



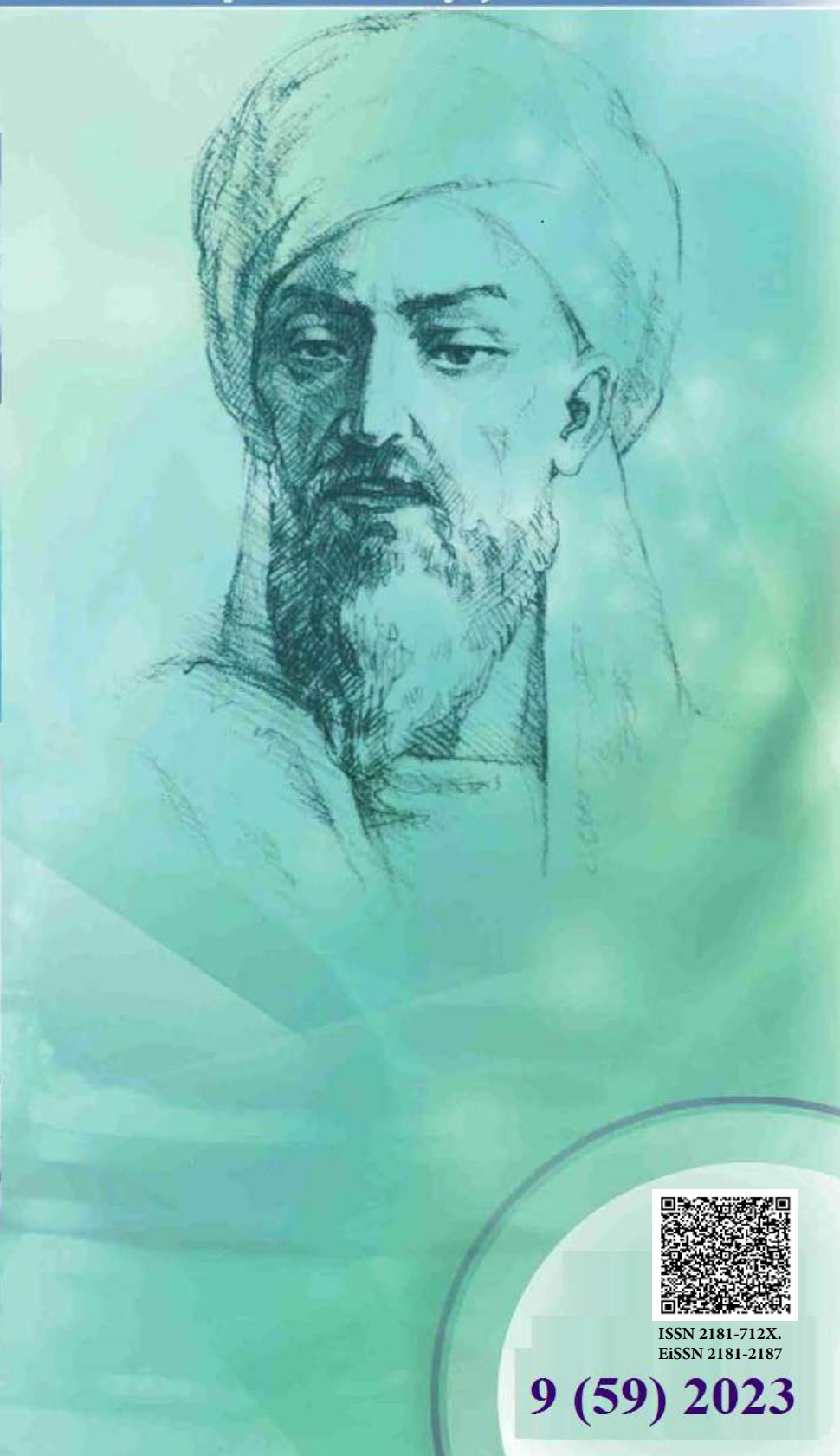
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O‘TKIR VIRUSLI DIARREYADA TURLI PROBIOTIKLARNING SAMARADORLIGI

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Respublika ixtisoslashtirilgan epidemiologiya, mikrobiologiya yuqumli va parazitlar kasalliklar ilmiy-amaliy tibbiyot markazi, 100070, Ozbekiston, Toshkent sh., Uchtepa tumani, Zakovat ko'chasi, 2-uy. г.Ташкент, 998 (71) 243-36-05

