40 days [11]. In this regard, there is a restructuring of energy metabolism from carbohydrate to fat, and since at this time a lack of glucose and oxygen is already developing in the body, oxidation of fatty acids is inhibited at the stage of the formation of acetone, acetocus and p-oxyx acids [1] .

Under the current conditions of hypoxia, the function of all systems of the body suffers, but the nervous system is more sensitive to it: with the complete cessation of blood flow, the recognition of damage to the cerebral cortex is found after a few minutes. A decrease in oxygen consumption by 20 % structures of the brain causes loss of consciousness. After 5-6 minutes of brain anoxia, deep structural changes in neurons and an oblong brain occur-after 10-15 minutes. In the heart muscle, the small foci of necrosis are 3-5 minutes from the moment of

ischemia, and a large-focal heart attack is formed after 20-30 minutes [3]. The transition of acidosis to an uncompensated phase leads to alteration of myocardial structures. In the zone of acidosis, the processes of membrane spheres, electromechanical conjugation are violated, anomalous electrical activity is formed and the processes of cellular aliteration are activated. The consequence of this is the decrease and complete loss of contractile activity of the heart, the occurrence of arrhythmias and myocardial infarction [1, 10].

In parallel, the development of endogenous intoxication as a non -specific syndrome of non-compliance between the formation and excretion of products of normal obstacle and impaired metabolism occurs. In conditions of endo- and exogenous intoxication, tissue macrophages activated by tissue decay products and microbial antibodies are cleaned to produce a number of pro-inflammatory cytokines. This mechanism is universal in nature controlled by the immune system, which prevents the uncontrolled release of cytokines and other inflammation mediators, ensuring an adequate reaction of the body to inflammation [13]. But a significant number of traumatic damage does not obey the general laws, due to which the conditions for continuous (multiple) intake of antigenic structures in the tissue are created. This leads to the predominance of pro -inflammatory stimulation of the body, which triggers the pathological mechanism of the systemic inflammatory reaction. Prospective cytokines, according to many authors [6, 12], strengthen the expression of the Villebrand factor, the tissue factor and fibrinolysis inhibitors, as well as chemokin. All this leads to the appearance of new portions of thrombin and contributes to the occurrence of DIC and thrombosis. At the same time, the permeability of blood vessels and the transmigration of leukocytes in the extra -vascular space increases, which leads to the development of blankets and edema. A considerable role in this process belongs to the endothelium of blood vessels containing interferons receptors. As a result of the excitation of R-Afna, the proliferation of endothelial cells is inhibited, but their apoptosis is enhanced. The stimulation of the R-Finy leads to increased expression on the endothelium of the antigens of the main histocompatibility complex of the 2nd class, as well as IL-1ß and ICAM-1 products, which is accompanied by the involvement of endotheliocytes in the reaction of cellular and humoral immunity [6]. The accumulation of excessive concentration in the blood flow system of pro-inflammatory mediators entails a change in the organs and systems of a person and the development of multiple organ failure [15].

One of the mechanisms of the occurrence of the gender is the

development of mitochondrial dysfunction against the background of metabolic acidosis [2, 5]. Violation of the structure of mitochons with lactatat-acydosis leads to a sharp increase in calcium ions in the cytosol. With an excess of intracellular calcium, the processes of swelling of mitochondria are aggravated, ATP deficiency is intended and all energy -dependent reactions in the cell are suppressed [26].

An increase in the concentration of lactate is several times compared to the physiological level, regardless of the size of the pH, can cause swelling of the mitochondria, which is accompanied by activation of breathing, and the division of oxidative phosphoriling [17]. Even a short -term change in the concentration of hydrogen ions (protons) in liquid media leads to a change in enzymes and the treatment of physiological processes. A decrease in the level of creatine phosphate (CF) in the development of metabolic disorders in the nervous tissue and myocardium occurs after a few seconds, while the brain tissue loses about 70 % of the CF, and after 40-45 with the CF completely exhausts [5]. Thus, with ischemia, the content of adenine nucleotides in cardiomyocytes (CMC) decreases, which further complicates the synthesis of ATP. The degree of decrease in the level of ATP depends on the rate of the occurrence of ischemia and its severity.

Using the direct measurement method of intramicocardial pH during heart-tank resuscitation, F. Kette et al. [17] showed that even a short period of cardiac arrest caused by fibrillation is characterized by a deep myocardial acidosis - after 5 minutes of cardiac arrest, when the pH of arterial blood still remains normal, and mixed venous is 7.26, the intramicocardial pH is reduced to 6.95 . In turn, the excessive accumulation of hydrogen ions and biologically active compounds leads to a sharp increase in the permeability of biological membranes due to structural transitions in proteins and lipids and the activation processes of free radical oxidation [7].

Therefore, in conditions of hypoxia and acidosis of various genes, oxidation of fatty acids in tissues are blocked, acidic products accumulate in excess, metabolic acidosis is formed and, accordingly, ATP deficiency develops, and all energy -dependent reactions are suppressed. Violation of bioenergy caused by hypoxia, high level of catecholamines in the blood and metabolic acidosis can be carried out to the processes of the floor in critical conditions, which ultimately leads to a massive formation of free radicals and toxic peroxide compounds [3, 14]. Oxidizing stress leads to damage to the vascular wall, an increase in the pro -cargulant activity of plasma and platelets, which is one of the leading moments

in the development of atherosclerosis [4], and damage to platelet membranes, erythrocytes and endothelia is the trigger mechanism for the development of acute myocard infarction, as well as violations cerebral circulation. Strengthening lipoperoxidation reduces the stability of the lipid layer, which can lead to electrical breakdown of cardiomyocytes with its own membrane potential [10]. The above mechanisms primarily lead to electrophysiological disorders, to diastolic, and then to systolic myocardial dysfunction and only then to the occurrence of pain in the chest. This sequence of changes is called the "ischemic state." Obviously, the angianous attack is its final stage, in fact the “tip of the iceberg”, at the basis of which are the changes in myocardial metabolism that have arisen due to perfusion disorders and, above all, mitochondrial dysfunction, which in this case is secondary, acquired in nature.

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GENETIC FEATURES OF THE RISK OF ARTERIAL HYPERTENSION IN PATIENTS WITH ABDOMINAL OBESITY

U.I. Usmanova[1], U.Kh. Musashaikhov[1], M.J. Tursunov[2]
Andijan State medical institute
Republican emergency medical center

Abstract.

In recent years, researchers have been paying more and more attention to the study of molecular genetic factors of hypertension, the search for genes and the analysis of the association of their polymorphisms with various components of the metabolic syndrome. The ethnic features of predisposition to the development of hypertension have been revealed, which confirms the role of genetic factors. Significant changes in arterial hypertension within the framework of the metabolic syndrome are mutations of genes responsible for the balance of pressor and depressor pathogenetic links.

Key words: arterial hypertension, genes, polymorphism, metabolic syndrome, obesity.

ABDOMINAL SEMIZLIK BILAN BEMORLARDA ARTERIAL GIPERTENZIYA RIVOJLANISH XAVFINI IRSIY XUSUSIYATLARI

U.I. Usmonova[1], U.X.Musashayxov[1], M.J. Tursunov[2]
Andijon Davlat tibbiyot instituti
Respublika shoshilinch tez tibbiy yordam ilmiy markazi,

Annotatsiya

So'nggi yillarda tadqiqotchilar arterial gipertenziyaning molekulyar genetik omillarini o'rganishga, genlarni izlashga va ularning polimorfizmlarining metabolik sindromning turli tarkibiy qismlari bilan bog'liqligini tahlil qilishga tobora ko'proq e'tibor qaratmoqdalar. Gipertenziya rivojlanishiga moyillikning etnik xususiyatlari aniqlandi, bu genetik omillarning rolini tasdiqlaydi. Metabolik sindrom doirasida arterial gipertenziyadagi muhim o'zgarishlar pressor va depressor patogenetik bog'lanishlar muvozanati uchun javob beradigan genlarning mutatsiyasidir.

Kalit so'zlar: arterial gipertenziya, genlar, polimorfizm, metabolic sindrom, semizlik.

ГЕНЕТИЧЕСКИЕ ОСОБЕННОСТИ РИСКА РАЗВИТИЯ

АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ У БОЛЬНЫХ С АБДОМИНАЛЬНЫМ ОЖИРЕНИЕМ

У.И. Усманова[1], У.Х. Мусашайхов[1], Ж.М. Турсунов[2]
Андижанский государственный медицинский институт
Республиканский научный центр экстренной медицинской помощи

Аннотация.

Последние годы исследователи всё более пристальное внимание уделяют изучению молекулярно-генетических факторов артериальной гипертензии, поиску генов и анализу ассоциации их полиморфизмов с различными компонентами метаболического синдрома. Выявлены этнические особенности предрасположенности к развитию гипертонической болезни, что подтверждает роль генетических факторов. Значимыми изменениями при артериальной гипертензии в рамках метаболического синдрома являются мутации генов, ответственных за баланс прессорных и депрессорных патогенетических звеньев.

Ключевые слова: артериальная гипертензия, гены, полиморфизм, метаболический синдром, ожирение

Arterial hypertension (AH) remains a pressing problem in cardiology, occupying a leading position among diseases of the cardiovascular system due to its high prevalence. Currently, significant interest has represented correlation to the disease with metabolic disorders. The frequent combination of hypertension with abdominal obesity, disorders of carbohydrate and lipid metabolism, and the presence of a close pathogenic connection between them served as the basis for identifying the concept of “metabolic syndrome” (MS) [1].

The prevalence of this pathology in Europeans is 20–30% with an approximately equal distribution by gender. In the general population it ranges from 14 to 40%.In Russia, MS occurs among men under 40 with the percentage of 18.6 and women 7.3% and people under 40- 55 in 44,4% and 20.8 respectively [2,3].

According to the results of numerous epidemiological studies, one of the most common components of the syndrome is hypertension. The prevalence of hypertension in patients with MS is 30.5% [2,3]. The problem of high blood pressure (BP) as a component of MS is one of the most significant for modern medicine due to the predicted increase in the incidence of this pathology in the future and the increasing proportion of mortality from cardiovascular pathology.

The pathogenetic links of hypertension in MS are determined by the development of hyperinsulinemia. It, in turn, activates the sympathetic-adrenal

and renin-angiotensin-aldosterone systems (RAAS), proliferative processes in vascular smooth muscle cells, and increases sodium reabsorption in the proximal and distal tubules of nephrons. All this ultimately leads to vasospasm, an increase in total peripheral vascular resistance and an increase in blood pressure [5].

The most relevant are the polymorphisms of the genes for angiotensin converting enzyme (ACE), angiotensinogen (AGT), angiotensinogen receptor type 1 II (AGTR1), 5,10-methylenetetrahydrofolate reductase (MTHFR), endothelial NO synthetase type 3 (NOS3). Various polymorphic states of these genes are to a certain extent associated with hypertension, and these associations are largely autonomous in nature. However, the results of numerous studies of these polymorphisms in hypertension are ambiguous and often contradictory [8]. Therefore, population genetic studies emphasize the need to take into account the ethnicity, as well as the geographic area of residence of the studied patients [8].

