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WAYS TO CORRECT INTESTINAL DYSBIOSIS IN HIV-INFECTED CHILDREN SUFFERING FROM INFECTIOUS DIARRHEA

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Abstract: In HIV-infected children with increasing severity of acute diarrhea, a significant increase in severe forms of intestinal dysbacteriosis was observed. In such cases, complex treatment and an individualized approach are necessary. Among the probiotic preparations included in the complex treatment, Lactobacillus rhamnosus, Saccharomyces boulardii, and Bacillus clausii demonstrated high effectiveness in alleviating dehydration. The effect of Bacillus cereus and Bifidobacterium bifidum was limited in some cases, and no significant differences were observed in the main group. The obtained results indicate the need for an individualized approach to selecting probiotics for the treatment of diarrhea.

Key words: HIV infection, children, diarrhea, probiotics

Relevance of the problem. It is known that the total number of microorganisms living in human intestines (1014) is twice the total number of cells in the body. Close interaction between the microbiome and the mucous membrane is the most crucial condition for intestinal homeostasis. Changes in the microbiome (dysbiosis) are associated not only with various intestinal diseases but also with multi-organ pathologies, including HIV infection [1, 7]. This opens up prospects for influencing the infectious process by correcting dysbiotic changes in the intestines of people infected with HIV [3, 8].

In HIV-infected patients, probiotics can have beneficial effects by restoring the balance of beneficial and pathogenic microflora present on the surface of the intestinal mucosa, as well as by improving the function of the epithelial barrier, increasing CD4 count, enhancing immune translation, reducing bacterial permeability, and alleviating signs of infection. There is evidence that the beneficial effects of probiotics are strain-dependent, and not all treatment methods are equally effective. One of the approaches used to maintain beneficial microflora in the gastrointestinal tract under various conditions is the use of probiotics [4, 6]. The use of *Lactobacillus rhamnosus GG* in the treatment and prevention of gastrointestinal pathology in children is justified by its immunological and antimicrobial properties [2, 10]. A placebo-controlled study evaluated the effectiveness of *Lactobacillus rhamnosus* in relation to intestinal symptoms in HIV-infected individuals. This probiotic had a significant effect on reducing the daily frequency of diarrhea and improving stool consistency. However, it did not have a positive effect on HIV RNA copies and CD4+ cell counts in the blood, which remained stable throughout the entire course of treatment [5]

Bifidobacterium bifidum in combination with thermophilic streptococcus demonstrates a positive effect when used for 2 months in HIV-infected children compared to 40 HIV-infected children who received a placebo. This is manifested by an increase in the number of CD4+ cells and a decrease in the level of bacterial DNA in the bloodstream of people with HIV [9].

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Research objective: To conduct a comparative analysis of various therapeutic approaches and identify effective methods for balancing the intestinal microbiome in HIV-infected children with infectious diarrhea.

Research Materials and Methods. The study was conducted from 2020 to 2025 at the Specialized Infectious Diseases Clinic of the Republican AIDS Center and the "HIV Infection" Department of the Research Institute of Virology under the Scientific and Practical Medical Center for Epidemiology, Microbiology, Infectious and Parasitic Diseases of the Ministry of Health of the Republic of Uzbekistan. It involved the examination of 499 children aged 3 to 18 years with HIV infection and acute diarrhea. The study subjects were divided into two groups: Group 1 consisted of 261 HIV-infected children with acute infectious diarrhea, while Group 2 comprised 247 children with acute diarrhea without HIV infection. The diagnosis of "HIV infection" in children was established based on the Order No. 270 dated 19.08.2023 "On protocols for the prevention and treatment of human immunodeficiency virus infection" and Order No. 122 dated 25.03.2015 "On improving measures to combat typhoid fever, paratyphoid fever, salmonellosis, and acute intestinal diseases among the population of the republic" issued by the Ministry of Health of the Republic of Uzbekistan.