✓ *Rezume*

Tadqiqotning maqsadi virus etiologiyali o'tkir ichak infeksiyasi bilan kasallangan bolalarda turli probiyotiklarning klinik samaradorligini qiyosiy baholash bo'ldi. Tadqiqotga o'tkir diareya bilan kasallangan bolalar olindi va 6 hil probiyotiklarning samaradorligi baholandi. Tadqiqot guruhlaridagi natijalar o'rtasidagi katta farqqa qaramasdan, deyarli barcha preparatlar diareyani kamaytirishda probiyotiklarning foydali ta'siri va klassik probiyotiklarni qabul qilgan bolalarda bakterial bo'lmagan probiyotiklarga nisbatan diareya sindromini kamaytirish uchun ko'proq vaqt kerak bo'lishini ko'rsatdi.

Kalit so'zlar: o'tkir ichak infeksiyasi, virusli diareya, bolalar, probiyotiklar

EFFECTIVENESS OF DIFFERENT PROBIOTICS IN ACUTE VIRAL DIARRHEA

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✓ *Resume*

The purpose of the study was to compare the clinical effectiveness of different probiotics in children with acute intestinal infection of viral etiology. Children with acute diarrhea were included in the study and the effectiveness of 6 probiotics was evaluated. Despite the large difference between the results in the study groups, almost all preparations showed a beneficial effect of probiotics in reducing diarrhea, and it took longer to reduce the diarrhea syndrome in children who received classical probiotics compared to non-bacterial probiotics.

Keywords: acute intestinal infection, viral diarrhea, children, probiotics

ЭФФЕКТИВНОСТЬ РАЗЛИЧНЫХ ПРОБИОТИКОВ ПРИ ОСТРОЙ ВИРУСНОЙ ДИАРЕЕ

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✓ Резюме

Целью исследования являлось сравнить клиническую эффективность различных пробиотиков у детей с острой кишечной инфекцией вирусной этиологии. В исследование были включены дети с острой диареей и оценена эффективность 6 пробиотиков. Несмотря на большую разницу между результатами в исследуемых группах, практически все препараты показали благоприятный эффект пробиотиков в уменьшении диареи, а уменьшение диарейного синдрома у детей, получавших классические пробиотики, заняло больше времени по сравнению с небактериальными пробиотиками.

