ALKOGOLSIZ YOG'LI JIGAR KASALLIGI VA 2-TUR DIABET: KONYUGATSIYA VA RIVOJLANISH BOSQICHLARI MUAMMOSI

НЕАЛКОГОЛЬНАЯ ЖИРОВАЯ БОЛЕЗНЬ ПЕЧЕНИ И САХАНЫЙ ДИАБЕТ 2 ТИПА: ПРОБЛЕМА СОПЯЖЕННОСТИ И ЭТАПНОСТИ РАЗВИТИЯ

NON-ALCOHOLIC FATTY LIVER DISEASE AND TYPE 2 DIABETES MELLITUS: THE PROBLEM OF CONJUNCTION AND PHASING

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Аннотация

Широкая распространенность неалкогольной жировой болезни печени (НАЖБП) и сахарного диабета 2 типа (СД2), а также их взаимосвязи определяет необходимость прицельного рассмотрения данной патологии с целью оптимиза- ции подходов к диагностике и лечению пациентов с НАЖБП и СД2. Являясь компонентами метаболического синдро- ма, эти два заболевания во многом имеют схожие механизмы развития и прогрессирования, синергично повышая риск неблагоприятных исходов у коморбидных пациентов. Несмотря на общность патофизиологических механизмов, актуальным остается вопрос о последовательности развития НАЖБП и СД2.

По результатам анализа литературы выделено две основных теории: алиментарная и метаболическая. Согласно алиментарной теории, первичным звеном патогенеза выступают ожирение и сопряженное с ним избыточное нако- пление свободных жирных кислот и триглицеридов в печени, приводящее впоследствии к инсулинорезистентности и развитию СД2. В противоположность этому, в метаболической теории в качестве первичного удара рассматрива- ется сопутствующая диабету инсулинорезистентность, которая независимо от ожирения создает предпосылки для повреждения печени. Помимо этого, в обзоре уделено особое внимание рассмотрению новой концепции — мета- болически ассоциированной жировой болезни печени (МАЖБП), рассматриваемой в качестве печеночного компо- нента метаболического синдрома. В рамках данной концепции выделяют различные клинические фенотипы НАЖБП, определяющие путь, по которому развиваются рассматриваемые заболевания. В заключение в обзоре обсуждается патогенетически обоснованная терапия, акцент в которой сделан на

преодоление инсулинорезистентности, коррек- цию атерогенной дислипидемии и восстановление структуры и функции клеток печени.

Ключевые Слова

неалкогольная жировая болезнь печени; сахарный диабет 2 типа; ожирение; инсулинорезистентность; мета- болический синдром;

Abstract

The widespread prevalence of non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM), as well as their combination, determines the need for a targeted analysis of this pathology in order to optimize approaches to the diagno- sis and treatment of patients with NAFLD and T2DM. As components of the metabolic syndrome, these two diseases have largely similar mechanisms of development and progression, simultaneously increasing the risk of adverse outcomes in comorbid patients. Despite the common pathophysiological mechanisms, the question of the development of NAFLD and T2DM remains significant.

Upon conducting literature analysis, two main theories have been identified: alimentary and metabolic. According to the ali- mentary theory, the primary link in the pathogenesis is obesity and the associated excessive accumulation of free fatty acids and triglycerides in the liver, which subsequently leads to insulin resistance and the development of T2DM. In contrast, the metabolic theory considers diabetes-related insulin resistance as the first hit, which, regardless of obesity, creates precondi- tions for liver damage. In addition, the review focuses on the consideration of the new concept of Metabolic associated fatty liver disease (MAFLD) as a hepatic manifestation of the metabolic syndrome and considers the clinical phenotypes identified within this pathology. In conclusion, pathogenically based treatment goals in patients with NAFLD and T2DM are overcom- ing insulin resistance, correcting atherogenic dyslipidemia, and restoring the structures and functions of liver cells.

