THE USAGE OF PROBIOTICS ENTEROL IN COMBINED THERAPY OF COLON MICROBIOCENOSIS IN CHILDREN WITH TYPE 1 DIABETES MELLITUS

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Abstract*. The article presents the results of studying the efficacy of probiotic Enterol in the complex therapy of patients with intestinal microbiocenosis type 1 diabetes mellitus. To accomplish the results of clinical and bacteriological examination of 33 children with type 1 diabetes aged 10 to 18 years.*

Aim. The purpose of the study was to study the use of the probiotic enterol in the complex therapy of intestinal microbiocenosis disorders in order to correct the intestinal microbiome in patients with type 1 diabetes mellitus.

Materials and methods. To accomplish the results of clinical and bacteriological examination of 33 children with type 1 diabetes aged 10 to 18 years. The analysis of the effectiveness of probiotic Enterol in the complex therapy of patients with intestinal microbiocenosis type 1 diabetes. The control group consisted of 30 healthy individuals.

Conclusions. Conducts bacteriological analysis of the intestinal microflora. All of the surveyed children with type 1 diabetes, in the intestinal microflora are disbiotic changes. The results indicate the feasibility of active correction dysbiotic changes in diabetes mellitus type 1 enzyme preparations such as enterol.

Keywords*: probiotic enterol, type 1 diabetes mellitus, intestinal microbiocenosis.*

Recently, there has been a significant increase in the incidence of diabetes mellitus (DM) in all highly developed countries. Despite the successes in the diagnosis and treatment of diabetes mellitus, a number of unresolved issues remain. Various clinical manifestations associated with gastrointestinal tract disorders are quite common (up to 70%) in patients with DM [1,3]. In type 1 diabetes mellitus, patients often experience latent or asymptomatic chronic diseases of the stomach and duodenum. Complaints from patients with DM regarding the digestive organs often have a dyspeptic nature and are not dominant [1]. Some gastroenterologists attribute significant importance in the pathogenesis of gastrointestinal tract (GIT) lesions in patients with diabetes mellitus to changes in intestinal microbiocenosis, which provides a basis for further studying the role of intestinal microflora in the development and course of type 1 diabetes [2,4]. The intestinal microbiota is a complex association of microorganisms that mutually influence their vitality and are in constant interaction with the macroorganism.

One of the most important functions of normal intestinal flora is its direct involvement in the formation of the body's immunological reactivity. Type 1 diabetes is a disease for which a complete cure is currently not possible. Due to the increasing incidence of type 1 diabetes, its "rejuvenation," and its significant social importance, the task of studying factors exacerbating the course of this disease and finding ways to combat them comes to the forefront, as this disease leads to disability in many patients during the most active period of their lives. Various pathological

changes have been noted by many researchers in patients with type 1 diabetes affecting the kidneys, liver, stomach, and multiple disorders in the function and morphology of the intestines [2]. It is not always easy to determine the causes of diarrhea in patients with diabetes mellitus. It is characteristic that many patients suffering from this disease are prone to constipation, which is explained by the development of intestinal pseudo-obstruction syndrome in diabetes due to progressive diabetic neuropathy. At the same time, diarrhea is detected in 20% of patients in the clinical picture of the disease. Diarrhea is more common in type 1 diabetes mellitus, predominantly in middle-aged individuals, and more often in men than in women. Usually, diarrhea is a late symptom of diabetes mellitus. Diarrhea often occurs at night, is often profuse, and is not always accompanied by pain. The stool becomes watery, and steatorrhea may occasionally occur. Diarrhea may be intermittent, sometimes alternating with constipation, and in some cases may last for weeks and months, proving refractory to the administration of antidiarrheal drugs. The mechanism of diarrhea and steatorrhea development in diabetes may be due to concomitant exocrine insufficiency of the pancreas or celiac disease. The features of nutrition in patients with diabetes mellitus, particularly the intake of sugar substitutes such as xylitol and sorbitol acting as osmotic laxatives, also have certain significance. However, diarrhea syndrome in patients with diabetes mellitus often develops because of diabetic neuropathy [1]. This may be indicated by the presence of other signs of this complication in the clinical picture of the disease, such as bladder dysfunction and fecal incontinence due to anal sphincter innervation disorders, which create serious problems for the patient up to social isolation. Intestinal motility disorders contribute to bacterial overgrowth in the small intestine, which in itself can be an important cause of diarrhea. Hormonal regulation disorders observed in patients with diabetes mellitus also play an additional role. The treatment of diarrhea in diabetes is primarily aimed at comprehensive correction of carbohydrate metabolism. Symptomatic therapy involves normalizing intestinal motility using enzyme preparations and antibacterial agents when necessary.