The medical and social significance of hypertension within MS lies in the fact that a combination of factors leads to a higher risk of developing cardiovascular diseases and type 2 diabetes. The combination of hypertension with metabolic disorders in women is associated with an increase in the risk of diseases of the circulatory system by 5.9 times, in men - by 2.3 times [5]. On the other hand, MS is a reversible condition, and with appropriate treatment and strengthening of preventive measures, it is possible to achieve the disappearance or reduction of the severity of its manifestations [6].

According to statistical data, MS in patients with hypertension occurs in approximately 28.2% of cases. Similar results were obtained in a study conducted in Italy—34% [6]. In a survey of the Greek population, the prevalence of metabolic disorders among patients with high blood pressure was 23.6% [7]. Results close to those presented were also obtained in population studies in Spain, Turkey, and the USA, where the frequency of MS ranged from 20 to 40% [5].

Subclinical target organ damage in the form of LVH, IMT thickening, and AU are important markers that determine the prognosis in patients with hypertension [4]. Some authors argue that the presence of MS itself is a less significant predictor of organ changes than specific individual components, in particular hypertension and obesity; others, on the contrary, indicate that MS enhances the effect of each components on the condition of the heart, blood vessels and kidneys [4,5]. Some studies have established an increase in the

proportion of respondents with LVH and increased IMT thickness in the group of patients with hypertension as part of MS compared to the group with isolated hypertension. Similar results were obtained in an American sample (n=356): with an increase in the number of MS components, the frequency of detection of LVH and atherosclerotic plaques increased [9]. In one of the foreign studies (n=354), patients with hypertension and MS had higher AU (measured as the ratio of albumin to creatinine) and left ventricular myocardial mass index [7]. A survey of office workers in St. Petersburg aged 20 to 65 years revealed an increase in the percentage of detection of atherosclerotic plaques with an increase in metabolic disorders among patients with hypertension [10].

Since the formation of hypertension within MS may depend on genetic factors involved in the processes of blood pressure regulation, researchers have studied the contribution of candidate genes of the endothelial system to the development of this pathology. The high incidence of elevated blood pressure in MS confirms that hypertension is less likely to manifest itself in isolation and is more often combined with other components of MS - abdominal obesity or disorders of carbohydrate and lipid metabolism. An established genetic predisposition to the development of hypertension as part of MS will undoubtedly help in the development and implementation of population-based prevention programs. On the one hand, assessing the frequency of MS contributes to the provision of timely preventive measures in the group of respondents with a high risk of developing CVD; on the other hand, MS can be used as a control for the correction of its individual components in the treatment of patients with hypertension.

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OBESITY AS A POWERFUL RISK FACTOR FOR ARTERIAL HYPERTENSION

U.I. Usmanova, U.Kh. Musashaikhov
Andijan State medical institute

Abstract.

In recent years, researchers have been paying more and more attention to the study of molecular genetic factors of hypertension, the search for genes and the analysis of the association of their polymorphisms with various components of the metabolic syndrome. The ethnic features of predisposition to the development of hypertension have been revealed, which confirms the role of genetic factors. Significant changes in arterial hypertension within the framework of the metabolic syndrome are mutations of genes responsible for the balance of pressor and depressor pathogenetic links.

Key words: arterial hypertension, genes, polymorphism, metabolic syndrome, obesity.

SEMIZLIK ARTERIAL GIPERTENSIYA RIVOJLANISHINI KUCHLI OMILI SIFATIDA

U.I. Usmonova, U.X.Musashayxov
Andijon Davlat tibbiyot instituti

Annotatsiya

So'nggi yillarda tadqiqotchilar arterial gipertenziyaning molekulyar genetik omillarini o'rganishga, genlarni izlashga va ularning polimorfizmlarining metabolik sindromning turli tarkibiy qismlari bilan bog'liqligini tahlil qilishga tobora ko'proq e'tibor qaratmoqdalar. Gipertenziya rivojlanishiga moyillikning etnik xususiyatlari aniqlandi, bu genetik omillarning rolini tasdiqlaydi. Metabolik sindrom doirasida arterial gipertenziyadagi muhim o'zgarishlar pressor va depressor patogenetik bog'lanishlar muvozanati uchun javob beradigan genlarning mutatsiyasidir.

Kalit so'zlar: arterial gipertenziya, genlar, polimorfizm, metabolic sindrom, semizlik.

ОЖИРЕНИЕ КАК МОЩНЫЙ ФАКТОР РИСКА АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ

У.И. Усманова, У.Х. Мусашайхов
Андижанский государственный медицинский институт

Аннотация.

Последние годы исследователи всё более пристальное внимание уделяют изучению

молекулярно-генетических факторов артериальной гипертензии, поиску генов и анализу ассоциации их полиморфизмов с различными компонентами метаболического синдрома. Выявлены этнические особенности предрасположенности к развитию гипертонической болезни, что подтверждает роль генетических факторов. Значимыми изменениями при артериальной гипертензии в рамках метаболического синдрома являются мутации генов, ответственных за баланс прессорных и депрессорных патогенетических звеньев.

Ключевые слова: артериальная гипертензия, гены, полиморфизм, метаболический синдром, ожирение

Relevance. A sharp increase in the incidence of overweight and obesity in adolescents was first noted in the 80s of the 20th century, with a subsequent rise in the incidence of arterial hypertension (AH) and prehypertension. Trends in blood pressure (BP) lag behind body mass index (BMI) by about 10 years, which appears to explain some of the variability in the relationship between BP and BMI. Long-term trends in changes in these indicators in young people indicate a relationship between excess weight and hypertension [3].

Currently, the generally accepted criteria for diagnosing and classifying high blood pressure in adolescents are the criteria proposed by the National High Blood Pressure Education Program (NHBPEP). According to this classification, blood pressure levels between the 90th and 95th percentiles in patients according to their gender, age and height indicate the presence of a "pre-hypertensive" state; A blood pressure value between the 95th and 100th percentiles indicates the presence of arterial hypertension. The classification applies to adolescents up to 17 years of age inclusive. When assessing blood pressure in young people aged 18–19 years, the adult classification is used [1].

The main proportion of patients with increased blood pressure are those with signs of prehypertension. Although the relationship between obesity and hypertension has now been demonstrated in a number of studies, the mechanism by which obesity contributes to the development of hypertension is still debated.

A number of studies have shown that the relationship between blood pressure and BMI is not linear. Specifically, the researchers demonstrated that there was a downward trend in BP between 1963 and 1988, but BMI values remained constant during the same period. C. Koebnick et al. [2] showed that the prevalence of hypertension among adolescents 12–19 years old with overweight (2.1%) is twice as high as that among adolescents with normal weight (0.8%). The frequency of detection of high blood pressure increases stepwise with increasing weight in young people of both sexes and of any age. These data were

confirmed by the results of a number of studies, which showed that the likelihood of developing hypertension at a young age with excess body weight is significantly higher than in individuals with normal and low weight [7].

Currently, overweight and obesity are considered key risk factors for hypertension, although a number of other risk factors are known. Thus, hypertension in adolescents is associated with the use of diets high in fat and sodium, a sedentary lifestyle, insufficient physical activity, the presence of cardiovascular diseases (primarily hypertension) in the family history, and low birth weight [5]. The influence of ethnicity and gender on the development of hypertension has less evidence, but it is assumed that these factors influence the severity of the relationship between blood pressure and obesity.

Activation of the sympathetic nervous system, accumulation of visceral fat and fat deposition in the vascular wall, sodium retention, and activation of the renin-angiotensin system are considered important elements in the pathogenesis of hypertension in overweight [6]. Genetic predisposition may be a major factor, although diet and physical activity have been shown to play a more significant role [4]. A sedentary lifestyle, psychological factors (depression, low self-esteem) and lack of sleep at night also significantly contribute to weight gain. Obesity is likely the result of the influence of a combination of factors, including genetic ones, which affect the implementation of satiety mechanisms and the rate of metabolic processes [9].

Large amounts of dietary fat may have a greater effect on weight than the overall caloric intake of the diet. A significant portion of the energy consumed from fat is stored in adipocytes, increasing body weight and waist circumference as the number and volume of adipocytes increases, while carbohydrates contained in cereals, breads, fruits and vegetables, as well as proteins, are catabolized almost immediately after consumption. In addition, high fat content in food leads to hypercholesterolemia [9].

A change in the ratio of fractions of saturated and unsaturated fatty acids (in favor of the former), circulating in the blood as part of fats, affects the function of the liver and kidneys, and also leads to direct damage to the walls of blood vessels due to the formation of atherosclerotic plaques. One of the mechanisms for the development of metabolic syndrome is damage to the media of large arteries due to cholesterol deposition in the vessel wall [10].

Fat accumulates in the wall of the vessel, narrowing its lumen and preventing normal blood flow. An increase in the thickness of the intima-media complex of the carotid artery in obese patients is observed even with normal

blood pressure values, which indicates an early onset of atherosclerotic changes in obesity. Fat accumulating in the wall of the vessel gradually forms plaques, which continue to grow, leading to stenosis of the vessel, up to its complete obliteration, as a result of which the blood supply to organs and tissues suffers, creating conditions for the development of a number of acute and chronic diseases, including lethal ones [10] .

Another negative effect of a high-calorie diet is an increase in the synthesis and concentration of norepinephrine (an indicator of the activity of the sympathetic nervous system). It is assumed that a diet high in fat and carbohydrates leads to activation of peripheral adrenergic receptors, which causes an increase in blood pressure [8]. It has been shown that with simultaneous blockade of α- and β-adrenergic receptors, blood pressure in obese patients decreases.

The effect of obesity on the condition of many organs can lead to serious health problems, but the most obvious is the dependence of the condition of the kidneys on body weight. Accumulation of adipose tissue around the kidney, together with increased intra-abdominal pressure, is considered an additional cause of impaired sodium reabsorption. Initially, obesity leads to vasodilation and glomerular hyperfiltration, which maintains sodium balance despite increased tubular reabsorption. Together with an increase in blood pressure and some other factors (inflammation, oxidative stress and lipotoxicity), this can aggravate kidney damage and lead to the formation of renal failure [9]. Clinically, this process is manifested by proteinuria, which usually precedes a decrease in glomerular filtration rate by several years.

Leptin, by inducing cytokine signalin, promotes kidney damage. Adipose tissue, especially visceral fat, has systemic effects by secreting various hormones and cytokines. A diet high in fat and carbohydrates, leading to hypercholesterolemia and an increase in the concentration of free fatty acids in the blood, directly affects the ion channels of the cell membranes of smooth muscle cells and cells of other tissues [9].