Keywords

non-alcoholic fatty liver disease; type 2 diabetes mellitus; obesity, insulin resistance; metabolic syndrome;

Mavzuning Dolzarbligi

Alkogolsiz yog'li jigar kasalligi (AYJK) va 2 -tur diabet (QD2) ning keng tarqalishi, shuningdek ularning o'zaro bog'liqligi AYJK va QD2 bilan og'rigan bemorlarni tashxislash va davolashga yondashuvlarni optimallashtirish uchun ushbu patologiyani diqqat bilan ko'rib chiqish zarurligini belgilaydi. Metabolik sindromning tarkibiy qismlari bo'lgan bu ikki kasallik ko'p jihatdan o'xshash rivojlanish va rivojlanish mexanizmlariga ega bo'lib, komorbid bemorlarda salbiy natijalar xavfini sinergik ravishda oshiradi. Patofiziologik mexanizmlarning umumiyligiga qaramay, AYJK va QD2 rivojlanishining ketma-ketligi masalasi dolzarb bo'lib qolmoqda.

Adabiyot tahlili natijalariga ko'ra ikkita asosiy nazariya aniqlandi: alimentar va metabolik. Alimentar nazariyaga ko'ra, patogenezning asosiy bo'g'ini semirish va jigarda erkin yog ' kislotalari va triglitseridlarning ortiqcha qo'shilishi bo'lib, keyinchalik insulin reziztentligi va QD2 rivojlanishiga olib keladi. Bundan farqli o'laroq, metabolik nazariyada diabet bilan birga keladigan insulin reziztentligi asosiy orin sifatida ko'rib chiqiladi, bu semirishdan qat'i nazar,

jigar shikastlanishi uchun zarur shart - sharoitlarni yaratadi. Bundan tashqari, maqolada yangi kontseptsiyani - metabolik bilan bog'liq yog'li jigar kasalligini ko'rib chiqishga alohida e'tibor qaratilgan. Ushbu kontseptsiya doirasida AYJK ning turli xil klinik fenotiplari ajralib turadi, ular ko'rib chiqilayotgan kasalliklarning rivojlanish yo'lini belgilaydi. Xulosa qilib aytganda, maqolada patogenetik asoslangan terapiya muhokama qilinadi, unda insulin reziztentligini yengishga, aterogen dislipidemiyaning korrelyatsiyasiga va jigar hujayralarining tuzilishi va funktsiyasini tiklashga e'tibor qaratiladi.

Kalit so'zlar

alkogolsiz yog'li jigar kasalligi; 2-tur diabet; semizlik; insulin reziztentligi; metabolik sindromi;

Bugungi kunda to'plangan bilimlar metabolik sindrom (MS) muammosiga sezilarli darajada kengroq qarashga, ma'lum xavf omillarini diqqat bilan ko'rib chiqishga va diagnostika va davolashga ko'proq moslashtirilgan yondashuvlarni tanlashga imkon beradi.

Ushbu maqola doirasida alkogolsiz yog'li jigar kasalligi (AYJK) va QD2 patogenezining dolzarb nazariyalari tahlil qilindi, bunda insulin reziztentligi va semirish asosiy o'rinni egallaydi. Adabiyotlarga nazar soladigan bolsak "alkogolsiz yog'li jigar kasalligi"," 2-tur diabet"," insulin rezistentligi"va" semizlik "so'zlari bilan Pubmed va Elibrary.ru 1998 yildan 2021 yilgacha bo'lgan davrni o’z ichiga oladi,

ALKOGOLSIZ YOG'LI JIGAR KASALLIGI VA METABOLIK SINDROMNING TARKIBIY QISMLARI SIFATIDA 2-TUR DIABET

MS bilan bog'liq kasalliklardan biri AYJK hisoblanadi [5, 6]. Rossiya gastroenterologlari ilmiy jamiyati (NOGR) va Rossiya terapevtlar ilmiy tibbiyot jamiyati (RNMOT) ning so'nggi klinik tavsiyalariga ko'ra, AYJK jigarni toksik shikastlanishining ekzogen omillari bo'lmagan odamlarda metabolik genezisning surunkali jigar kasalligi bo'lib, jigar asosini tashkil etuvchi hujayra elementlarida lipidlarning to'planishi natijasida kelib chiqadi. Morfologik jihatdan steatoz, steatogepatit, fibroz bilan tasdiqlangan, siroz yoki adenokarsinoma [7].