Ключевые слова: острая кишечная инфекция, вирусная диарея, дети, пробиотики

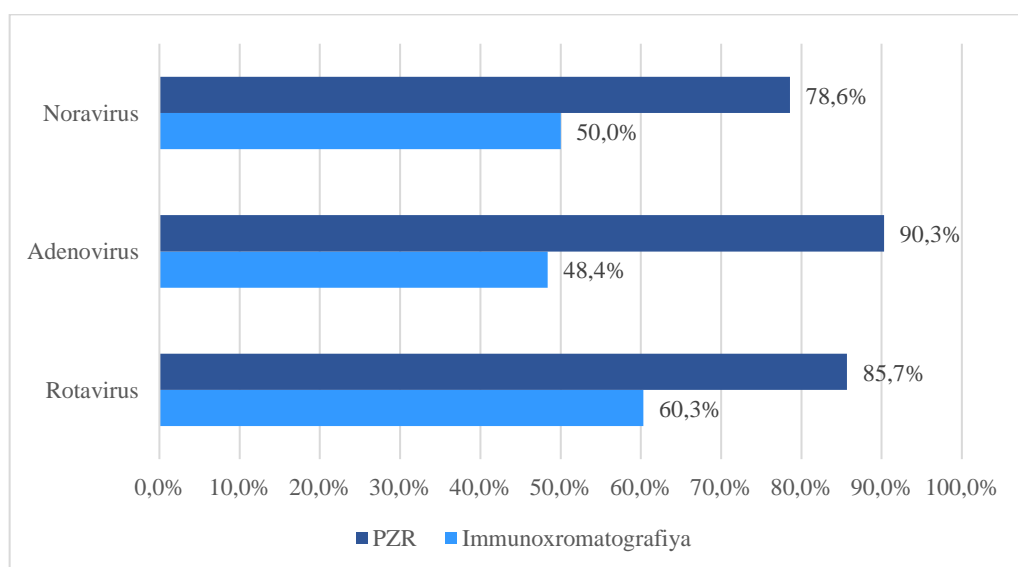
Dolzarbligi

Волалик davrida o'tkir ichak infeksiyalarini (OII) davolashni optimallashtirish masalalari o'z dolzarbligini yo'qotmaydi [1]. O'tkir yuqumli diareyada terapevtik vositalar sifatida probiyotiklarning samaradorligini tasdiqlovchi ko'plab klinik tadqiqotlar va meta-tahlillarning juda ko'p natijalari mavjud [2-4]. Probiyotiklarni qo'llash diareya davomiyligini o'rtacha 1 kunga qisqartirishga imkon berdi, bunda kasallikning qo'zg'atuvchisi va og'irligidan, ishlatiladigan dorilarning shtammlari va dozalaridan, shuningdek, tadqiqotlar o'tkaziladigan joy – rivojlanayotgan yoki iqtisodiy rivojlangan mamlakatlar bo'lishidan qat'i nazar [2]. Shu bilan birga, probiyotiklar erta buyurilganda (<48 soat) ularning terapevtik ta'siri maksimal bo'lgan [5]. Probiyotikni tayinlashda shuni esda tutish kerakki, mikrobiota tarkibining buzilishi bilan bog'liq barcha kasalliklarni davolash va oldini olish uchun samarali bo'lgan universal bakteriyalar shtammi yo'q, shuning uchun nozologiyaga qarab probiyotik shtammini tanlash muhimdir [6].

Tadqiqot maqsadi. Virus etiologiyali o'tkir ichak infeksiyasi (AII) bilan kasallangan bolalarda turli probiyotiklarning klinik samaradorligini qiyosiy baholash.

Material va usullar

Tadqiqot Respublika ixtisoslashtirilgan epidemiologiya, mikrobiologiya, yuqumli va parazitarni kasalliklar ilmiy – amaliy tibbiyot markazi klinikasi bazasida 2021-yil avgust oyidan boshlab 2022-yil iyul oyiga qadar o'tkazildi. Bolalar o'tkir ichak infeksiyalari hamda reanimatsiya va intensiv davolash bo'limlarida statsionar davolanayotgan 6 oylikdan 18 yoshgacha bo'lgan har ikki jinsdagi 360 nafar bolalar tekshirildi. Bolalarning O'rtacha yoshi $9,4 \pm 0,8$ yilni tashkil qildi, ular orasida 163 nafar qiz (45,2%) va 197 nafar o'g'il (54,8%) bolalar bo'lgan. Tadqiqot kogort, prospektiv, randomizatsiyalangan, bir nechta taqqoslash guruhlarini bilan o'tkazildi.



1-rasm. Bolalarda virusli diareyalarning etiologik tuzilmasi.

Diareyaning etiologik omilini aniqlash uchun umumiy klinik tadqiqot usullaridan tashqari, bemorlarning najaslari PZR – diagnostikasi, immunoxromatografiya va 3 marotaba bakteriologik tahlil bilan tekshirildi. Laboratoriya tekshiruv natijalariga ko'ra, 165 bolada (45,8%) bakterial infeksiya, virusli diareya (VD) bilan og'riq bolalar 30% ni va protistlar – kriptosporidiyalar aniqlangan bolalar 3,6% ni tashkil qildi. Qolgan 74 nafar (20,6%) bemorda diareya sababi noma'lum bo'lib qoldi (1-rasm).

Kasalxonaga yotqizilgan birinchi kunlarda, laboratoriya usullaridan foydalangan holda, ichak infeksiyalarining patogenlarini aniqlashda, shuningdek, virusli agentlarni aniqlashda PZR – diagnostikasi samaraliroq bo'ldi (1-jadval). Shu bilan birga, rotavirusli diareyani aniqlash darajasi 58,3% (63 bemor), noraviruslar esa deyarli 2 baravar kam uchradi (28,7%) va eng kam hollarda – 13% adenovirus infeksiyasi aniqlandi.