Free fatty acids can also activate phosphorylation of the calcium-independent protein kinase C isoenzyme, an important element of cellular regulation. The binding of free fatty acids to Na+/K+-ATPase leads to the formation of multiple signaling modules, resulting in the activation and synthesis of the epidermal growth factor receptor and an increase in the concentration of reactive oxygen species [10]. Changes in endothelial function result from decreased NO synthesis due to activation of oxidative stress or under the

influence of proinflammatory cytokines. Increased production of cytokines, activation of oxidative stress and decreased NO concentrations lead to vasoconstriction and increased overall vascular resistance, which in turn contributes to the development of venous insufficiency, venous thrombosis and pulmonary embolism, cardiovascular diseases, especially hypertension [10].

Conclusion. The mechanisms of the pathogenesis of hypertension in overweight have not been sufficiently studied; this applies to all age groups. Most researchers point to the similarity of the mechanisms of development of hypertension in obesity in young and adulthood. Recording risk factors and subclinical markers is useful in identifying young people who are overweight and at high risk of developing hypertension. Hypertension in combination with overweight or obesity is more likely to contribute to the development of cardiovascular disease than either condition alone. That is why hypertension, associated with excess body weight at a young age, has been the subject of close attention of the medical community in recent years. There are no universal recommendations for determining the low risk of hypertension in overweight at a young age. However, European, North American and International guidelines emphasize the importance of assessing the complications and comorbidities associated with excess weight. Most guidelines recommend BP screening in all overweight and obese adolescents.

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GENETIC FEATURES OF THE RISK OF DEVELOPING ARTERIAL HYPERTENSION IN OVERWEIGHT PERSONS

U.I. Usmanova, Sh.M. Musashaikhova
Andijan State medical institute

Abstract.

Obesity is considered a non-communicable pandemic, and the increase in its spread is a serious medical and social problem. High body mass index values are closely correlated with hypertension and its complications, however, the effect of obesity on the realization of hereditary predisposition to hypertension remains poorly understood. This article presents a review of the literature on the association of gene polymorphism with the development of hypertension, depending on the presence of obesity.

Key words: arterial hypertension, polymorphism, obesity, cardio-vascular system.

ORTIQCHA VAZNLI ODAMLARDA ARTERIAL GIPERTENZIYA RIVOJLANISH XAVFINING GENETIK XUSUSIYATLARI

U.I. Usmonova, Sh.M.Musashayxova
Andijon Davlat tibbiyot instituti

Annotatsiya

Semizlik yuqumli bo'lmagan pandemiya hisoblanadi va uning tarqalishining ko'payishi jiddiy tibbiy va ijtimoiy muammo hisoblanadi. Tana massasi indeksining yuqori ko'rsatkichlari arterial gipertenziya va uning asoratlari bilan chambarchas bog'liq, ammo semirishning gipertenziyaga irsiy moyillikni amalga oshirishga ta'siri yaxshi tushunilmagan. Ushbu maqolada semizlik mavjudligiga qarab gipertoniya rivojlanishi bilan gen polimorfizmi assotsiatsiyasi adabiyotlari haqida umumiy ma'lumot berilgan.

Kalit so'zlar: arterial gipertenziya, polimorfizm, semizlik, yurak qon-tomir sistemasi.

ГЕНЕТИЧЕСКИЕ ОСОБЕННОСТИ РИСКА РАЗВИТИЯ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ У ЛИЦ С ИЗБЫТОЧНОЙ МАССОЙ ТЕЛА

У.И. Усманова, Ш.М. Мусашайхова
Андижанский государственный медицинский институт

Аннотация.

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Conclusion. The mechanisms of the pathogenesis of hypertension in overweight have not been sufficiently studied; this applies to all age groups. Most researchers point to the similarity of the mechanisms of development of hypertension in obesity in young and adulthood. Recording risk factors and subclinical markers is useful in identifying young people who are overweight and at high risk of developing hypertension. Hypertension in combination with overweight or obesity is more likely to contribute to the development of cardiovascular disease than either condition alone. That is why hypertension, associated with excess body weight at a young age, has been the subject of close attention of the medical community in recent years. There are no universal recommendations for determining the low risk of hypertension in overweight at a young age. However, European, North American and International guidelines emphasize the importance of assessing the complications and comorbidities associated with excess weight. Most guidelines recommend BP screening in all overweight and obese adolescents.

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COMPARISON OF CLINICAL EFFECTIVENESS OF LOOP DIURETICS IN COMPLEX THERAPY OF CHRONIC HEART FAILURE

O.M. Makhsudov
Andijan State medical institute

Abstract.

The article discusses the features of the mechanism of action of diuretics. A comparative analysis of diuretics is carried out depending on the point of action, as well as a comparison of the pharmacological properties of drugs of the same class (loop diuretics - furosemide and torsemide). The authors observed patients with chronic heart failure (CHF).

Purpose of the study: to evaluate the effectiveness and safety of torasemide (Lotonel, Vertex) in patients with CHF.

Material and methods: The study involved 58 patients with CHF who were randomized into 2 groups: 20 patients received torsemide (Lotonel, Vertex) in addition to the main therapy for 3 months, and 38 patients received furosemide. Patients included in the study had clinical signs of stage II-III CHF. The examination of patients included determination of the NYHA FC of CHF, the severity of the clinical condition using the Clinical Status Assessment Scale (CSAS), registration of a 12-lead ECG, echocardiography, blood sampling to determine indicators of electrolyte metabolism and creatinine, as well as a 6-minute walk test.

Results and conclusion: Initially and after 3 months. During therapy, all patients were assessed for their clinical condition, hemodynamic status, quality of life and functional state of the left ventricle (LV), and the levels of electrolyte metabolism and creatinine were determined. The effect of both diuretics on body weight, edema, and shortness of breath was comparable. In both groups, according to EchoCG data after 3 months. There was a decrease in end-diastolic volume (EDV), as well as a significant increase in LVEF. In the torasemide group, there was a significant increase in the 6-minute walk distance; torasemide had a lesser effect on potassium excretion. The safety and effectiveness of the use of torasemide and furosemide to improve the clinical condition and quality of life of patients with moderate compensated CHF were confirmed. However, the clinical and hemodynamic characteristics of torasemide were superior to those of furosemide.

Key words: Patients with CHF, chronic heart failure, diuretics, torasemide, furosemide.

SURUNKALI YURAK YETISHMOVCHILIGINI KOMPLEKS DAVOLASHDA DIURETIKLARNING KLINIK SAMARADORLIGINI QIYOSLASH

O.M. Maxsudov
Andijon Davlat tibbiyot instituti

Annotatsiya

Maqolada diuretiklarning tasir qilish mexanizmining xususiyatlari ko‘rib chiqiladi. Diuretiklarning qiyosiy tahlili tasir nuqtasiga qarab, shuningdek bir xil sinfdagi dorilarning farmakologik xususiyatlarini taqqoslash (petleviy diuretiklar - furosemid va torsemid) o‘tkazildi. Muallif surunkali yurak etishmovchiligi (SYuE) bo‘lgan bemorlarni kuzatdi.

Tadqiqot maqsadi: SYuE bilan og‘rigan bemorlarda torasemidning (Lotonel, Vertex) samaradorligi va xavfsizligini baholash.

Material va usullar: Tadqiqotda SYuE bilan kasallangan tasodifiy 2 guruxda 58 bemor ishtirok etdi: 20 bemor 3 oy davomida asosiy terapiyaga qo‘shimcha ravishda torsemid oldi, 38 bemor furosemid oldi. Tadqiqotga kiritilgan bemorlarda SYuE II-III bosqichining klinik belgilari mavjud edi. Bemorlarni tekshirish CYuE ning NYHA VS ni aniqlash, Klinik holatni baholash shkalasi (KXBSh) bo‘yicha klinik holatning og‘irligini, 12 tarmoqli EKGni ro‘yxatdan o‘tkazish, ExoKG, elektrolitlar almashinuvi va kreatinin ko‘rsatkichlarini aniqlash. Qon namunalarini olish va 6 daqiqalik yurish testi o‘tkazishdan iborat.

Natijalar va xulosa: Dastlab va 3 oydan keyin. Terapiya davomida barcha bemorlarda klinik holat, gemodinamik holat, hayot sifati va chap qorincha (ChQ) funktsional holati baholandi, elektrolitlar almashinuvi va kreatinin darajasi aniqlandi. Ikkala diuretikning tana vazniga, shish va nafas qisilishiga tasiri o‘xshash edi. Ikkala guruhda ham 3 oydan keyin ExoKG malumotlariga ko‘ra. Diastolik end-diastolik hajmda (EDV) pasayish, shuningdek, FV ChQ da sezilarli o‘sish kuzatildi. Torsemid guruhida 6 daqiqalik yurish masofasida sezilarli o‘sish kuzatildi; Torsemid kaliyning chiqarilishiga kamroq tasir ko‘rsatdi. O‘rtacha kompensatsiyalangan SYuE bo‘lgan bemorlarning klinik holati va hayot sifatini yaxshilash uchun torasemid va furosemiddan foydalanish xavfsizligi va samaradorligi tasdiqlangan. Biroq, torasemidning klinik va gemodinamik xususiyatlari furosemid-nikidan ustun.

Kalit so‘zlar: ChF bilan og‘rigan bemorlar, surunkali yurak etishmovchiligi, diuretiklar, torasemid, furosemid.

СРАВНЕНИЕ КЛИНИЧЕСКОЙ ЭФФЕКТИВНОСТИ ПЕТЛЕВЫХ ДИУРЕТИКОВ В КОМПЛЕКСНОЙ ТЕРАПИИ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ

О.М. Махсудов

Андижанский государственный медицинский институт

Аннотация.

В статье рассматриваются особенности механизма действия диуретиков. Проведен сравнительный анализ диуретиков в зависимости от точки действия, а также сравнение фармакологических свойств препаратов одного класса (петлевые диуретики - фуросемид и торасемид). Авторы наблюдали больных хронической сердечной недостаточностью (ХСН).

Цель исследования: оценить эффективность и безопасность торасемида (Лотонел, Вертекс) у больных ХСН.

Материал и методы: В исследовании приняли участие 58 больных ХСН, которые были рандомизированы на 2 группы: 20 больных получали торасемид (Лотонел, Вертекс) в дополнение к основной терапии в течение 3 мес, 38 больных получали фуросемид. Patsienты, включенные в исследование, имели клинические признаки ХСН II-III стадии. Обследование больных включало определение ФК ХСН по NYHA, тяжести клинического состояния по шкале оценки клинического статуса (CSAS), регистратsiю ЭКГ в 12 отведениях, эхокардиографию, забор крови для определения показателей электролитного обмена и креатинина, а также тест 6-минутной ходьбы.