Bugungi kunga kelib, AYJK tarqalishi 25% ni tashkil etadi va ushbu ko'rsatkichning barqaror o'sishiga nisbatan tendentsiya mavjud [8]. AYJK bugungi kunda butun dunyo bo'ylab surunkali jigar kasalliklari etiologiyasida etakchi o'rinni egallashi tashvishga soladi. Shu bilan birga, u ko'pincha jigar sirrozi va gepatotsellulyar karsinomaga o'tishga moyil bo'ladi, shuningdek, umumiy va jigar kasalliklari bilan bog'liq o'lim xavfini oshiradi. Bundan tashqari, AYJK va uning oqibatlari ko'pincha jigar transplantatsiyasi zarurligiga olib keladi [9].

Shunday qilib, yuqorida aytib o'tilganidek, AYJK metabolik kasalliklar bilan bog'liq va ba'zi ma'lumotlarga ko'ra, uning o'zi MS bo'lib, uning jigar tarkibiy qismi hisoblanadi [10, 11]. Shunday qilib, 2020 yilda xalqaro ekspert konsensus bayonoti e'lon qilindi, unda barcha mutaxassisliklar shifokorlariga yangi ta'rif -metabolik bilan bog'liq yog'li jigar kasalligi (metabolic dysfunction associated fatty)[12]. Ushbu ta'rif yog ' gepatozining metabolik kasalliklar bilan bog'liqligini to'liq aks ettiradi boshqa organ tizimlariga ta'sir ko'rsatadigan va jigardan tashqarida kechadigan ushbu kasallikning ko'p qirraliligi ko’zda tutiladi.

Bugungi kunda tibbiy hamkorlikda faol muhokama qilinayotgan metabolik sindromning eng yuqori cho'qqilaridan biri bu AYJK. MS bilan bog'liq yana bir jiddiy muammo QD2. Shunday qilib, 2019 yilda 20 yoshdan 79 yoshgacha bo'lgan diabet bilan og'rigan bemorlarning soni 463 millionni tashkil etdi [13]. Shu bilan birga, xalqaro diabet Federatsiyasi prognozlariga ko'ra, 2030 yilga kelib har o'ninchi kattalar QD2 bilan og'riydilar. [14]. Diabetni jigar kasalliklari bilan bog'lab, shuni ta'kidlash kerakki, ko'pincha QD2 bilan og'rigan bemorlarda AYJK bilan kasallanish umumiy aholi sonidan ikki baravar yuqori, bu raqamlarda 55,5% ni tashkil qiladi [15].

Shuni ta'kidlash kerakki, odatdagi endokrinologiya amaliyotida diabetik bemorlarda jigar patologiyasi ko'pincha etibordan chetda qoladi [16]. Birlamchi tibbiy yordam shifokori tomonidan tegishli ogohlantirishning yo'qligi yomon oqibatlariga olib keladi. Ushbu ikkita patologiyaning kombinatsiyasi nafaqat AYJK va ushbu holat bilan bog'liq kasalxonaga yotqizishning yanada og'ir formalarining rivojlanish xavfini oshiradi, balki diabet bilan og'rigan odamlarda glikemik nazoratga erishishni qiyinlashtiradi va aterogen dislipidemiya rivojlanishiga yordam beradi [17].

Shunday qilib, QD2 va AYJK ko'pincha bir - biri bilan birga yashaydi, sinergik ravishda ushbu muammoga duch kelgan shaxslar orasida xavfini oshiradi [18-22]. Uglevod va yog ' almashinuvini tartibga soluvchi asosiy organ sifatida jigar AYJK va QD2 birlashtiradi. Insulin rezistentligi va semirish - bu jigar asosiy organlardan biri sifatida tanlangan ikkita patologik holat. Shu bilan birga, AYJK va QD2 bilan bir qatorda ichki muhit buzilishlarining ketma - ketligi va rivojlanish mexanizmlari masalasi dolzarb bo'lib qolmoqda: bu ikki kasallik parallel ravishda ketadi, MS holatini og'irlashtiradi va shu bilan yurak-qon tomir o'lim xavfini oshiradi.

