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THE ROLE OF GUT MICROBIOTA ALTERATIONS IN THE DEVELOPMENT OF HEPATIC ENCEPHALOPATHY IN PATIENTS WITH LIVER CIRRHOSIS

Ismoilova Robiyaxon Shuxrat qizi
Master's Student of the Department of
"Internal Diseases in Family Medicine,"
Specialty "Therapy,"
CAMU International Medical University
ORCID ID: https://orcid.org/0009-0003-3876-2799
robiyaxonismoilova22@gmail.com +998907830424

Ph.D., **Kenjayev Olimjon Obidjonovich**
Head of the Department of "Internal Diseases in Family Medicine,"
CAMU International Medical University
ORCID ID: https://orcid.org/0009-0002-9209-2282
+998916786624

ABSTRACT

This article is devoted to the study of structural changes in the gut microbiota of patients with liver cirrhosis and their impact on the course of the disease. During the progression of liver cirrhosis, disruption of the intestinal microecological balance may lead to alterations in metabolic processes and further deterioration of liver function. In this article, qualitative and quantitative changes in the gut microbiota were analyzed. The findings demonstrated that dysbiosis, characterized by a reduction in beneficial bacteria and an increase in certain opportunistic microorganisms, is widespread among patients with liver cirrhosis. Such alterations in the gut microbiota may contribute to dysfunction of the gut–liver axis and create conditions for the accumulation of toxic metabolites in the body. Furthermore, changes in microbiota composition were found to be associated with the clinical course and severity of the disease. The conclusions obtained indicate that the assessment of gut microbiota is of significant importance in determining the developmental characteristics of liver cirrhosis. The study findings provide a scientific basis for improving preventive and therapeutic approaches aimed at restoring intestinal microecology.

Keywords: liver cirrhosis, gut microbiota, dysbiosis, gut–liver axis, metabolic disorders, toxic metabolites, opportunistic bacteria, liver function, microecology

JIGAR SIRROZI BILAN OG'RIGAN BEMORLARDA ICHAK MIKROBIOTASINING O'ZGARISHI VA JIGAR ENSEFALOPATIYASI RIVOJLANISHIDAGI O'RNI

Annotatsiya.

Ushbu maqolada jigar sirrozi bilan og'rigan bemorlarda ichak mikrobiotasining tarkibiy o'zgarishlari va ularning kasallik kechishiga ta'sirini o'rganishga bag'ishlangan. Jigar sirrozi rivojlanishi davomida ichak mikroekologik muvozanatining buzilishi organizmda metabolik jarayonlarning o'zgarishiga hamda jigar faoliyatining yanada izdan chiqishiga olib kelishi mumkin. Quyidagi maqolada ichak mikrobiotasining sifat va miqdor jihatdan o'zgarishlari tahlil qilindi. Olingan xulosalar foydali bakteriyalar sonining kamayishi va ayrim shartli patogen mikroorganizmlarning ko'payishi bilan tavsiflanadigan disbioz holati jigar sirrozi bilan og'rigan bemorlarda keng tarqalganligini ko'rsatdi. Ichak mikrobiotasidagi bunday o'zgarishlar ichak–jigar o'qi faoliyatining buzilishiga hamda toksik metabolitlarning organizmda to'planishiga sharoit yaratishi mumkinligi aniqlandi. Shuningdek, mikrobiota tarkibidagi o'zgarishlar

kasallikning klinik kechishi va og‘irlik darajasi bilan bog‘liq ekanligi qayd etildi. Olingan xulosalar shundan iboratki, ichak mikrobiotasini baholash jigar sirrozining rivojlanish xususiyatlarini aniqlashda muhim ahamiyatga ega ekanligini ko‘rsatadi. Tadqiqot ma’lumotlari ichak mikroekologiyasini tiklashga qaratilgan profilaktik va terapevtik yondashuvlarni takomillashtirish uchun ilmiy asos bo‘lib xizmat qiladi.

Kalit so‘zlar: jigar sirrozi, ichak mikrobiotasi, disbioz, ichak–jigar o‘qi, metabolik buzilishlar, toksik metabolitlar, shartli patogen bakteriyalar, jigar funksiyasi, mikroekologiya.

Dolzarbligi.

Jigar sirrozi — bu surunkali jigar kasalligi bo‘lib, unda sog‘lom jigar to‘qimalari fibroz to‘qima va regenerativ tugunlar bilan almashinadi. Natijada jigar tuzilishi buziladi va uning funksional faoliyati izdan chiqadi . Ushbu kasallik butun dunyo bo‘ylab muhim sog‘liqni saqlash muammosi hisoblanadi va uning global tarqalishi taxminan 1,3 % ni tashkil etadi Tarqalishidan tashqari, jigar sirrozi kasallanish va o‘limning asosiy sabablaridan biri bo‘lib, bemorlarning hayot sifatiga salbiy ta’sir ko‘rsatadi hamda nogironlik tufayli yo‘qotilgan hayot yillarning sezilarli qismini tashkil qiladi.