Результаты и заключение: Первоначально и через 3 месяца. В ходе терапии у всех patsientов оценивали клиническое состояние, гемодинамический статус, качество жизни и функциональное состояние левого желудочка (ЛЖ), определяли уровень электролитного обмена и креатинина. Влияние обоих диуретиков на массу тела, отеки и одышку было сопоставимым. В обеих группах по данным ЭхоКГ через 3 мес. Отмечалось снижение конечно-диастолического объема (КДО), а также значительное увеличение ФВЛЖ. В группе торасемида наблюдалось значительное увеличение дистанции 6-минутной ходьбы; торасемид оказывал меньшее влияние на экскрецию калия. Подтверждена безопасность и эффективность применения торасемида и фуросемида для улучшения клинического состояния и качества жизни patsientов с умеренной компенсированной ХСН. Однако клинические и гемодинамические характеристики торасемида превосходили показатели фуросемида.

Ключевые слова: Больные ХСН, хронической сердечной недостаточностью, диуретики, торасемид, фуросемид.

Introduction. In recent years, there has been an increase in the number of patients with CHF all over the world. This is associated with increased life expectancy and disease comorbidity. By 2050, the prevalence of CHF is expected to increase by 60% compared to 2010 [1, 2].

The main causes of CHF development are arterial hypertension (AH) (88% of cases), coronary heart disease (CHD) (59% of cases). The combination of these diseases occurs in every second patient with CHF [3]. Moreover, among all cardiac patients, the main reason for hospitalization in 16.8% of cases is decompensation of CHF [4]. Particularly important is the fact that mortality among patients with stage III-IV CHF. very high - 50% of patients die within 1 year [2].

Clinically, decompensation of CHF is manifested by increased shortness of breath, congestion in the lungs and edema of the lower extremities. The main directions of therapy are the normalization and regulation of the volume or composition of body fluids, which is achieved by prescribing diuretics [5]. The choice of diuretics is very important, since irrational prescription of drugs in this group is one of the causes of decompensation of CHF [6].

Diuretics are a diverse group of drugs that increase the volume of urine

produced. Diuretics also increase the excretion of sodium and water, suppressing the mechanism of sodium reabsorption in different parts of the renal tubules. In addition, these drugs affect the excretion of potassium, magnesium, chlorine, phosphates and bicarbonates, which, with long-term use, results in various side effects. Diuretics differ in their mechanism and strength of action, ability to influence acid-base balance, speed of onset and duration of action. They are used in complex therapy of hypertension, because they have a hypotensive effect and enhance the effectiveness of other antihypertensive drugs. In the treatment of CHF, the property of diuretics to reduce pulmonary edema and venous pulmonary hypertension is used [7–9].

According to the mechanism of action, drugs are divided into 6 classes (Table 1) [7, 10–12].

CLASSIFICATION OF DIURETICS			
Name	Scene	Force of action	Mechanism of action
Loopback	Ascending loop of henle	Powerful	Sodium potassium and chlorine transport inhibitors
Thiazide	Distal tubule	Moderate	Sodium and chlorine transport inhibitors
Carbonic anhydrase inhibitors	Proximal tubule	Weak	Carbonic anhydrase inhibitors
Potassium-sparing diuretics	Terminal part of the proximal Canadian and collecting ducts	Weak	Renal epithelial sodium channel blockers
Mineralocorticoid receptor antagonists	Terminal part of the proximal Canadian and collecting ducts	Weak	Mineralocorticoid receptor blockers
Osmotic diuretics	Proximal tubule	Strong	Osmotic diuretics

Thiazide and thiazide-like diuretics (TDs) are very common due to their effectiveness. With CHF I stage. their intake does not require too strict restriction

of salt intake [13, 14]. This group consists of hydrochlorothiazide and non-thiazide sulfonamides (chlorthalidone, indapamide, clopamide). The main site of action of TD is the initial part of the distal convoluted tubule. The proximal region is an additional site of action.

The main differences between TD and loop diuretics are a decrease in calcium excretion and an increase in sodium concentration in the distal nephron, which leads to increased exchange of sodium for potassium with increased excretion of the latter [15].

TDs do not alter renal blood flow and reduce glomerular filtration rate (GFR) under certain conditions. A representative of this group, indapamide, increases GFR and has a hypotensive effect in hypertensive patients with normal and reduced renal function. The ability of TD to reduce vascular resistance and cause a hypotensive effect is associated with the main saluretic effect of these drugs.

Low doses of TD are used in the treatment of hypertension. Higher doses are used in the treatment of edema syndrome and CHF; in this case, noticeable shifts in plasma concentrations of potassium, uric acid, glucose and lipids are observed, which creates contraindications [16].

Carbonic anhydrase inhibitors (CA). Currently, drugs in this group have limited use as diuretics. A representative of IC is acetazolamide, which is a sulfonamide derivative. Acetazolamide inhibits the enzyme carbonic anhydrase, which catalyzes the formation of hydrogen ions in tubular epithelial cells. Hydrogen ions in the lumen of the tubule are exchanged for sodium ions, which enter the epithelial cell. During this exchange involving carbonic anhydrase decreases sodium reabsorption and increases the excretion of bicarbonates, which is accompanied by the development of metabolic acidosis. Acetazolamide blocks carbonic anhydrase in the proximal tubule region. In the treatment of CHF, it is used as an additional agent during long-term treatment with strong diuretics to normalize urine pH and restore sensitivity to loop diuretics when resistance occurs. The most common indications are edema syndrome in combination with alkalosis, glaucoma, intracranial hypertension [12, 14,].

Potassium-sparing diuretics (KDs). According to the mechanism of action, KDs are divided into 2 groups: agents that block sodium channels of renal epithelial cells and mineralocorticoid receptor antagonists. The most commonly used CDs are veroshpiron, spironolactone, and triampur. These drugs have one serious side effect - the risk of hyperkalemia, especially in patients with diabetes mellitus, renal failure, or when combined with ACE inhibitors or potassium supplements[11].

Sodium channel blockers. KDs block sodium channels of the epithelium in the distal tubules and collecting ducts. However, the diuretic effect of drugs in this group is weakly expressed, since the reabsorption capacity of the collecting ducts is limited and amounts to approximately 2% of the total filtered volume of salts.

Mineralocorticoid receptor antagonists (MCRA). Spironolactone enhances the effect of diuretics of other groups. Indications for use, in addition to CHF, are edema in liver cirrhosis, primary hyperaldosteronism (Conn's disease). Due to the possibility of hyperkalemia, strict laboratory monitoring is necessary. A better alternative to spironolactone is eplerenone, a competitive selective AMCR in the distal nephron.

AMKR exhibit maximum effect in combination with other neurohormonal modulators (ACE inhibitors or sartans, beta blockers). These drugs are used for triple neurohormonal blockade in the treatment of CHF. The goal of therapy is to reduce the risk of cardiovascular complications and mortality in patients with left ventricular dysfunction (EF<40%) and clinical manifestations of CHF after a recent myocardial infarction. In case of severe decompensation and worsening of CHF, CDs are used in high doses in combination with loop diuretics [10].

The level of potassium in plasma must be determined before the start of therapy, then after 1 week, 1 month; also when changing the dose and periodically during treatment (especially in the elderly, with renal failure, diabetes mellitus). With potassium values in plasma 5.5–5.9 mmol/l requires a dose reduction; more than 6 mmol/l – discontinue the drug [15].

Osmotic diuretics (OD). Representatives of this class are mannitol, urea, glycerin, isosorbide. These diuretics act in the proximal tubule. Being osmotically active substances, they increase the osmolarity of plasma and tubular fluid. The drugs are not reabsorbed, as a result they prevent the movement of water into the interstitium, the concentration of sodium in the tubules is significantly reduced, which leads to the cessation of its reabsorption. At the level of the loop of Henle, ODs also act, although to a lesser extent than loop ones. As a result of taking OD, the volume of extracellular fluid increases, blood viscosity decreases, renal blood flow increases, and oncotic pressure in the glomeruli decreases. Indications for the prescription of diuretics of this group are attacks of glaucoma, cerebral edema, and prevention of a decrease in GFR during surgical interventions [11, 14, 16].

Loop diuretics (LDs). They have the most powerful diuretic effect, and their use is recommended for patients with severe manifestations of CHF [5]. PDs

cause dilatation of renal and peripheral vessels [14].

One of the widely used drugs in this class is furosemide. However, its constant use causes a decrease in the quality of life in patients, which is expressed in the imperative urge to urinate in the first 2 hours after taking the drug, and severe hypotension is recorded. In general, all these effects lead to a decrease in compliance [8]. It is known that diuretic therapy (most often furosemide) using small doses of the drug and a "weekend" regimen (taking the drug every other day or on weekends) is unjustified and provokes the development of decompensation of heart failure [2, 6]. The unique properties of torasemide, including its favorable pharmacokinetic profile for outpatient administration (longer half-life and duration of action, as well as higher bioavailability compared with those of furosemide), may overcome these difficulties and concerns of maintenance diuretic therapy. In recent ears, the PD torasemide has been successfully used .

Torasemide, unlike furosemide, also blocks the effects of aldosterone, i.e., it increases renal excretion of potassium to a lesser extent. This reduces the risk of hypokalemia, one of the main side effects.

The pharmacokinetic properties of torasemide differ from those of furosemide; the differences are presented in Table 2 .

COMPARATIVE CHARACTERISTICS OF FUROSEMIDE AND TORASEMIDE		
Characteristics	Furosemide	Torasemide
Bioaailability (%)	50	80 - 100
Reduced bioavailability with food	Yes	No
Metabolism	50 - 50	Kidneys/liver 20 - 80
Onset of action after oral admin-istration min	30 - 60	30 - 60
T1/2(h) with CHF	2,7	3- 6
T1/2(h) with renal dysfunction	2,8	4 - 5
T1/2(h) with liver dysfunction	2,5	8

The largest study of torsemide is the open randomized trial TORIC (TORsemide in Congestive heart failure), which compared fixed doses of 40 mg/day furosemide and 10 mg/day torsemide in more than 2 thousand patients with CHF. A significantly lower ($p<0.05$) overall and cardiovascular mortality was proven in the group of patients taking torasemide. Treatment with torasemide was superior in terms of functional class reduction and was less likely to cause hypokalemia[12].

Standard doses of torasemide for the treatment of CHF are 10–20 mg/day. For cirrhosis of the liver with ascites, torasemide is taken together with aldosterone antagonists on a low-salt diet.

The mechanism of action of torasemide is the reversible binding of torasemide to the sodium/chlorine/potassium ion cotransporter located in the ascending segment of the loop of Henle, as a result of which the reabsorption of sodium and water is reduced or completely inhibited, and the osmotic pressure of the intracellular fluid decreases. Torsemide blocks myocardial aldosterone receptors, reduces the progression of fibrosis and improves myocardial diastolic function.

The antialdosterone effect of torasemide causes less hypokalemia than that of furosemide, while torasemide is more active and its action is longer .