PATOGENETIK BOG'LANISHLARNING UMUMIYLIGI

ALKOGOLSIZ YOG'LI JIGAR KASALLIGI VA 2-TUR DIABETNING RIVOJLANISHIDA

AYJK va QD2 o'rtasidagi munosabatlar muammosining asosi, yuqorida aytib o'tilganidek, insulin reziztentligidir. Semizlik, shartli ravishda, yurak - qon tomir patologiyasi, yurak tomirlari kasalligi va saratonning ayrim turlarini o'z ichiga olgan ko'plab kasalliklarning rivojlanishining asosi deb hisoblansa ham QD2 eng yuqori tana massasi indeksi (TVI) bilan bog'liq. Shunday qilib, semirish QD2 bilan og'rigan odamlarning 44 foizini tashkil qiladi [23].

Qandli diabet bilan bir qatorda, AYJK insulin reziztentligi ushbu kasallikning rivojlanishining asosiy mexanizmlaridan biri sifatida ham hisobga oladi, bu uglevod va keyinchalik yog ' almashinuvining buzilishida namoyon bo'ladi, natijada jigar hujayralarida lipidlar to'planadi [25-27].

ALIMENTAR NAZARIYA

Zamonaviy nazariyalardan biriga ko'ra, AYJK bilan erkin yog ' kislotalari va triglitseridlarning (tg) haddan tashqari to'planishi insulin retseptorlarining shikastlanishiga va insulin reziztentligining rivojlanishiga olib keladi, bu esa o'z navbatida insulin sekretsiyasining asta-sekin buzilishiga va QD2 namoyon bo'lishiga olib keladi [28].

Ushbu nazariyani tushunish oson bo'lib, jigar yog’ infiltratsiyasining buzilishini natiyjasida tushuntiradi. Ta'riflangan nazariyani alimentar deb atash mumkin, chunki unga ko'ra jigarda

lipidlarning ortiqcha to'planishi ularning bevosita toplanishi bilan bog'liq [29]. Darhaqiqat, AYJK qorin bo'shlig'idagi yog’larning toplanishi va MS bilan og'rigan bemorlarning 100 foizida aniqlanadi [30], ularning 20-47 foizida alkogolsiz steatogepatit mavjud - prognostik jihatdan yomonroq — AYJK ning turi hisoblanadi [31].

Alimentar omil va natijada semirishning jigar va uglevod almashinuviga ta'siri mexanizmi batafsilroq quyidagicha tushintiriladi.

I. Jigar steatozi.

Hayvonlarga boy yog ' va oson hazm bo'ladigan uglevodlarni ortiqcha iste'mol qilish oshqozon - ichak traktidan qon oqimiga, so'ngra to'qimalarga ko'p miqdordagi xolesterinlarning paydo bo'lishiga olib keladi. Adipotsitlar gipertrofiyasi - gipperplaziyasi bilan ifodalangan lipidlar to'planadi. Yog ' to'qimasi ichki sekretsiya bezining funktsiyasiga ega bo'lib, uning sekretor faolligini o'zgartiradi va ko'p miqdordagi yallig'lanish jarayonini keltirib chiqara boshlaydi (o'simta nekrozi omili - alfa (Tnf - a), FFA, interleykin-6 va boshqalar), bu asta-sekin progressiv surunkali yallig'lanishning rivojlanishiga olib keladi [32]. Ushbu jarayon, shuningdek, jigar portal tizimiga va jigarga yog’larning ortiqcha etkazib berilishi bilan birga keladi. Jigarga lipidlarning kirib kelishi, ularning sintezi va utilizatsiyasi o'rtasidagi nomutanosiblik mavjud bo'lib, bu gepatotsitlarda triglitsridlarni o'z ichiga olgan yog ' vakuolalarining to'planishi, ya'ni steatozning rivojlanishi bilan namoyon bo'ladi [33].