From modern perspectives, the normal human microbiota is considered to be a balanced ecosystem characterized by a specific composition occupying various biological niches. This microbiota includes over 500 species of bacteria, with a total number reaching 1014, exceeding the number of human body cells. The evolutionarily developed symbiosis of the intestinal microbiota is in a state of biological equilibrium with human body cells but is subject to frequent disruptions due to unfavorable factors in the external and internal environments.

Disorders in the qualitative and quantitative composition of the symbiotic microflora, as formulated by A.F. Bilbilin, are associated with "the manifestation of adaptation failure, disruption of protective and compensatory adaptations of the body," which serve as the triggering mechanism for disturbances in metabolic processes, development of allergic reactions, and the onset of various somatic diseases.

The idea of correcting the internal environment of the human body through targeted changes in the composition of the microbiota belongs to the founder of domestic and world microbiology, Nobel laureate I.I. Mechnikov (1908). It was he who discovered: "Numerous diverse associations of microorganisms inhabiting the human digestive tract significantly determine the mental and physical health of a person." His proposed method of enteral administration of live cultures of lactic acid bacteria as antagonists of putrefactive microbes laid the foundation for modern work on the creation of biopreparation. Lactobacillin by I.I. Mechnikov

was acidified milk produced as a result of the activity of cultures of the Lactobacillus bulgaricus and lactic streptococcus isolated from yogurt.

An actual direction in modern medicine is the use of means to correct intestinal microbiota (probiotics, prebiotics, synbiotics) for treating many diseases and pathological conditions of the human body. The groups of drugs of the probiotic and prebiotic series used are diverse; therefore, it is advisable to use the most studied agents with proven clinical effectiveness. One such probiotic drug is "Enterol" [5]. Enterol (France) contains the lyophilized biomass of a dry culture of a special strain of Saccharomyces boulardii yeast, supplemented with lactose and sucrose, available in hard gelatin capsules or packaged in sachets. One dose contains 1 billion live microbial cells resistant to antibiotics. Its use is indicated for the treatment and prevention of intestinal dysfunction caused by antibiotic therapy, treating of acute intestinal infections, preventing tube feeding-associated diarrhea, treating of irritable bowel syndrome, etc. The advantage of this drug is the rapid onset of antidiarrheal effect (10-20 minutes) and the permissibility of simultaneous use with antibiotics.

The aim of our study was to investigate the use of the probiotic Enterol in the complex therapy of intestinal microbiota disorders aiming at correcting the intestinal microbiome in patients with type 1 diabetes.

Materials and methods of the study. This study presents the results of clinical and bacteriological examination of 33 children with type 1 diabetes, aged 4–18 years, under the observation of endocrinologists. The control group consisted of 30 practically healthy individuals. The diagnosis of type 1 diabetes was verified based on clinical signs of periodic hyperglycemia (increased thirst, polyuria, episodes of dry mouth), anamnestic data (previous episodes of ketoacidosis or ketoacidotic coma, absolute dependence on insulin therapy, early established clinical diagnosis of type 1 diabetes).

The microbiota of the large intestine was studied according to the methodological recommendations of Kasatkin E.P. et al. (1996). The state of the intestinal microbiota and the severity of dysbiotic shifts were assessed according to the generally accepted criteria for dividing intestinal microbiota disorders [4]. The results of the study were processed using parametric statistical methods with the Excel package adapted for medico-biological research.

Results and Discussion. When studying intestinal microbiota disorders in all children with type 1 diabetes, changes in the composition of the intestinal flora of pronounced or moderate nature were identified. Only 5 (15.2%) patients had minor dysbiotic deviations. In the slow-progressing stages of type 1 diabetes, regardless of the clinical stage of the disease, minor dysbiotic changes were noted.