Jigar sirrozining kelib chiqish sabablari ko‘p omilli hisoblanadi. Surunkali alkogol iste’moli hanuzgacha ushbu kasallikning eng keng tarqalgan sababidir. Biroq, virusli gepatitlar, ayniqsa B va C gepatitlari ham muhim o‘rin tutadi. . So‘nggi yillarda skrining usullarining takomillashuvi va samarali antivirus davolash usullarining joriy etilishi natijasida virusli gepatitlarning global tarqalishi kamaymoqda. Aksincha, semizlik va metabolik sindromning dunyo bo‘ylab keng tarqalishi tufayli alkogol bilan bog‘liq bo‘lmagan yog‘li jigar kasallig(Jigar yog’li gepatozi) bilan bog‘liq sirroz holatlari ortib bormoqda. Bundan tashqari, autoimmun gepatit, irsiy kasalliklar, masalan, Vilson kasalligi va gemoxromatoz, shuningdek birlamchi biliar sirroz kabi xolestatik jigar kasalliklari ham sirrozning nisbatan kam uchraydigan sabablariga kiradi

Kirish.

Jigar sirrozi surunkali jigar kasalliklarining yakuniy bosqichi bo‘lib, butun dunyo bo‘ylab yuqori kasallanish va o‘lim ko‘rsatkichlariga sabab bo’luvchi omillardan biri hisoblanadi. Uning rivojlanishida ichak-jigar o‘qi (gut-liver axis) muhim o‘rin tutadi. Bu tizim ichak mikrobiotasi va jigar o‘rtasidagi ikki tomonlama o‘zaro aloqani ta’minlaydi. Ushbu o‘qning buzilishi, jumladan ichak devori funksiyasining izdan chiqishi natijasida ingichka ichak pathogen bakteriyalarining ortiqcha ko‘payishi hamda mikrobiota disbiozi yuzaga keladi. Bular esa jigar sirrozining eng og’ir asoratlaridan biri jigar ensefalopatiyasi rivojlanishiga sababbo’ladi.

Jigar sirrozi SJKning progressiv bosqichi bo‘lib, qaytariluvchi fibrozning qaytarilmas fibrotik to‘qima va regenerativ tugunlarga aylanishi bilan xarakterlanadi. Ushbu jarayon oxir-oqibat portal gipertenziya va uning asoratlari, jumladan, qizilo‘ngach va oshqozon varikoz venalaridan qon ketishi, jigar ensefalopatiyasi (JE), assit hamda gepatorenal sindrom rivojlanishiga olib keladi [7]. Bundan tashqari, sirroz surunkali jigar kasalliklari oqibatlari va gepatotsellyulyar karsinoma rivojlanish xavfining asosiy omillaridan biri hisoblanadi [8].

Patofiziologik nuqtai nazardan, jigar sirrozi jigar hujayralarining uzoq muddatli shikastlanishi natijasida yuzaga keladi. Bu jarayon surunkali yallig‘lanish va fibrozning rivojlanishini qo‘zg‘atadi. Fibroz jarayonida jigar yulduzsimon hujayralari (hepatic stellate cells) markaziy rol o‘ynab, hujayradan tashqari matritsa komponentlarini ishlab chiqaradi va ularning asta-sekin to‘planishiga sabab bo‘ladi. Fibroz chuqurlashgani sari jigar o‘zining regenerativ qobiliyati hisobiga tugunlar hosil qiladi, bu esa organ tuzilishining yanada buzilishiga va jigar funksiyasining yomonlashishiga olib keladi. Vaqt o‘tishi bilan ushbu patologik qayta tuzilish portal gipertenziya, jigar ensefalopatiyasi hamda jigar hujayrali karsinomasi rivojlanish xavfining ortishi kabi og‘ir asoratlarni keltirib chiqarishi mumkin

Jigar sirrozi kasalligini davolashda bemorlarning to'g'ri va taabiiy mahssulotlar bilan ovqatlanishi, ularning kunlik ratsioniga tolaga bboy va o''simlik mahsulotllaridan ko'proq iste'mol qilishini nazorat qilish lozim.

Muhokama.

So'nggi yillarda olib borilgan ko'plab tadqiqotlar ichak mikrobiotasi inson organizmidagi eng yirik mikroekotizim ekanligini va uning gastroenterologik, nevrologik, respirator, metabolik hamda yurak-qon tomir tizimi kasalliklariga ta'sir ko'rsatishini namoyon etdi. Jigar ovqat hazm qilish tizimidan tashqarida joylashgan va ichak mikrobiotasi hamda uning metabolitlari bilan birinchi bo'lib to'qnashadigan eng yaqin organ hisoblanadi. Ichak mikrobiotasi va jigar o'rtasidagi o'zaro aloqa "ichak–jigar o'qi" (gut-liver axis) deb ataladi va keng o'rganilib kelmoqda [9].