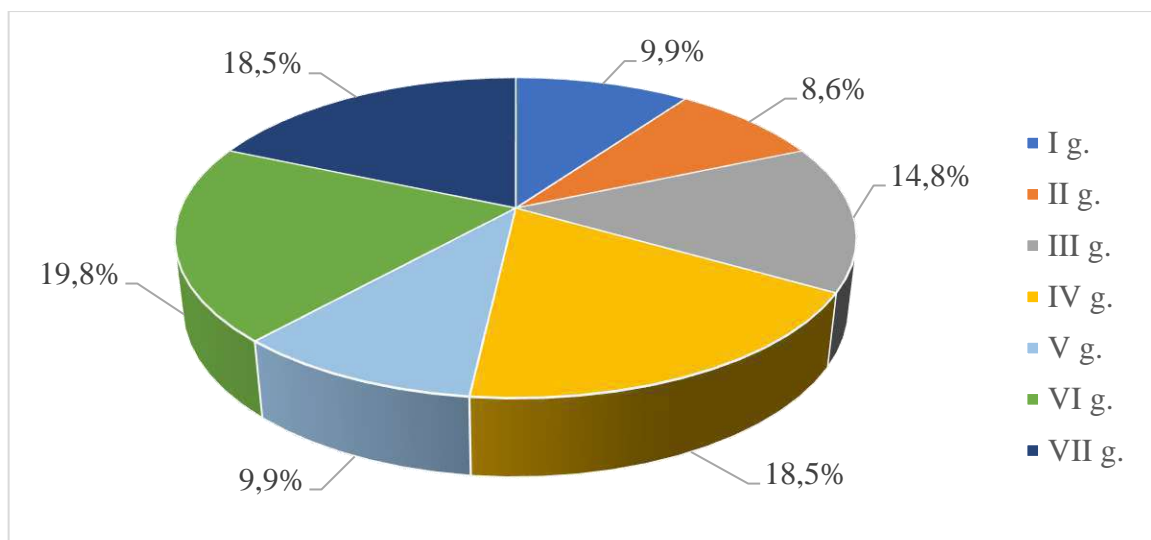
Barcha bolalarga odatitij davo – oral regidratsiya aralashmalari, Sink preparati, zarur holatlarda – parenteral regidratsiya eritmalari va simptomatik vositalar (Drotaverin, Metaklopromid va boshq.) tavsiya etildi. Bundan tashqari, davolash sxemasiga ma'lum bir probiyotik kiritilgan bo'lib, u yoshga qarab belgilanadi. Bir yoki boshqa probiyotikni tayinlash quyidagicha amalga oshirildi:

1) agar bola uyda probiyotik preparati bilan davolangan bo'lsa, xuddi shu preparat bilan davolash davom ettiriladi;

2) agar bola kasalxonaga yotqizilishidan oldin probiyotikni qabul qilmagan bo'lsa, un holda uni qo'llash uchun ko'rsatmalar mavjud bo'lgan taqdirda, probiyotikni tanlash randomizatsiya usuli orqali amalga oshirildi. Va bunda Drag Audit ma'lumotlariga ko'ra O'zbekiston Respublikasida ko'p qo'llaniladigan probiyotiklar yoki tadqiqot vaqtida klinika dorixonasida mavjud bo'lgan dori vositalariga ko'ra buyurildi. Ularga quyidagi tarkibga ega probiyotiklar kirdi:

- *Lactobacillus acidophilus (L.gasseri)*, *Bifidobacterium infantis*, *Enterococcus faecium*;
- *Bacillus clausii* sporalari;
- *Lactobacillus acidophilus*, *Bifidobacterium longum*, *Bifidobacterium bifidum*, *Bifidobacterium infantis*;
- *Saccharomyces boulardii* CNCM I-745;
- *Lactobacillus helveticus*, *Lactococcus lactis ssp.*, *Bifidobacterium longum*, *Lactobacillus rhamnosus*, *Bifidobacterium breve*, *Streptococcus thermophilus*, *Bifidobacterium bifidum*, *Lactobacillus casei*, *Lactobacillus plantarum*;
- *Bifidobacterium longum*, *Propionibacterium avidum 1*, *Lactobacillus acidophilus*, *Lactobacillus bulgaricum*, *Streptococcus diacetilactis*, *Streptococcus thermophilus*.

Bolalarning guruhlar bo'yicha taqsimlanishi 2-rasmda ko'rsatilgan (2-rasm).



2-rasm. Bolalar davolash sxemasidagi probiotikka nisbatan taqsimlanishi.

Shunday qilib, I guruhga quyidagi ko'pkomponentli preparatni qabul qilgan 9,9% bolalar kiritilgan: *Lactobacillus acidophilus*, *Bifidobacterium infantis*, *Enterococcus faecium* (LEK d.d., Sloveniya).

II guruhga *Bacillus clausii* (Opella Healthcare Italia S.R.L., Italiya) shtammlarini o'z ichiga olgan dori buyurilgan bolalar 8,6% ni tashkil etdi.