The diuretic effect of torasemide lasts up to 18 hours. The absence of frequent urination in the first hours after taking the drug significantly improves the patient's quality of life and increases compliance. The purpose of this study was to compare the safety of long-term therapy and the effect of torasemide (Lotonel, Vertex, Russia) and furosemide on the course of the disease and quality of life, LV function and electrolyte levels in patients with compensated CHF who do not require intravenous PD.

Material and methods. We observed 58 patients over the age of 40 ears with clinical signs of stage II–III CHF. The CHF therapy received at the start of the study was stable over the past 4 months. The study did not include patients with clinical signs of obvious fluid retention in the body requiring intravenous administration of PD (edema of the lower extremities, hepatomegaly, swelling of the jugular veins, moist rales in the lungs). Non-inclusion criteria also included: clinical signs of hypovolemia, hypokalemia, hemodynamically significant lesions of the heart valves; pulmonary heart; ACS in less than 3 months. before the start of the study; inflammatory diseases, serum creatinine >30 μmol/l.

All patients underwent a clinical examination with determination of the FC of CHF according to NYHA, the severity of the clinical condition using the Clinical Status Assessment Scale (CSAS). An ECG was recorded in 12 leads, an EchoCG was performed according to standard methods, and blood was taken to determine indicators of electrolyte metabolism and creatinine. A 6-minute walk test was conducted. All patients were randomly divided into 2 comparable groups: 1st received torasemide 10–20 mg/day (n=20), 2nd received furosemide 10–60 mg/day (n=18). The starting dose of torasemide was selected depending on the diuretic therapy used at the time of initiation of therapy. All patients

received standard therapy for CHF (ACE inhibitors or sartans, β-blockers, aldosterone antagonists, cardiac glycosides as indicated). Both drugs were prescribed in combination with 50–100 mg/day of veroshpiron. At the same time, at visits 1 (after 7 days) and 2 (after 1 month), a clinical examination and blood sampling were performed, and at the final visit 3 (3 months), in addition, echocardiography was performed at rest. Therapy with the study drugs was not accompanied by clinically significant fluctuations in blood pressure and heart rate. None of the patients had adverse reactions that required exclusion from the study.

Results. Positive dynamics in the clinical condition of patients and the severity of CHF were noted in both groups. The effects of both diuretics on body weight, edema, and dyspnea were comparable. A more rapid reduction in symptoms of shortness of breath, palpitations, disappearance of peripheral edema or pastosity in combination with effective blood pressure control was observed among patients in the torasemide group (differences not significant). Daily diuresis was 2.24 and 2.46 l/day, respectively, in the torasemide and furosemide groups (the differences are not significant).

During the study, in both groups there was a significant decrease in the average NYHA FC by 11% in the torasemide group and by 6% in the furosemide group ($p < 0.05$).

According to echocardiography after 3 months. in both groups there was an improvement in the functional state of the left ventricle in the form of a decrease in EDV. In group 1, there was a decrease in EDV from 170.1 to 163.4 ml, in group 2 – from 168.5 to 164.3 ml ($p<0.05$), as well as a significant improvement in systolic function (increased EF LV from 46.7% to 50.2% in the torsemide group and from 46.2% to 48.7% in the furosemide group).

In the torasemide group there was a significant increase in the 6-minute walk distance - from 280 to 350 (+70) m, in the furosemide group - from 270 to 310 (+40) m.

However, torasemide had a lesser effect on potassium excretion. During the study, an insignificant decrease in plasma potassium levels was observed in the torasemide and furosemide groups. The average creatinine level in both groups also remained virtually unchanged.

During diuretic therapy, the appearance of extrasystole (supraventricular and ventricular) was noted according to ECG data. In the torasemide group, extrasystole occurred in 2 (5%) patients, in the furosemide group - in 5 (17%) patients.

Conclusion. Thus, furosemide and torasemide (Lotonel) have a strong natriuretic and, accordingly, diuretic effect. However, the use of torasemide (Lotonel) is the most reasonable choice for long-term treatment of heart failure. The drug has a pronounced diuretic effect, has high bioavailability, a longer duration of action, and an optimal cost-effectiveness ratio. There was a significant decrease in the severity of shortness of breath, an increase in exercise tolerance and an improvement in the quality of life of patients with CHF.

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РОЛЬ ГЕНЕТИЧЕСКОГО МАРКЕРА В НАРУШЕНИИ ТРОМБОЦИТАРНОГО ЗВЕНА ГЕМОСТАЗА (ITGB3) В ПАТОГЕНЕЗЕ ИШЕМИЧЕСКОГО ИНСУЛЬТА

У.Х. Мусашайхов
Андижанский государственный медицинский институт

Аннотация.

В ходе исследования, у 35 больных с ишемическом инсультом, было проанализировано ассоциативный связь Leu33Pro в гене интегрин бета-3 (ITGB3) в формировании ИИ. В исследованных группах фактическое распределение генотипов полиморфизма C807T соответствовало ожидаемым при равновесии Харди-Вайнберга (РХВ) (p<0.05).

Ключевые слова: ишемический инсульт, генетический полиморфизм Leu33Pro ITGB3.

GEMOSTAZNING TROMBOTSITAR XALKA BUZILIShI (ITGB3) GENETIK MARKERINING IShEMIK INSULT PATOGENEZIDAGI ROLI

U.X. Musashayxov
Andijon Davlat tibbiyot instituti

Annotatsiya

Tadqiqot davomida ishemik insult bilan og‘rigan 35 ta bemorda II ning shakllanishida integrin beta-3 (ITGB3) genidagi Leu33Pro ning assotsiativ munosabati tahlil qilindi. O‘rganilgan guruhlarda C807T polimorfizm genotiplarining haqiqiy taqsimoti Xardi-Vaynberg muvozanati (RHB) (p<0,05) da kutilganlarga mos keldi.

Kalit so‘zlar: ishemik insult, Leu33Pro (ITGB3) genetik polimorfizmi.

THE ROLE OF THE GENETIC MARKER OF PLATELET HEMOSTASIS DISORDER (ITGB3) IN THE PATHOGENESIS OF ISCHEMIC STROKE

U.H. Musashaykhov
Andijan State medical institute

Abstract.

In the course of the study, in 35 patients with ischemic stroke, the associative relationship of Leu33Pro in the integrin beta-3 (ITGB3) gene in the formation of AI was analyzed. In the studied groups, the actual distribution of the genotypes of the C807T polymorphism corresponded to those

expected at the Hardy-Weinberg equilibrium (RHB) (p<0.05).

Keywords: ischemic stroke, genetic polymorphism Leu33Pro ITGB3.

Актуальность. В последние годы обнаруживается повышение доли ишемических инсультов (ИИ) среди молодых – около 20% от всех инсультов [4]. Заболеваемость, по разным данным, варьирует от 3 до 23 на 100000 человек [2]. В качестве провокатора в данных ситуациях чаще всего можно рассматривать наследственную тромбофилию, так как у части пациентов при обследовании выявляется окклюзия церебральных артерий вследствие внутрисосудистого тромбоза [1, 6]. Тромбофилия определяется как нарушение гемостаза и гемореологии, характеризующееся повышенной склонностью к развитию тромбозов или внутрисосудистого свертывания, в основе которого лежат приобретенные и генетически обусловленные нарушения в различных звеньях гемостаза и гемореологии [3]. Среди факторов, повышающих риск развития тромбоза, очень важны гены тромбоцитарных рецепторов. В данном случае проводится анализ генетического маркера гена тромбоцитарного рецептора к коллагену (ITGA2 807C>T) и фибриногену (ITGB31565T>C). При дефекте гена рецептора к коллагену усиливается прилипание тромбоцитов к эндотелию сосудов и к друг к другу, что ведет к повышенному тромбообразованию. При анализе генетического маркера ITGB31565T>C можно выявить эффективность или неэффективность антиагрегантной терапии аспирином. При нарушениях, обусловленных мутациями в этих генах, повышается риск тромбозов, инфаркта миокарда, ишемического инсульта [5].

Материал и методы исследования. В ходе генетического исследование нами было обследовано 35 больных с ИИ находившихся в неврологическом отделение клиники Андижанского государственного медицинского института . Диагностика ИИ осуществлялась в соответствии с принятыми в настоящее время клиническими рекомендациями. Выделение молекулы ДНК из периферической крови проводили при помощи набора «Ампли Прайм РИБО_преп». Генотипирование полиморфизма Leu33Pro ITGB3 осуществляли на основе метода Tag Man-зондов на амплификаторе Rotor-Gene Q (Quagen, Германия), с использованием коммерческого тест-набора ООО «Литех» (Россия).

Статистическую обработку результатов выполняли с помощью стандартного пакета прикладных программ OpenEpi V.9.2. Анализ

отклонения эмперических частот генотипов от теоретически ожидаемого распределения Харди–Вайнберга осуществляли с помощью пакет программы Statistica 6.0.

Целью исследование является, изучение частоты распределения и оценка взаимосвязи полиморфизма Leu33Pro в гене интегрин бета-3 (ITGB3) у больных с ИИ.

Полученные результаты и их обсуждение. В ходе исследовании у больных в подгруппе с ИИ и в контрольной группе доля дикиго аллеля Leu и неблагоприятного аллеля Pro составила 88.6% и 11.4% против 95.6% и 4.4% соответственно. При статистической обработке выявлена достоверное уменьшение частоты благоприятного аллеля Leu в исследуемой группе пациентов (88.6% против 95.6% в контрольной группе при χ2=4.5; P=0.03; OR=0.3; 95%CI:0.13 – 0.96). При наличии данного аллеля риск развития ИИ отсутствует, соответственно наличия дикого аллеля Leu свидетельствует о возможном защитном эффекте в отношении формирования ИИ. Выявлено значимое увеличению доминирующего, мутантного аллеля Pro у больных с ИИ по сравнению условно-здоровыми донорами (11.4% против 4.4%). Рассчитанный коэффициент отношения шансов показал, что шанс обнаружения функционального неблагоприятного аллеля Pro у респондентов с ИИ повышался в 2.8 раза по сравнению у представителей контрольной группы (χ2=4.5; P=0.03; OR=2.8; 95%CI:1.05–7.63).