Sog'lom inson ichak mikrobiotasining asosiy qismini to'rtta yirik bakterial bo'lim — **Bacteroidetes, Firmicutes, Proteobacteria va Actinobacteria** tashkil qilad.. Biroq sirroz rivojlanishi jarayonida mikrobiologik xilma-xillikning sezilarli kamayishi kuzatiladi. Bu holat ichak devori funksiyasining buzilishi natijasida yuzaga keladigan ingichka ichak bakterial ko'payishi (small intestinal bacterial overgrowth) va bakterial translokatsiya bilan kechadi.

Probiotiklar inson organizmi uchun foydali ta'sir ko'rsatadigan bakteriyalar yoki achitqi kabi mikroorganizmlardir. Klinik tadqiqotlardan birida 6 oy davomida VSL-3 probiotigi qabul qilgan bemorlarda jigar ensefalopatiyasi rivojlanish chastotasi, shuningdek Child–Pugh va MELD ko'rsatkichlari nazorat guruhiga nisbatan past bo'lgani aniqlangan. Boshqa tadqiqotlar ham jigar ensefalopatiyasi kabi og'ir jigar kasalliklarini probiotiklar, prebiotiklar va antibiotiklar yordamida ichak mikrobiomini modulyatsiya qilish orqali davolash mumkinligini ko'rsatgan .

Xulosa qilib aytganda, jigar sirrozi surunkali jigar kasalliklarining keng tarqalgan terminal bosqichi bo'lib, uning rivojlanishi ichak bakteriyalarining ortiqcha ko'payishi va disbioz bilan chambarchas bog'liq. Bakterial toksinlarning portal vena yoki tizimli qon aylanishiga tushishi bevosita gepatotsitlar nobud bo'lishiga olib kelishi mumkin. Bundan tashqari, mikrobiota muvozanatining buzilishi ichak to'sig'i funksiyasiga salbiy ta'sir ko'rsatib, bakteriyalar translokatsiyasini kuchaytiradi va natijada infeksiya, tizimli yallig'lanish hamda qon tomirlarining kengayishiga sabab bo'ladi. Bu esa o'tkir dekompensatsiya va ko'p a'zoli yetishmovchilik rivojlanishiga olib kelishi mumkin. Shu sababli ichak mikrobiotasi va jigar sirrozi o'rtasidagi munosabatlarni chuqur o'rganish muhim ahamiyatga ega. Biroq, ichak mikrobiotasi surunkali jigar kasalliklarining rivojlanishi va progressiyasida muhim rol o'ynashiga qaramay, uning sirroz rivojlanishiga bevosita sababiy ta'sirini tasdiqlovchi dalillar hanuz yetarli emas

Xulosa.

Hozirgi kunda ichak disbiozi va jigar ensefalopatiyasi kelib chiiqiishini oldini olish uchun bemorlarning to'g'ri ovqatlanishi , tolaga boy va o'simlik mahsulotlariga asoslangan parhezlar, shuningdek prebiotiklar, probiotiklar yoki sinbiotiklar bilan qo'shimcha davolash ichak mikrobiotasining muvozanatini tiklash, qondagi ammiak miqdorini kamaytirish va jigar ensefalopatiyasi natijalarini yaxshilashda istiqbolli usullar sifatida ko'rilmoqda. Hozirgi klinik tavsiyalar yetarli miqdorda oqsil iste'mol qilishni, ayniqsa o'simlik manbali yoki kazein tarkibli oqsillarni tavsiya etad.Parhez va ovqatlanishni optimallashtirish jigar sirrozini davolashda istiqbolli qo'shimcha yondashuv hisoblanadi.

Ushbu maqola shuni ko'rsatadiki, jigar sirrozi bilan og'rigan bemorlarda ichak mikrobiotasidagi disbioz gepatik ensefalopatiya rivojlanishida muhim rol o'ynaydi. Ichakdagi foydali bakteriyalarning kamayishi va patogen bakteriyalarning ko'payishi, shuningdek,

toksinlar va ammiak darajasining ortishi, ichak–jigar–miya o‘qi orqali markaziy asab tizimiga salbiy ta’sir ko‘rsatadi. Natijada jigar ensefalopatiyasi rivojlanish xavfi oshadi

Adabiyotlar ro’yxati.

1. Ouyang Li [1 2], Han Xu [1 3], Dayoung Kim [1 3], Fan Yang [1 3], Zhijun Bao [1 2 3]
[1] Shanghai Key Laboratory of Clinical Geriatric Medicine, Shanghai, China
[2] Department of Gastroenterology, Huadong Hospital Affiliated to Fudan University, Shanghai, China
[3] Department of Gerontology, Huadong Hospital Affiliated to Fudan University, Shanghai, China
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