III guruhga kirgan bolalar 14,8% ni tashkil etdi ular ham ko'pkomponentli probiyotiklarni qabul qilgan: *Lactobacillus acidophilus*, *Bifidobacterium longum*, *Bifidobacterium bifidum*, *Bifidobacterium infantis* (GM Pharmaceuticals Ltd, Gruziya).

IV guruhga *Saccharomyces boulardii CNCM I-745* (BIOCODEX, Fransiya) preparatini qabul qilgan 18,5% bolalar kirgan.

V guruhga 9,9% bolalar kirgan, ularga buyurilgan probiyotiklar tarkibi quyidagicha bo'lgan: *Lactobacillus helveticus*, *Lactococcus lactis ssp.*, *Bifidobacterium longum*, *Lactobacillus rhamnosus*, *Bifidobacterium breve*, *Streptococcus thermophilus*, *Bifidobacterium bifidum*, *Lactobacillus casei*, *Lactobacillus plantarum* (Adipharm LTD, Bolgariya).

VI guruhni 19,8% ni tashkil qildi, ular qabul qilgan preparatning tarkibi quyidagicha bo'lgan: *Bifidobacterium longum*, *Propionibacterium avidum 1*, *Lactobacillus acidophilus*, *Lactobacillus bulgaricum*, *Streptococcus diacetilactis*, *Streptococcus thermophilus* (OOO NATUREX, O'zbekiston).

VII guruh – nazorat guruhini probiyotiklarsiz, faqat an'anaviy terapiya olgan bolalardan iborat edi (18,5%).

Barcha guruhlardagi bolalar yoshi, jinsi va diareya og'irligi bo'yicha taqqoslangan. Shuni ta'kidlash kerakki, bakterial probiyotiklarni tayinlashda antibakterial preparatlar tavsiya etilmagan.

Natija va tahlillar

VD bilan kasallangan barcha tekshirilgan bolalar orasida sutkalik diareya 3-5 marta kuzatilgan bolalar faqat 16% ni tashkil qildi. Kkunlik diareya 5-7 martagacha bo'lganlar ko'pchilikni (45,7%) va 1 sutkada diareyaning soni 7-10 marta kuzatilgan bolalar esa 32,1% ni tashkil qildi. Najasning chastotasi kuniga 10 martadan ko'p bo'lgan bemorlar 6,2% hollarda kuzatilgan.

Preparatni qo'llashdan keyin 3-kundan so'ng VD kompleks terapiyasida probiyotiklarning klinik samaradorligi tahlil qilindi. Bunda asosiy natija etib diareya davomiyligi olindi. Biroq, o'z-o'zidan, bu chora optimal deb hisoblanmaydi. Shu bilan birga, maqsadli daraja (MD) sifatida kuniga 3 marta yoki undan kam suyuq axlat kelishi soni hisoblangan va bu darajaga etgan bolalarning umumiy soni 66,7% ni tashkil etdi. Muayyan probiyotikga qarab kunlik diareya kamaygan bolalar soni haqidagi ma'lumotlar 1-jadvalda keltirilgan (1- jadval).

1-jadval

Virulli diareya bilan og'rigan bolalarda probiyotikga qarab kunlik diareya kamayishi.

Maqsadli darajaga etgan bemorlar soni	Tekshirilgan guruhlar, n=108						
	I	II	III	IV	V	VI	VII
abs	7	16	12	18	7	4	8
%	63,6	76,1	75	90	63,6	44,4	40

Jadvaldan ko'rinib turibdiki, kunlik diareya soni 3 martadan kam bo'lgan bemorlarning katta qismi (90%) IV guruhdagi bemorlardir. II va III guruhlardagi bolalarda diareya sindromining pasayishi mos ravishda 76,1% va 75% bolalarda kuzatildi. I va V guruhlarda diareya bo'yicha MD ga etgan bemorlar soni bir xil - har bir guruhda 63,6%, VI guruhda esa bu ko'rsatkich kamroq bolalarda (44,4%) qayd etilgan. Diareya sindromi kamaygan bemorlarning eng kam soni VII guruhdagi bolalarda qayd etilgan bo'lib, 40% ni tashkil etdi.

Bundan tashqari, probiyotiklarning klinik samaradorligini baholashning yana bir mezoni VD bilan og'rigan bemorlarda klinik simptomlarning o'rtacha davomiyligi bo'lib, natijalari 2-jadvalda ko'rsatilgan, ular orasida kun davomida ich kelish chastotasi eng muhimi hisoblangan (2- jadval).