Ассоциативная связь между полиморфизмом Leu33Pro в гене интегрин бета-3 (ITGB3) в группах пациентов и контроля

Исследуемые группы	Аллели и генотипы	Статистическое различие в отношении контрольной группы					
		Relative risk		Odds ratio		χ2	p-value
		RR	95% CI:	OR	95% CI:		
Ишемический инсульт (n=35)	Leu	0.51	0.29 – 0.88	0.3	0.13 – 0.96	4.5	0.03*
	Pro	1.97	1.14 – 3.40	2.8	1.05 – 7.63		
	Leu/Leu	0.52	0.28 – 1.0	0.4	0.13 – 1.12	3.2	0.07*
	Leu/Pro	1.74	0.87 – 3.51	2.2	0.73 – 6.83	2.1	0.1
	Pro/Pro	4.36	3.15 – 6.03	****	****	3.3	0.07*

Частоты Leu/Leu, Leu/Pro, Pro/Pro генотипов Leu33Pro в гене интегрин бета-3 (ITGB3) в исследованных группах пациентов с ИИ и контроля

составили: 80.0%, 17.1% и 2.9% против 91.3%, 8.7% и 0.0%, соответственно. Как видно, частота дикого генотипа Leu/Leu и мутантного маркера Pro/Pro среди пациентов с ИИ оказались незначимых количествах, чем в группе контроля (χ2=3.2; P=0.07; OR=0.4; 95%CI: 0.13–1.12 и χ2=3.3; P=0.07). Выявлена тенденция к увеличению количества гетерозиготного генотипа Leu /Pro у пациентов с ИИ (17.1 против 8.7 при χ2=2.1; P=0.1; OR=2.2; 95% CI: 0.73 – 6.83). (табл.1). Рассчитанный относительный риск развития ИИ при наличии неблагоприятного маркера Leu /Pro повышается в 2.2 раза.

Заключение. Таким образом проанализированные данные исследование показали что наличие дикого аллеля Leu свидетельствует о возможном защитном эффекте в отношении формирования ИИ. При выявление неблагоприятного аллеля Pro у респондентов с ИИ, риск развитие данной патологии резко возрастает на 2.8 раза. А также при обнаружении гетерозиготного генотипа Leu /Pro в основной группе риск развития ИИ был низким.

Таким образом, можно заключить, что неблагоприятные генотипические варианты полиморфизма Leu33Pro в гене интегрин бета-3 (ITGB3) могут играть роль в развитии тромбоэмболических осложнений как ИИ, но целесообразно будет проводит анализы в месте с другими генами тромбоцитарного звена гемостаза.

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MORFOLOGICAL CHARACTERISTICS OF CEREBRAL BLOOD VESSEL ANEURYSMS

E.A. Eshbaev[1], Q.B. Isakov[2], A.B. Gafurov[2]
Tashkent Medical Academy[1]
Andijan State Medical Institute[2]

Abstract.

The brain undergoes various secondary changes against the background of chronic damage of arterial blood vessels, atherosclerosis and hypertension. Histochemical staining methods provide reliable information when studying the development of destruction and defragmentation of fibrous structures, which are components of vascular components. In this study, cerebral blood vessels were studied using the Schiff and Van Gieson method. Based on the analysis of the obtained results, it was found that most of the destruction and defragmentation process continues with the accumulation of acidic mucopolysaccharides between the walls of the vessels and sharp swellings between the layers and the decrease of the high pressure tolerance of the vessel wall. As a result, angiosclerosis and angiofibrosis continue with the development of foci.

Key words: aneurysm, histochemical method, cerebrovascular disease, angiosclerosis, atherosclerosis, brain, morphology.

BOSH MIYA QON TOMIRLARI ANEVRIZMALARNING MORFOLOGIK XUSUSIYATLARI

E.A. Eshbayev[1], Q.B. Isaqov[2], A.B. Gafurov[2]
Toshkent tibbiyot akademiyasi[1]
Andijon Davlat tibbiyot instituti[2]

Annotasiya.

Bosh miya arterial qon tomirlarining surunkali zararlanishi, ateroskleroz va gipertoniya kasalligi fonida xar xil ikkilamchi o'zgarishlarga uchraydi. Aynan tomir komponenetlari tarkibiy qismlari bo'lgan tolali tuzilmalarning destruksiyasi va defragmentasiyasini rivojlanishini o'rganishda gistokimyoviy bo'yash usullari ishonarli ma'lumotlarni beradi. Ayni tadqiqot ishmizda, Shiff va Van Gizon usulida bosh miya qon tomirlarini o'rganildi. Olingan natijalar taxlili bo'yicha aksariyat destruksiya va defgragmentasiya jarayoni tomirlar devorining oralig'ida nordon mukopolisaxaridlarning to'planishi va qavatlar oralig'ida keskin shishlar va tomir devorining yuqori bosimga bardoshlilik xususiyatni pasayishi bilan davom etishi aniqlandi. Oqibatda, angioskleroz va angiofibroz o'choqlarining takomil topishi bilan davom etadi.

*Kalit so'zlar***:** *anevrizma, gistokimyoviy usul, serebravaskulyar kasallik, angioskleroz, ateroskleroz, bosh miya, morfologiya.*

МОРФОЛОГИЧЕСКАЯ ХАРАКТЕРИСТИКА АНЕВРИЗМ СОСУДОВ ГОЛОВНОГО МОЗГА

Э.А. Эшбаев[1], Қ.Б. Исақов[2], А.Б. Гафуров[2]
Ташкентская медицинская академия[1]
Андижанский государственный медицинский институт[2]

Аннотация.
Головной мозг претерпевает различные вторичные изменения на фоне хронического поражения артериальных сосудов, атеросклероза и гипертонической болезни. Методы гистохимического окрашивания дают достоверную информацию при изучении развития деструкции и дефрагментации фиброзных структур, входящих в состав сосудистых компонентов. В данном исследовании кровеносные сосуды головного мозга изучались по методу Шиффа и Ван Гизона. На основании анализа полученных результатов установлено, что в большинстве случаев процесс деструкции и дефрагментации продолжается с накоплением кислых мукополисахаридов между стенками сосудов и резкими вздутиями между слоями и снижением толерантности сосуда к высокому давлению. стена. В результате ангиосклероз и ангиофиброз продолжаются с развитием очагов.

Ключевые слова: аневризма, гистохимический метод, цереброваскулярное заболевание, ангиосклероз, атеросклероз, головной мозг, морфология.

Relevance of the topic: 12.6% of all vascular diseases in the world are cerebrovascular diseases, of which 40% are intracranial aneurysms of the internal carotid arteries, 25% are branches of the posterior lateral artery and 20% are the middle cerebral artery, and 20% are the vertebral basilar artery. and it is 5%, and it has not yet been studied whether pathological expansions in the arteries depend on a specific cause. According to the teaching of English scientists, the main factors of aneurysm of cerebral blood vessels are caused by abnormalities of vascular walls during embryonic development, hypertension, and separation and expansion of the vascular wall after atherosclerosis.

Morphological changes in the intracranial arteries of the brain continue with various changes mainly against the background of hypertension and atherosclerosis [4, 6]. In particular, at the age of 55-59, atherosclerotic changes occur in the blood vessel wall, narrowing of the vessel diameter, or dystrophic and sclerotic changes occur in the vessel wall in bifurcated or branched branches close to this branch [1]. When most of the patients with cerebrovascular diseases were studied, the most important of the changes that can occur in their vessels [9] are compression crushing of private blood vessels feeding the vessel walls, accumulation of sour mucopolysaccharides between elastic and collagen fibers,

mucoid thickening and fibrinoid structures in the vessel wall in atherosclerosis and hypertension. It is considered a chain of the problem that continues with improvement [3, 5, 7]. According to our scientists, most of the organic changes that occur in the blood vessels of our body are thinning of the vessel walls, separation into layers as a result of a sharp increase of the acidic structures that break the interrelationship of the layers between them, and they noted that it occurs in the form of an aneurysm [8, 11]. This, in turn, requires the morphological identification of the above processes, the use of special histochemical methods in the examination, and the preliminary assessment of possible changes.

The walls of blood vessels stained with Altzian blue and Van Gien methods, which are staining methods that provide accurate information for the assessment of morphological changes occurring in cerebral blood vessels, show the structures of rough fiber chaotic arrangement in the wall of vessels [10].

Purpose: To clarify the occurrence rate, risk factors, morphogenesis and pathomorphological changes of brain aneurysm.

Materials and methods: in 26 cases of acute blood circulation in the brain, the blood vessels of the artery were removed from the surgical practice and in total 21 cases of the autopsies of the dead patients, the autopsy materials of the blood vessels of the base of the brain and aneurysmal ruptured arteries were obtained. In the patients, the aneurysmal enlarged focus isolated from the branch of the brain base of the middle artery was fixed in a 10% formalin solution for 72 hours, and then placed in 96% alcohol for dehydration. Then the tissue pieces were embedded in Histamix brand paraffin and left in a thermostat at 57C for 72 hours. The tissues were then placed in cassettes in the form of paraffin blocks. Using a microtome, micropreparations cut with a thickness of 4-8 μm were immersed in xylene and 70, 80, 90, 100% alcohols and stained with Alcian blue and Van Gison dye. Acidic and neutral mucopolysaccharides are stained blue with the help of Altzian blue dye, which gives information about Schiff's positive structure in this area. By Van Gison staining, collagen fibers are colored red, giving information on the analysis of the changes in different levels of collagen fibers developed and destroyed in the vessel wall.

Research results and their discussion: According to the data studied in our research work, the main morphological substrate of the changes in cerebral blood vessels after atherosclerosis and hypertension is elastolysis of fibrous structures, which is manifested by the occurrence of various degrees of swelling. In particular, mucoid thickening of the arterial intima in hypertension causes a

sharp accumulation of sour mucopolysaccharides in the vessels of this area, which leads to the hydrolysis of fibers and destroys the integrity of the vessel. Alcian blue, a histochemical staining method, was used to detect these changes.

This dye clearly delineates foci by staining acidic mucopolysaccharides in a mauve blue color. At the same time, Schiff's positive (sour mucopolysaccharide) causes swelling of the fibrous structures in the collected branches, mutual inteposition of consecutive layers in the artery wall. And this can continue with the occurrence of pseudo-aneurysmal expansions in the aorta and cerebral blood vessels in the young contingent. In this study, the following morphological changes were identified in cases of aneurysms and pre-aneurysms in cerebral blood vessels.

For example, according to the analysis of the data studied with the help of altzian dye, it was found that the different intensity of sour mucopolysaccharides accumulated in the space between the blood vessels increases the hydrophilic property between the collagen and elastic fiber structures, which leads to the sharp development of interstitial swelling and the violation of nutrition of the vessel wall. This leads to the destruction of most of the fibrous structures in the vessel wall.

As a result, the formation of destroyed fibrous structures in different layers leads to a sharp decrease in the trajectory of the vessel wall and the surface tension and resistance properties and deformation of the wall.

At the same time, due to the development of small sparse fibrous structures around the centers of mucoid swelling and fibrinoid swelling in different projections, the contractility of the vessel is severely disrupted from a morphofunctional point of view, and it continues with the formation of microbumps (aneurysmal elevations). As a result, interstitial swellings developed in the space between the vessel wall can lead to deformation of the vessel wall and even rupture. (Figure 1).