Feces were used as the material for studying intestinal dysbiosis. The study isolated genes of bifidobacteria, lactobacilli, typical and lactose-negative *Escherichia* coli, opportunistic and pathogenic enterobacteria, non-fermenting gram-positive bacteria, staphylococci, hemolytic forms of microorganisms, enterococcus-like fungi, and yeasts. Identification of anaerobic microorganisms, opportunistic and pathogenic enterobacteria was carried out on the VITEK 2 Compact device using identification cards: ANC (244147910), GN (bioMerieux France). Fecal examination included bacteriological method and polymerase chain reaction (PCR) with determination of nucleic acids *of Campylobacter spp., Salmonella spp., Shigella spp., Escherichia coli, Y. pseudotuberculosis, Y. enterocolitica, Norovirus, Adenovirus, Astrovirus, Rotavirus.* The study was conducted using Xpect *Clostridium difficile* Toxin A/B (Oxoid) test systems. Data processing was carried out using *Excel* computer programs with parametric and non-parametric statistical methods. The significance of differences was determined by calculating the Chi-square and standard error at $P<0.05$.

Research results and their discussion. The criteria for determining the severity of acute diarrhea in HIV-infected children are the daily frequency of diarrhea, duration of diarrhea, stool volume, consistency, presence of pathological elements, degree of dehydration, and signs of intoxication.

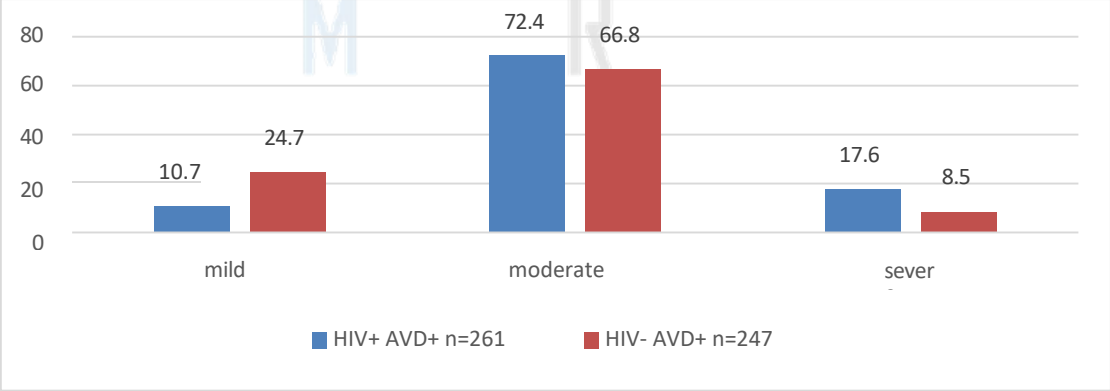

Figure 1. Severity levels of acute diarrhea in HIV-infected children.