VD bilan kasallangan bemorlarda diareya sindromining o'rtacha davomiyligi (3-kun baholash).

Klinik simptom	Klinik simptomning o'rtacha davomiyligi, marta/sut						
	I	II	III	IV	V	VI	VII
Diareya	3,3±0,4	4,2±0,5	3,3±0,5*	1,7±0,4*	3,3±0,4	3,9±0,5*	4,1±0,4**

Izoh:

* - solishtirilgan guruhlardagi ko'rsatkichlarning sezilarli farqi - $p < 0,05$

** - solishtirilgan guruhlardagi ko'rsatkichlarning sezilarli farqi - $p < 0,005$

Tadqiqot shuni ko'rsatdiki, IV guruhdagi bemorlarda probiyotikni qabul qilganidan keyin 2-kunida axlat kelish soni sezilarli darajada - kuniga $1,7 \pm 0,4$ martagacha kamaydi ($p < 0,05$). Ehtimol, bu probiyotikning bir qator ijobiy ta'siri, xususan, virusga qarshi faolligi va disaxaridazalarning tiklanishi bilan ifodalangan trofik ta'siri bilan bog'liq bo'lib, buning natijasida virus etiologiyali o'tkir ichak infeksiyalarida kuzatilgan osmotik diareya davomiyligining qisqarishi kuzatildi. I va V guruhlardagi bolalarda najasning chastotasi bir xil bo'lib, kuniga $3,3 \pm 0,4$ martani tashkil etdi va III guruhda bir oz farq kuzatildi, bunda najas chastotasi kuniga $3,3 \pm 0,5$ martani ($p < 0,05$) tashkil etdi. VI guruhda axlat kelish sonining kamayishi kuniga $3,9 \pm 0,5$ martani tashkil etdi. II guruhda najas chastotasining sezilarli darajada yuqori ko'rsatkichlari qayd etildi - kuniga $4,2 \pm 0,5$ martani tashkil etdi. ($p < 0,05$). VII guruhda probiyotiklarni qo'llamasdan an'anaviy davolanagan bolalarda axlat kelish soni sezilarli darajada yuqori bo'lgan - kuniga $4,1 \pm 0,4$ marta ($p < 0,005$).

Shunday qilib, laktobakteriyalar va bifidobakteriyalarni o'z ichiga olgan klassik probiyotiklarni qabul qilganlar guruhlarida diareya sindromini kamaytirish uchun ko'proq vaqt talab etilishi aniqlandi, sababi bu bakteriyalar mukozal proteksiya qobiliyatiga ega emas va shikastlangan ichak shilliq qavatini tiklash uchun qo'shimcha vaqt talab etiladi. Shuningdek, ularning ichak devoriga adgeziya bo'lishi va kolonizatsiyasi uchun vaqt kerak bo'ladi.

Tadqiqot guruhlaridagi natijalar o'rtasidagi katta farq mavjudligiga qaramasdan, deyarli barcha preparatlar diareyani kamaytirishda probiyotiklarning foydali ta'sirini ko'rsatdi va ba'zida bu ta'sir statistik ahamiyatga ega ko'rsatkichlarda bo'ldi. Biroq, bu tahlil uslubiy cheklavlarga ega bo'lgan, jumladan, noaniq yoki etarli darajada taqsimlashni yashirish, ITT tahlilining yo'qligi va boshq. Tadqiqotning cheklavlari orasida tekshirilgan bolalar soni kamligi, diareyani to'xtatishning umumiy qabul qilingan ta'rifining yo'qligi, bolalarning yoshga bog'liq xususiyatlari, VD mono- yoki mikst-infeksiya ko'rinishidagi diareya bo'lganligi va bemorda premorbid fon mavjudligi kiradi.

Xulosa

Tadqiqot shuni ko'rsatdiki, bolalarda VDni davolashda probiyotiklar qo'shilishi diareya davomiyligini qisqartirishi, davolash boshlanganidan 2-kundan boshlab terapevtik ta'sirni oshirishi va kasalxonada davolanish muddatini qisqartirishi mumkin. Shuningdek, eng kop qollaniladigan probiyotik preparatlarning qiyosiy tahlili, preparatda virusli diareya bilan bog'liq bir qator ijobiy ta'sir mexanizmlari mavjudligi bois *Saccharomyces boulardii* CNCM I-745 ning bakterial probiyotiklardan o'z ustunligini namoyish etdi.

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