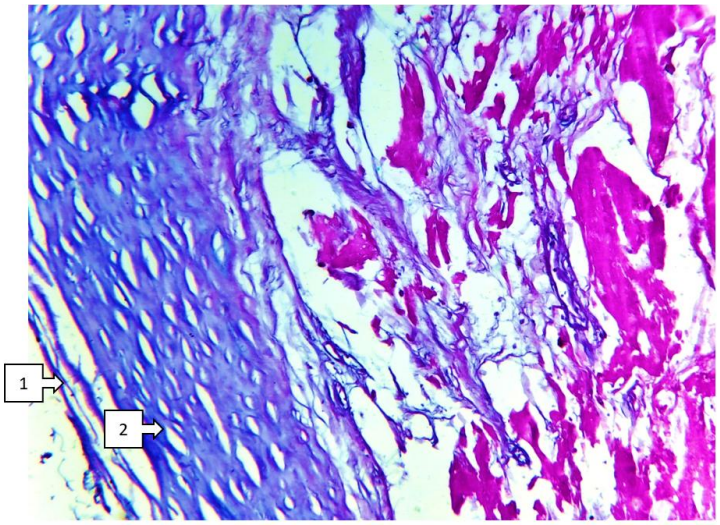

Figure 1. The tissue of the branch of the left lateral artery of the middle brain. Artery wall has different thickness (1). Blue-blue layer saturated with acidic mucopolysaccharides Schiff positive structure this view shows the process of elastolysis in fibrous structures (2) Stain Altzian blue. The size is 40x10.

Macrophages and fibroblasts are concentrated at different levels between most vascular walls.

At the same time, the proliferation of fibroblasts and the location of similar foci along the blood vessel perimeter confirm the development of angiosclerotic process and rapid synthesis of tropocollagen fibers. This leads to the development of centers of chaotic arrangement of collagen fibers of various degrees along the perimeter and wall of normal vessels and the violation of the integrity of the vessel wall. (See Figure 2).

A similar situation occurs after atherosclerosis, as a result of sudden accumulation of foamy cells located in the subendothelial layer, bulging of the endothelium into the vessel cavity, disruption of the interconnected set of fibrous structures, and displacement of the muscle and adventitia layers, the vessel wall causes a violation of the surface tension force, resulting in a turbulent flow. under its influence causes the vessel wall to bulge at different levels.

Therefore, in the tests with Alcian blue dye, between different layers of the vascular wall, it is possible to determine the sharp accumulation of Schiff positive structures, destruction and elastolysis in fibers. At the same time, the intensity of the Schiff positive interruptions in the vessels stained with Altian blue allows for the rapid development of the process, its localization and prospective prognosis.

Our next method of examination, Van Gison staining with acidic picrofuscin stain, allows to identify and study collagen and procollagen fibers developed or pathologically synthesized in the vessel wall, showing the position of the fibers in a specific projection. In this research work, it was found that in diseases of cerebral blood vessels with atherosclerosis and hypertension, collagen fibers

along the vessel wall are painted in red color and most of them are chaotically located, which leads to violation of the histioarchitectonics of the vessel.

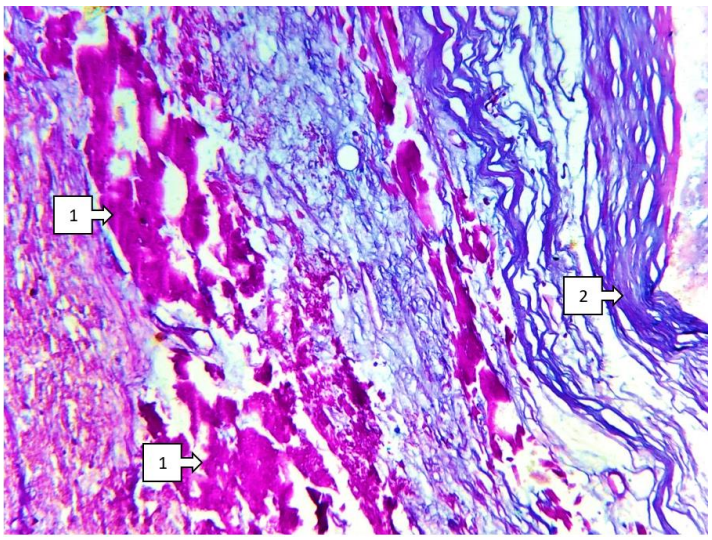

Figure 2. Collapsing aneurysm of the left side of the middle cerebral artery. It is fibrinoid necrosis and interstitial swelling of the middle layer and the intima area (1), foci of sour mucopolysaccharides absorbed into fibers and elastolysis (2). Paint Altsian blue. The size is 40x10.

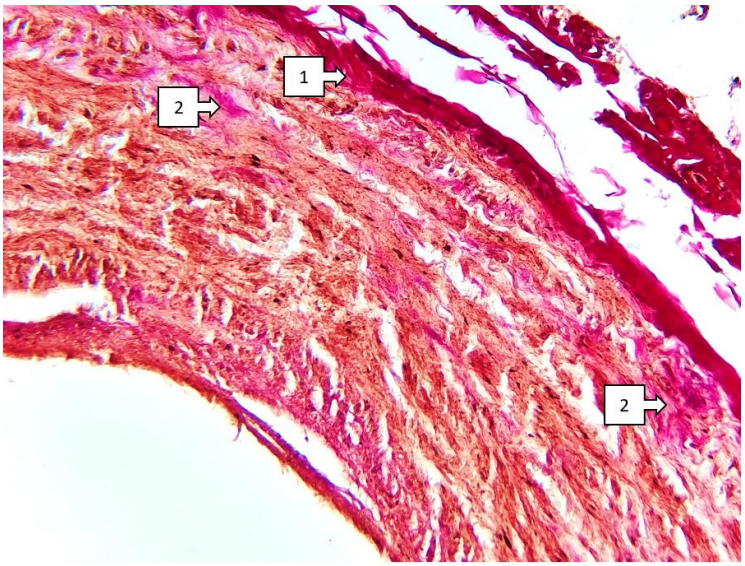

Figure 3. The tissue of the branch of the left lateral artery of the middle brain. The wall of the artery has different thickness (1). Between the thickened branches, chaotically located bundles of red collagen fibers are identified (2), destruction and defragmentation foci are identified (3). Paint Van Gison Size 20x10.

In hypertension, it was found that the collagen fibers were surrounded by yellow sparse fibrous structures around the procollagen stage and lost their clear relief appearance, the anastamosed borders of most collagen fibers were sharply expanded, and the interstitial swellings developed sharply in the interval. This mechanism is considered the main pathogenetic link that leads to a sharp loss of the strength of the vessel wall and bulging of the wall under the influence of

turbulent flow inside the vessel (see Fig. 3).

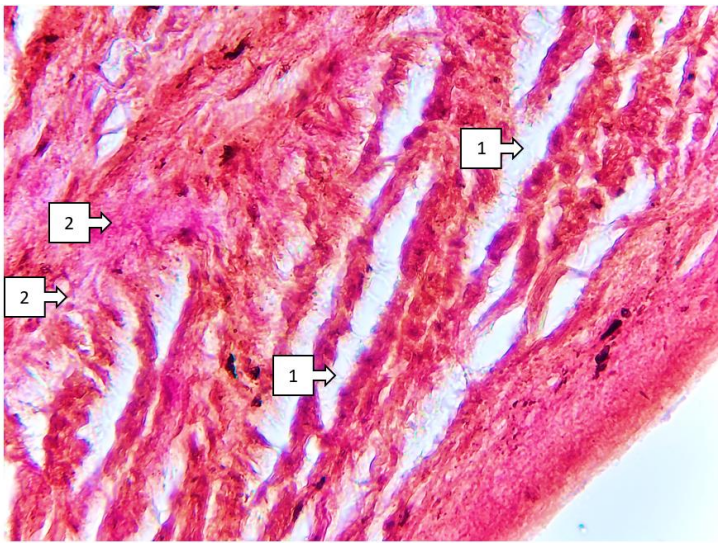

Figure 4. The tissue of the branch of the left lateral artery of the middle brain. Interstitial swelling between the fibrous structures of the intima layer of the artery (1). Foci of coarse sclerosis of collagen fibers are identified in thickened branches (2). Paint Van Gieson. The size is 40x10.

Arterial aneurysm is characterized by sudden changes between the middle layer of the vessel and the tuams of the muscle layer, mainly by the hypertrophy of muscle cells, the development of atrophic and sclerotic changes in the muscle tufts in the affected areas. These changes are based on the macroscopically sharp deformation of the vessel wall and the appearance of the morphological signs of the collapsing aneurysm. It is interstitial edema around the hypertrophied foci of the muscle layer, interstitial cysts between all layers of the atrophic and sclerotized branches, sharp separation of the borders of the layers of the vascular wall, destruction and elatolysis in the fibrous structures, almost no detection of vascular vessels (vasa vasorum) in the adventitial branches, the gap in this area a large accumulation of products is characterized by the formation of dystrophic and necrotic foci.

Violation of the sequence of mutual anastamotic connections of different fractions of collagen fibers, causing uneven appearance on the vessel wall, distribution of surface tension force at various levels, and sharp pressure on functional stress points play an important role in the occurrence of aneurysmal dilatations in these areas.

Conclusions.

Therefore, according to the analysis of the results obtained by histochemical tests, the focal increase of fibrous structures from the qualitative changes in the blood vessel wall, the large accumulation of acidic Schiff positive

structures in the space, causes the appearance of foci of disorganization in the wall, and the deformation of the vessel wall in various ways. At the same time, it was found that the pathological fibrous structures restored in place of the morphologically lost or damaged fibrous structures form surfaces that lead to a sharp change in the relief of the vessel wall and hemodynamic resistance from the morphofunctional point of view. These changes are studied in advance and serve as a source for the production of instructions to eliminate the foci of pathological disorganization expected through appropriate recommendations. In order to prevent these changes in the 45-55-year-old contingent, it is first necessary to eliminate the pathogenetic links of hypertension and atherosclerosis diseases, and to prevent the disproportionate location of coarse fibrous structures developing in the vascular wall.

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РАЗВИТИЕ ОСЛОЖНЕНИЙ У МАТЕРИ И ПЛОДА У РОЖЕНИЦ С ЭПИЛЕПСИЕЙ

Ш.А. Зуфарова[1], Ф.Т. Косимхожиева[2]
Республиканский центр репродуктивного здоровья населения
Андижанский государственный медицинский институт

Аннотация.

Недостаточная изученность коморбидности эпилепсии у беременных, стоящей на стыке неврологии и акушерства и гинекологии зачастую вызывает немало необоснованных страхов или наоборот, остается без должно внимания.

Целью данной статьи было раскрыть возможные осложнения у матери и плода в зависимости от выбранной тактики противоэпилептической терапии и индивидуальных особенностей рожениц.

Материал и методы. Были проспективно изучены данные историй болезни 200 рожениц с эпилепсией. Также были изучены факторы, способствующие развитию этих осложнений и отягощающие течение беременности.

Результаты проведенного анализа показали, что риск развития осложнений у плода при проведении монотерапии ниже, чем при политерапии.

Ключевые слова: беременность, эпилепсия, тератогенный риск, противоэпилептические препараты, осложнения, антиконвульсанты.