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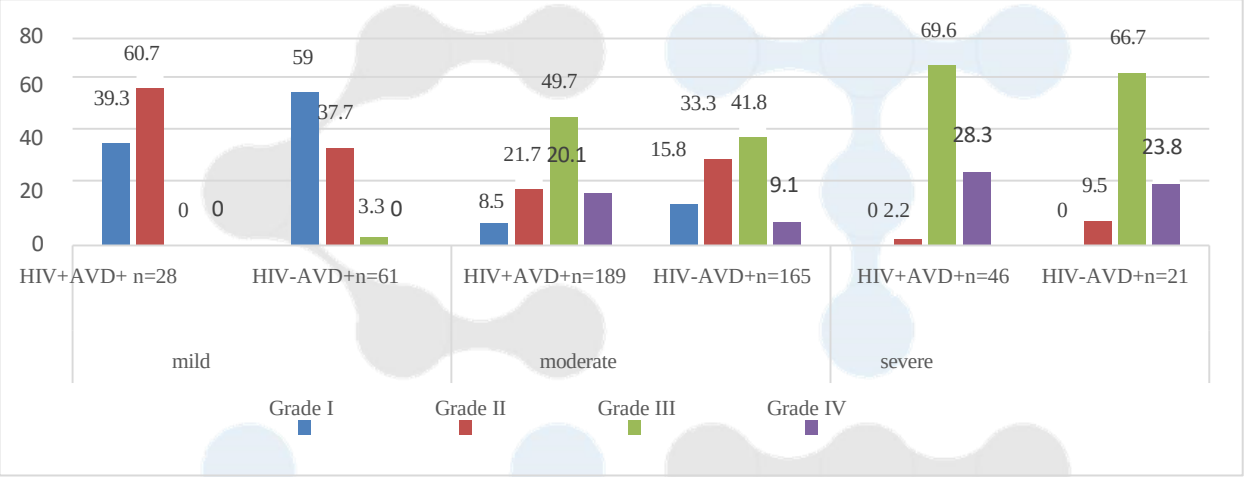
In children of the main group, mild diarrhea was observed 2.3 times less frequently than in the comparison group, while severe cases were recorded 2.1 times more often (10.7% and 24.7% vs. 17.6% and 8.5% respectively, P<0.05). However, no significant difference was found between the groups in terms of moderate severity (P>0.05).

Figure 2. Degrees of intestinal dysbiosis according to severity levels of acute diarrhea in HIV-infected children.

In the mild course of acute diarrhea, grade I intestinal dysbiosis was observed 1.5 times less frequently in children of the main group, while grade II was noted 1.6 times more often (39.3%;



59% and 60.7%; 37.7% of cases, respectively, P<0.05). Intestinal dysbiosis of grades III and IV was not observed. In the moderate course of acute diarrhea, grade I intestinal dysbiosis was noted in children of the main group 1.9 times less often than in the comparison groups, and grade II 1.5 times less frequently (8.5%; 15.8% and 21.7%; 33.3% of cases, respectively, P<0.05). Although no significant difference was found in the indicators of grade III intestinal dysbiosis between children of the main and comparison groups (P>0.05), significant differences in grade IV intestinal dysbiosis were 2.2 times more frequent (20.1% and 9.1% of cases, respectively, P<0.05). Grade I intestinal dysbiosis was not observed in children of either group with severe acute diarrhea, but grade II was detected in one (2.2%) patient in the main group and in 2 (9.5%) patients in the comparison group (P<0.05). In children of the main group, grade III intestinal dysbiosis developed 1.6 times less often, while grade IV intestinal dysbiosis developed 2.4 times more frequently (41.3%; 66.7% and 56.5%; 23.8% of cases, respectively, P<0.05).

To treat dysbiotic changes detected in HIV-infected children with acute infectious diarrhea, we used several probiotics for comparative coordination in the complex treatment plan. Among them, ***Lactobacillus rhamnosus***-containing combined drug Metaflora, *Bifidobacterium infantis, Lactobacillus acidophilus, Bifidobacterium breve, Streptococcus thermophilus, Lactobacillus casei, Lactobacillus bulgaricus;* ***Saccharomyces boulardii*** (Enterol), ***Bacillus cereus*** (Baktrimsubtil), ***Bacillus clausii*** (Enterojermina) and ***Bifidobacterium bifidum*** medications were given as 1 capsule twice a day for 5 days.

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Table 1.

Medications used in the treatment of dysbiotic changes identified in HIV-infected children with acute infectious diarrhea.

Medication	Main group HIV+ AVD+ n=145	Comparison group HIV- AVD+ n=200
	Abs.	Abs.
Lactobacillus rhamnosus	28	27
Saccharomyces boulardii	32	38
Bacillus clausii	26	45
Bacillus cereus	24	35
Bifidobacterium bifidum	35	55

The effectiveness of treatment after 5 days was assessed by the degree of dehydration, the daily number and duration of diarrhea, stool consistency, and the presence of pathological elements.