II. Steatogepatit va insulin rezistentligi.

Yog ' to'qimalari tomonidan faol ravishda chiqariladigan yallig'lanish jarayoni gepatotsitlar membranalariga bevosita zarar etkazadi, P450 sitokromining faollashishiga olib keladi, lipid peroksidatsiyasini kuchaytiradi va jigar hujayralariga zarar etkazadigan oksidlovchi nekroz rivojlanishiga sabab bo'ladi. Gepatotsitlarning o'limi apoptoz va nekroz mexanizmi bilan, shuningdek tolali toqimani to'planishi bilan sodir bo'ladi. Jigarda surunkali yallig'lanish asta - sekin rivojlanishiga olib keladi [34, 35]

METABOLIK NAZARIYA

Boshqa tomondan, jigar steatozi TVI, insulin rezistentligi bilan bog'liqligi haqidagi dalillar alimentar nazariyani shubha ostiga qo'yadi, bu yerda patogenezning asosiy bo'g'ini aynan qabul qilingan lipidlar va ularni sarif qilish o'rtasidagi nomutanosiblikdir., ya'ni alimentar omil [41]. Ushbu nazariya bilan birgalikda periferik insulin rezistentligi o'zi jigar hujayralarida yog’larning ortiqcha sintezi va to'planishini boshlaydi, bu ularning keyingi jigar shikastlanishi va patologiya rivojlanishi uchun zarur shart - sharoitlarni yaratadi. Agar adipocitlarda insulin retseptorlarining zichligi pasaysa, mushaklarda tirozin kinaza faolligining pasayishi kuzatiladi, bu esa glyukoza so'rilishining buzilishiga olib keladi [32].

Insulin ta'sirining normal to'qimalarga ta'siri qanday ifodalanadi? Insulinga sezgir bemorlarda insulin kontsentratsiyasining postprandial ko'tarilishi yog’ to'qimalarida lipaza faolligining pasayishiga, ya'ni lipolizning bostirilishiga olib keladi. Bu qon plazmasidagi yog’ kontsentratsiyasining pasayishi va natijada ushbu substratlarning jigarga etkazib berilishining pasayishi bilan ifodalanadi. Insulin rezistentligi holati vaziyatni tubdan o'zgartiradi: lipolizning insulinga bog'liq tasiri sodir bo'lmaydi, ya'ni yog’ning ko'pligi gepatotsitlarga "hujum qiladi" [42]. O'z navbatida, jigarga uzoq zanjirli yog ' kislotalarining ko'payishi jigar insulin rezistentligining rivojlanishiga moyil bo'lib, bu jigarda glyukoza neogenezining stimulyatsiyasi

va jigar tomonidan glyukoza chiqarilishining ko'payishi bilan ko’rinadi [43]. Shunday qilib, insulin darajasining oshishi bilan bir qatorda qon plazmasidagi glyukoza darajasi ham oshiradi. Bir vaqtning o’zida jigarida glyukoneogenezning faollashishi bilan-glikogen sintezining pasayishi, shuningdek yog’ning b - oksidlanishi, natijada gepatotsitlarda triglitseridlar to'planishi.

XULOSA

Shunday qilib, AYJK va QD2 ning konyugatsiyasiga qaramay, ularning rivojlanish ketma - ketligi masalasi ochiq qolmoqda. Maqolada ko'rib chiqilgan metabolik va alimentar nazariyalar asosida biz QD2 va AYJK rivojlanishining yo'llari va bosqichlari bemorning klinik fenotipiga qarab farq qilishi mumkin degan xulosaga kelishimiz mumkin. Yog ‘va uglevod almashinuvining buzilishining asosiy hodisalari sifatida ushbu kasalliklarning yuqori tez - tez kombinatsiyasini, shuningdek, bir jarayonning boshqasiga o'zaro ta'sir qilish imkoniyatini hisobga olgan holda, biz bemorlarning ikkala guruhiga diqqat bilan nazoratta bolishi kerekligini esda tutishimiz kerak QD2 nafaqat uglevod almashinuvining buzilishi, xuddi AYJK yog' almashinuvining buzilishi bilan cheklanmagani kabi gepatotsitlarda yog’ almashinuvi, insulin-rezistentligini bartaraf etish, aterogen dislipidemiyani tuzatish va jigar hujayralarini tiklash bu holda AYJK va QD2 muammosi bilan kasallangan bemorlarning ko'pchiligida qo'llanilishi mumkin bo'lgan kombinatsiya sifatida namoyon bo'ladi.

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