In the analysis of the quantitative and qualitative composition of the intestinal microbiota in children with type 1 diabetes, a significant decrease in bifidobacteria was found, by 7.45±0.15 lg CFU/g ($P<0.001$), similar changes were observed with lactobacilli, which also affected the total number of anaerobes. The detected deficit of anaerobes also affected the aerobic part of the intestinal microbiota. The most characteristic was the decrease in the number of lactose-positive Escherichia coli to 7.39±0.015 lg CFU/g against a sharp increase in the content of lactose-negative Escherichia coli, enterobacteria, staphylococci, Candida fungi, especially Protein.

The effectiveness of complex treatment of dysbiotic changes using the probiotic Enterol in children with type 1 diabetes was evaluated based on the results of bacteriological analysis. The data of bacteriological examination of the intestines of children with type 1 diabetes, presented in

Table 1, convincingly indicate that a single course of complex treatment led to the correction of the intestinal bacteriocenosis, bringing it to almost normal levels.

Thus, a significant increase in the number of bifidobacteria was noted, and the content of lactobacilli slightly increased, although initially their quantity was reduced but not as significantly as that of bifidobacteria. In all children with type 1 diabetes, the frequency of isolation of lactose-positive Escherichia coli increased, and, importantly, the percentage of hemolytic Escherichia coli decreased among them: before treatment, it was 30%, and after treatment, it was 8% (with a norm of 2%).

Table 1.

The state of intestinal microbiocenosis disorders in children with type 1 diabetes after treatment with the probiotic Enterol (n = 33)

Species of microorganisms	Number of Microbial Cells per 1 g of Feces (Mm) (in lg dilutions)		
	Practically healthy children, n=30	Before the treatment	After the course of treatment
Bifidobacteria	At least 9	7,45± 0,15	9,9± 0,3*
Lactobacilli	At least 7	5,9± 0,3	7,1 ±0,4*
Escherichia coli:			
lactose-positive	At least 8	6,1 ±0,1	7,39± 0,015*
hemolytic	2%	30%	8%
Staphylococcus aureus	No more than 4	5,2 ±0,8	3,7± 0,5*
Clostridia	No more than 5	5,8 ±0,6	4,5± 0,7
Yeast-like fungi	No more than 3	5,9± 0,5	4,2± 0,3*
Enterococci	No more than 5	5,1 ±0,1	3,5± 0,6*
Other enterobacteria	No more than 5	10,7 ±1,2	5,1± 0,4*
Gram-negative non-fermenting bacteria	No more than 5	9,2 ±0,5	4,7± 0,8*

*Note: * - $p < 0.05$*

Other representatives of enterobacteria and gram-negative non-fermenting bacteria were observed half as often after the course of treatment. However, it should be noted that although there was a significant decrease in the number of yeast-like fungi after the complex treatment, they nevertheless remained in quantities slightly exceeding the physiological norm.

As a result of treatment, dysbiotic changes in the intestine were observed in 63.64%, and 7 weeks after the start treatment, normal intestinal microbiota was established in 81.82% of the examined children with type 1 diabetes.

Conclusion:

1. All the children we examined with type 1 diabetes exhibited dysbiotic changes in the intestinal flora.

2. The characteristic feature of dysbiotic changes in children with type 1 diabetes was considered to be a decrease in the number of anaerobes and an increase in the quantity of

conditionally pathogenic flora, lactose-negative Escherichia coli, especially Candida fungi and Protei.

3. The obtained results indicate the expediency of active correction of dysbiotic changes in type 1 diabetes using enzymatic preparations such as Enterol.

REFERENCES

1. Avdeev V.G. Diabetic enteropathy //Pharmateca– No.3 – 2010 – pp.46-49
2. Dorofeev A.E. Intestinal diseases. – Gorlovka: Likhtar, 2010. — 532 p.
3. Kasatkina E.P., Voronin A.A., Taranenko L.A. Bacteriological diagnosis of intestinal dysbiosis in children with diabetes mellitus Method.rec.M1996.
4. Ibragimova L.I., Kolpakova E.A. et al. The role of the gut microbiota in the development of type 1 diabetes mellitus. // Diabetes mellitus, volume 24, No. 1, 2021.
5. Kotowska M., Albrecht P., Szajewska H. Saccharomyces boulardii in the prevention of antibion of antibiotic associated diarrhea in children: randomized double – blind placebo-controlled trial Aliment Pharmacol Ther.2005.Mar1;21(5);583-90.
6. Paun A., Yau C., Danska J.S. (2016). Immune recognition and response to the intestinal microbiome in type 1 diabetes. J. Autoimmun. 71, 10–18