Lactobacillus rhamnosus After administration of the drug, the disappearance of dehydration symptoms was observed in 89.3% of children in the main group, which is 1.8 times higher compared to pre-treatment indicators. In the comparison group, this indicator was almost 2 times higher, representing significantly more cases. Moderate dehydration persisted in 3 children of the main group and only in one child of the comparison group, which was significantly different from the pre-treatment indicators (40%; 10.7% and 42.5%; 3.7% of cases respectively, P<0.05). Severe dehydration was not detected in either group when this drug was used.

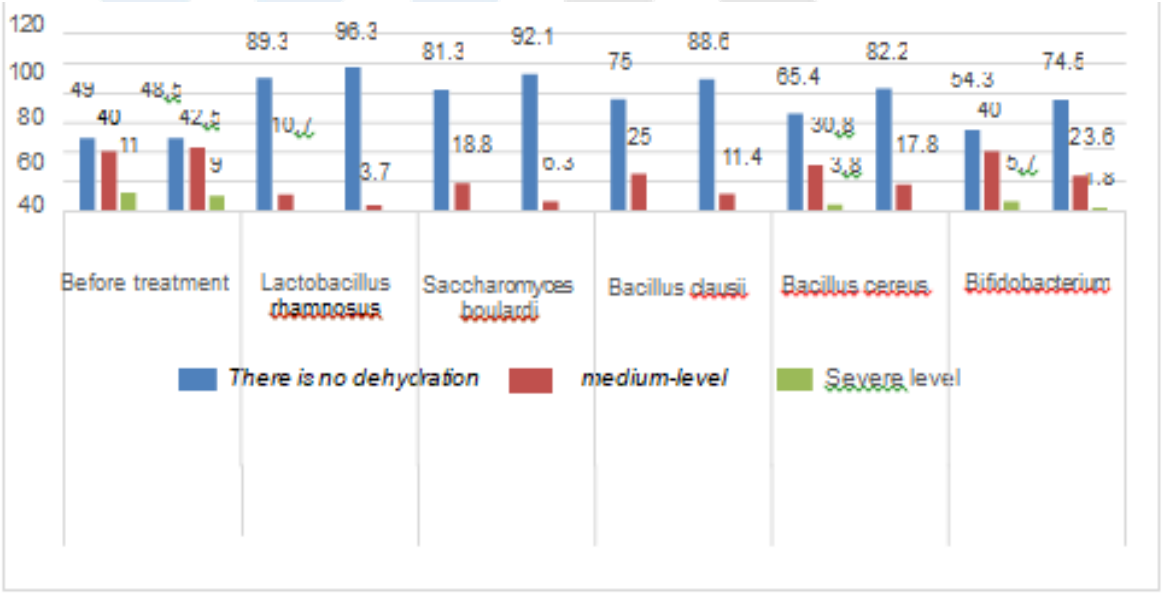

Figure 3. The effect of various probiotic drugs used in the treatment of acute diarrhea in HIV-infected children on the degree of dehydration.

Saccharomyces boulardii After administration of the drug, the disappearance of dehydration symptoms was observed in 81.3% of patients in the main group and 92.1% in the comparison group, which was 1.7 times and 1.9 times significantly more frequent compared to pre-treatment

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indicators (P<0.05). After treatment, moderate dehydration persisted in almost 1/5 (18.8%) of the main group and only in 3 patients (6.3%) of the comparison group (P<0.05). *Saccharomyces boulardii* When using this drug, severe dehydration was not observed in patients of either group.

After the administration *of Bacillus clausii*, the significant difference between pre- and post-treatment indicators was 1.5 times in children of the main group, while it was 1.8 times in the comparison group. In children of the main group, moderate dehydration after treatment was observed 1.6 times less frequently than before treatment, whereas in the comparison group, it was 3.7 times less frequent. Severe dehydration was not observed when this drug was used as part of a complex treatment plan.