EPILEPSIYASI BOR AYOLLARDA ONA VA HOMILADA ASORATLAR KUZATILISHI

Sh.A. Zufarova[1], F.T. Kosimhojiyeva[2]
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Annotasiya.

Nevrologiya va akusherlik va ginekologiya chorrahasida turgan homilador ayollarda epilepsiyaning komorbidligi haqida yetarli ma'lumot yo’qligi ko'plab asossiz qo'rquvlarni keltirib chiqaradi yoki aksincha, tegishli e'tiborsiz qolmoqda.

Ushbu maqolaning maqsadi antiepileptik terapiyaning tanlangan taktikasiga va tug'ruqdagi ayollarning individual xususiyatlariga qarab ona va homilada yuzaga kelishi mumkin bo'lgan asoratlarni aniqlash edi.

Materiallar va usullar. Epilepsiya bilan og'rigan 200 nafar homilador ayollarning ma'lumotlari istiqbolli o'rganildi. Ushbu asoratlarning rivojlanishiga yordam beruvchi va homiladorlikning kechishini og'irlashtiradigan omillar ham o'rganildi.

Tahlil natijalari shuni ko'rsatdiki, monoterapiya bilan homilada asoratlar xavfi politerapiyaga qaraganda pastroq.

Kalit so'zlar: homiladorlik, epilepsiya, teratogen xavf, antiepileptik dorilar, asoratlar, antikonvulsanlar.

COMPLICATIONS IN MOTHER AND FETUS IN WOMEN WITH EPILEPSY

Sh.A. Zufarova[1], F.T. Kosimhojieva[2]
Republican Center for Reproductive Health
Andijan State Medical Institute

Abstract.

Insufficient knowledge of the comorbidity of epilepsy in pregnant women, which stands at the intersection of neurology and obstetrics and gynecology, often causes many unfounded fears or, conversely, remains without due attention.

The purpose of this article was to reveal possible complications in the mother and fetus depending on the chosen tactics of antiepileptic therapy and the individual characteristics of women in labor.

Material and methods. Data from the medical records of 200 parturient women with epilepsy were prospectively studied. Factors contributing to the development of these complications and aggravating the course of pregnancy were also studied.

The results of the analysis showed that the risk of complications in the fetus with monotherapy is lower than with polytherapy.

Key words: pregnancy, epilepsy, teratogenic risk, antiepileptic drugs, complications, anticonvulsants.

Введение. Эпилепсия — распространенное, хроническое и серьезное неврологическое заболевание, лечение которого обычно необходимо продолжать во время беременности, что само по себе заставляет задуматься о тератогенности применяемых препаратов [3, 7, 8].

Беременность обычно не влияет на частоту припадков у рожениц с эпилепсией (РЭ). Хотя процентное соотношение варьируется в разных исследованиях, примерно у 60% пациенток частота приступов аналогична исходной частоте припадков до беременности, тогда как у 15% наблюдается увеличение частоты, а у 15% — снижение [1, 2]. Если у пациентки были приступы, если она здорова в течение 1 года до беременности, весьма вероятно (80%), что во время беременности у нее и дальше не будет припадков. Частота эпилептического статуса у беременных РЭ сопоставима с годовой частотой 1,6% в общей популяции эпилептиков [4, 6, 9].

Материал и методы исследования. Под нашим непосредственным наблюдением в Андижанском филиале Республиканского перинатального центра находились 200 рожениц с эпилепсией в период с 2020 по 2023 год. Условно все роженицы были поделены на две группы: 108 из них

проводилась политерапия (два или более антиконвульсанта), 82 – монотерапия. Основной контингент пациенток – 62 человека (59,1%) составляли домохозяйки. Возрастной ценз составил 18-38 лет.

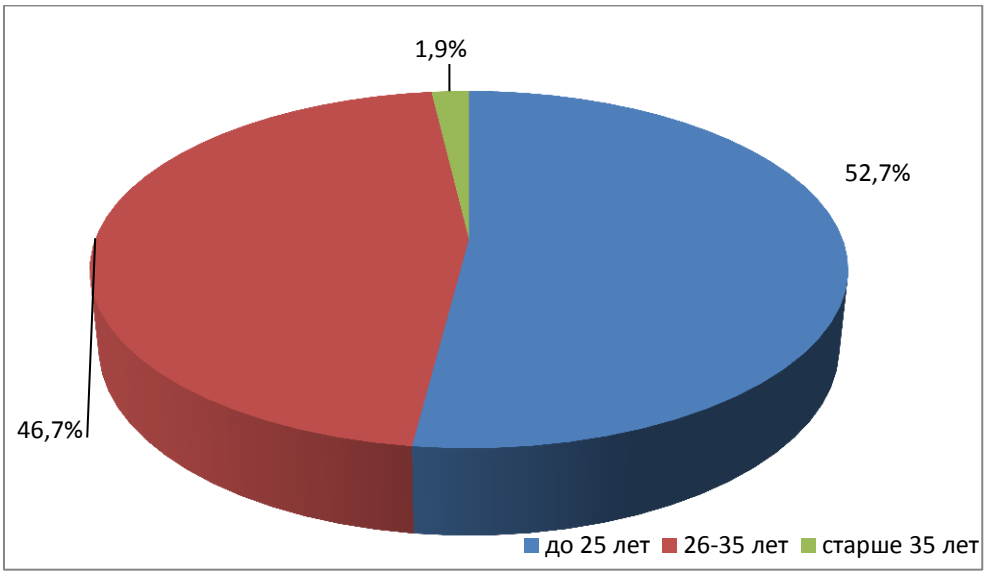

Рисунок 1. Возрастное распределение пациенток, получавших монотерапию.

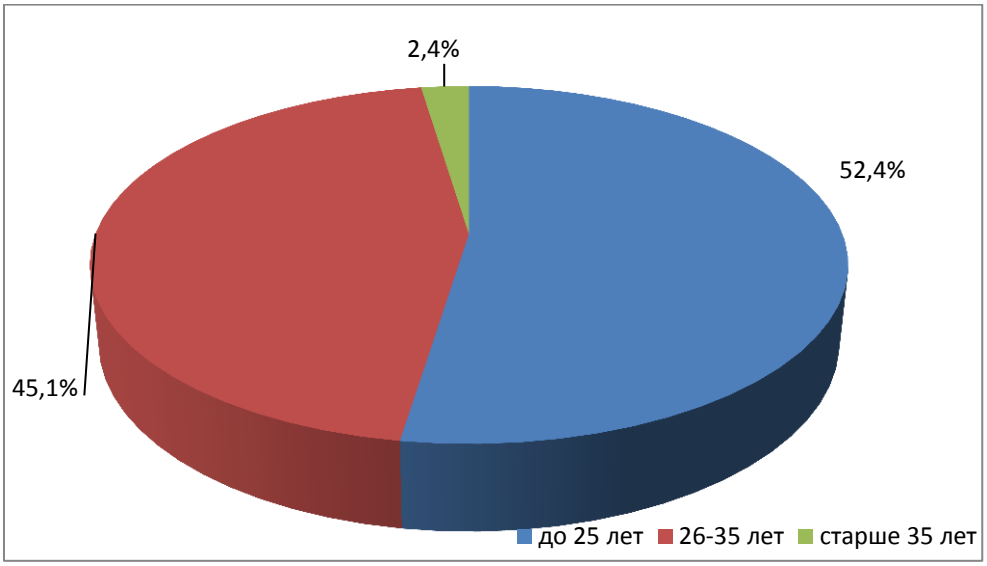

Рисунок 2. Возрастное распределение пациенток, получавших политерапию.

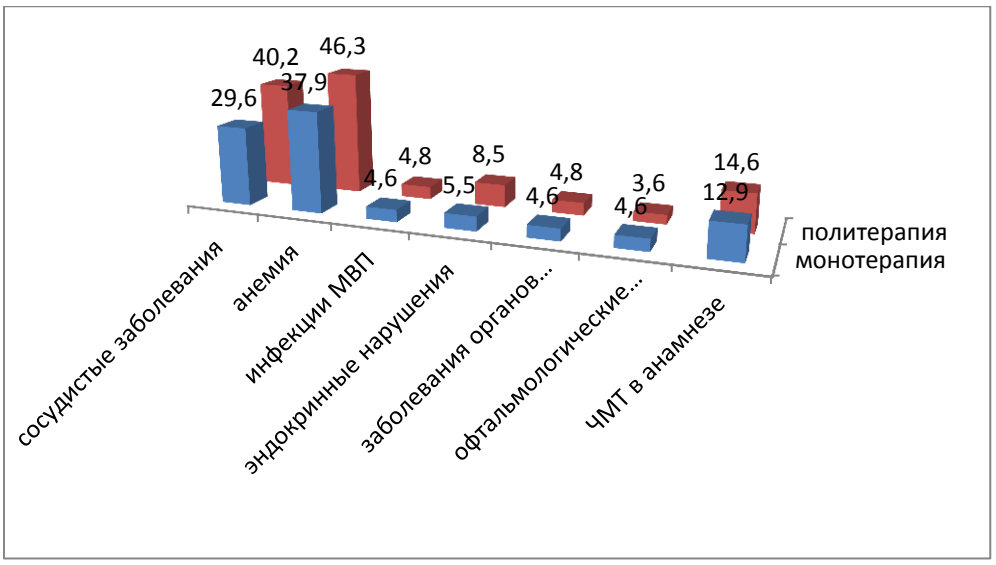

Рисунок 3. Наличие сопутствующих соматических патологий

В возрастном аспекте и в разрезе между группой пациенток, получавших монотерапию и группой, получавшей политерапию достоверной статистической разницы выявлено не было, из чего следует, что мы могли исключить погрешность в сравнении результатов исследования.

Результаты исследования. В качестве осложнений применения противоэпилептических препаратов нами учитывались низкая масса тела, признаки хронической фетоплацентарной недостаточности, острая гипоксия плода в родах, уродства плода, адинамия новорожденных.

Таблица 1.

Осложнения противоэпилептической терапии

Показатель	1 группа, N=108	2 группа, N=82
Средняя масса тела, г	3170±65	3040±75*
Признаки ХФПН, %	11,1	42,6 **
Признаки СОРП, %	12,9	32,9**
Признаки МФН, %	5,3	12,1*
Обвитие шеи пуповиной, острая гипоксия в родах, %	5,3	10,9**
Уродства плода, %	-	3,6
Адинамия новорожденных, %	12,9	34,1**

Среди осложнений разница в группах была статистически значимой ($p<0,05$).

Вывод. Наличие у матери эпистатуса и прием противоэпилептических препаратов безусловно влияет на течение беременности и развитие плода, но прекращать проведение противоэпилептической терапии конечно же было бы нецелесообразным. Тем не менее, можно отметить, что риск развития осложнений при проведении монотерапии значительно ниже, чем при использовании нескольких антиконвульсантов.

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Mundarija

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