In the main group of children receiving *Bacillus cereus,* signs of dehydration disappeared in 65.4% and moderate dehydration was detected in 30.8%, with no significant differences observed compared to pre-treatment indicators (P>0.05). In the comparison group, this difference was 1.7 times and 2.4 times greater, respectively (P<0.05). Only one child in the main group maintained a severe degree of dehydration, while in children of the comparison group, severe dehydration was not noted after taking *Bacillus cereus.*

There were practically no differences in the indicators of dehydration symptom resolution and moderate dehydration between the main group of patients receiving *Bifidobacterium bifidum* in the complex treatment plan (P>0.05), while differences in both degrees of dehydration in children of the comparison group were almost 1.5 times and 1.8 times less frequent (P<0.05). The difference between the indicators of severe dehydration before and after treatment was 1.8 times lower in children of the main group and 5 times significantly lower in children of the comparison group (P<0.05).

Conclusions:

1. The results of the study showed that in children with HIV infection, severe acute infectious diarrhea was recorded 2.1 times more often, and mild cases 2.3 times less often than in the comparison group (P<0.05).
2. With an increase in the severity of acute diarrhea in HIV-infected children, a significant increase in severe forms of intestinal dysbiosis was observed. In this case, complex treatment and an individual approach are required.
3. Among probiotic drugs during complex treatment, ***Lactobacillus rhamnosus, Saccharomyces boulardii*** *and* ***Bacillus clausii*** showed high effectiveness in eliminating dehydration. The effects of ***Bacillus cereus*** and ***Bifidobacterium bifidum*** were limited in some cases, and no significant differences were noted in the main group. These results indicate that diarrhea treatment requires an individualized approach to probiotic selection.

References:

1. Горобченко Е. Н. Коррекция бактериальными препаратами дисбиотических изменений кишечника ВИЧ-инфицированных / Е. Н. Горобченко, А. Г. Дьяченко, Е. М. Савинова, Т. В. Майстат // Туберкульоз, легеневі хвороби, ВІЛ-інфекція. - 2016. - № 3. - С. 58-63.
2. Захарова И.Н., Борзова Е.Ю., Симакова М.А. *Lactobacillus rhamnosus GG:* опыт применения в детской гастроэнтерологической практике. *Российский вестник перинатологии и педиатрии*. 2019;64(6):20-29. https://doi.org/10.21508/1027-4065-2019-64-6-20-29
3. Холодов А.А., Брюхачева Е.О., Примкулова М.В., Лавряшина М.Б., Пьянзова Т.В. Клиническая эффективность применения комплексной пробиотической терапии при наличии

синдрома кишечной диспепсии у больных туберкулезом с множественной лекарственной устойчивостью в сочетании с ВИЧ-инфекцией. Туберкулез и болезни легких. 2022;100(7):34-40. https://doi.org/10.21292/2075-1230-2022-100-7-34-40

4. Хрянин А.А., Пушкарёв Е.В., Бочарова В.К. ВИЧ-инфекция и микробиом кишечника. ВИЧ-инфекция и иммуносупрессии. 2023;15(4):25-35. https://doi.org/10.22328/2077-9828-2023-15-4-25-35
5. Carter GM, Esmaeili A, Shah H, Indyk D, Johnson M, Andreae M, Sacks HS. Probiotics in Human Immunodeficiency Virus Infection: A Systematic Review and Evidence Synthesis of Benefits and Risks. Open Forum Infect Dis. 2016 Jul 29;3(4):ofw164. doi: 10.1093/ofid/ofw164. PMID: 27747250; PMCID: PMC5063545.
6. D'Angelo C, Reale M, Costantini E. Microbiota and Probiotics in Health and HIV Infection. Nutrients. 2017 Jun 16;9(6):615. doi: 10.3390/nu9060615. PMID: 28621726; PMCID: PMC5490594.
7. Harper A, Vijayakumar V, Ouwehand AC, Ter Haar J, Obis D, Espadaler J, Binda S, Desiraju S, Day R. Viral Infections, the Microbiome, and Probiotics. Front Cell Infect Microbiol. 2021 Feb 12;10:596166. doi: 10.3389/fcimb.2020.596166. PMID: 33643929; PMCID: PMC7907522.
8. Reikvam DH, Meyer-Myklestad MH, Trøseid M, Stiksrud B. Probiotics to manage inflammation in HIV infection. Curr Opin Infect Dis. 2020 Feb;33(1):34-43. doi: 10.1097/QCO.0000000000000612. PMID: 31789692.
9. Sachdeva M, Sra HK, Agarwal A, Chauhan A, Pradhan P, Singh M, Singh M. Effect of Probiotics on the Frequency of CD4+ T-Cells in HIV-Infected Children and Adolescents: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Trop Pediatr. 2022 Feb 3;68(2):fmac006. doi: 10.1093/tropej/fmac006. PMID: 35137236.
10. Wilson NL, Moneyham LD, Alexandrov AW. A systematic review of probiotics as a potential intervention to restore gut health in HIV infection. J Assoc Nurses AIDS Care. 2013 Mar-Apr;24(2):98-111. doi: 10.1016/j.jana.2012.04.004. Epub 2012 Jul 31. PMID: 22853885.
11. Отажанов, Ш. З., Худайцулова, Г. К., & Муминова, М. Т. (2019). THE COURSE OF DIARRHEA OF VIRAL ETIOLOGY IN HIV INFECTED CHILDREN. *Новый день в медицине*, (4), 252-255.
12. Туйчиев Лазаз Нодирович, Худайкулова Гульнара Каримовна, Рахматуллаева Шахноза Бахадировна, & Муминова Махбуба Тешаевна (2023). СРАВНИТЕЛЬНЫЙ АНАЛИЗ КЛИНИКИ И ТЕЧЕНИЯ ОСТРЫХ ДИАРЕЙ У ДЕТЕЙ ПРИ ВИЧ-ИНФЕКЦИИ. Детские инфекции, 22 (2 (83)), 34-38.
13. Муминова, М. Т., Ильясова, М. М., & Рахматуллаева, Ш. Б. (2023). ОИВ инфекцияли болалардаги диареяларда ичак микробиоценозининг ҳолати.
14. Муминова, М. Т., Рахматуллаева, Ш. Б., & Садиков, Х. М. А. (2023). *ОИВ-инфекцияли болаларда диарея синдромини даволаш самарадорлиги* (Doctoral dissertation, Doctoral dissertation).
15. Муминова, М. Т., & Маматмусаева, Ф. Ш. Ўткир диареяли ОИВ зарарланган болаларда ичакнинг факультатив микрофлорасига Sachoromyces bouiladinинг таъсири. *Инфекция, иммунитет и фармокология2022*, 147-155.

ISSN: 2582-4686 SJIF 2021-3.261, 2022-2.889, 2023-5.384, 2024-6.875 ResearchBib IF: 9.948 / 2024

16. Туйчиев, Л. Н., Худайкулова, Г. К., & Муминова, М. Т. (2024). Опыт практического применения энтеросорбентов при лечении ВИЧ-инфицированных детей с синдромом диареи. *ВИЧ-инфекция и иммуносупрессии*, *16*(2), 100-105.
17. Худайкулова Гулнара Каримовна, Муминова Махбуба Тешаевна, & Отажанов Шамсиддин Зарифбаевич (2021). АНАЛИЗ ЭТИОЛОГИЧЕСКОЙ СТРУКТУРЫ ВИРУСНЫХ ДИАРЕЙ У ВИЧ-ИНФИЦИРОВАННЫХ ДЕТЕЙ. Journal of cardiorespiratory research, 2 (3), 31-34. doi: 10.26739/2181