DYSBACTERIOSIS IN CHILDREN

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ANNOTATION

The importance of intestinal microbiocenosis The most complex biotope of microbiocenosis is intestinal cooperation, represented by various populations of microorganisms. Intestinal microbiocenosis is a very important system of the body, performing or regulating its numerous functions to maintain homeostasis.

One of the most important functions of normal microflora is to provide colonization resistance, which prevents the colonization of the body by foreign microbes. With a decrease in colonization resistance, the number and spectrum of pathogenic bacteria increases, and the possibility of developing an infectious process arises.

Interestingly, the colonization ability of microorganisms (in particular, lactobacilli) is strictly specific to a particular individual. Studies on volunteers show that automicroorganisms provide a very rapid restoration of the normal state of intestinal microflora.

Key words: microbiocenosis, dysbacteriosis, children.

The immunomodulatory function of intestinal microflora is well known. The formation of an immune response is formed in the first hours of the neonatal period under the influence of microflora. In the absence of microorganisms, there is a decrease in the depth of the crypts of the intestinal mucosa, a decrease in the height of the villi, a thinning of the lamina propria, and a decrease in Peyer's patches. With their participation, lysozyme and other adjuvant-active compounds are released, which stimulate the body's immune system. Microorganisms carry out physiological and biochemical processes in the gastrointestinal tract (GIT) for the digestion and absorption of food. The metabolism of proteins, carbohydrates, fats, the production of vitamins, hormones, and a number of biological amines support the functionality of the entire organism and, in particular, the gastrointestinal tract. The motor function of the intestine is also regulated by the microbial flora, which is carried out through a number of mechanisms: formation and inhibition of substances such as bradykinin; production of prostaglandins of bacterial origin; changes in the

metabolism of bile acids with the formation of metabolites that accelerate motility. Amines formed during the life of microorganisms - histamine, bradykinin - regulate the sphincter activity of the gastrointestinal tract.
The detoxification activity of the intestinal microbial flora provides protection from xenobiotics: pesticides, amines, heavy metal salts, many drugs, nitrates, etc. A number of bacteria are known to have high nitrate reductase activity (propionibacteria, peptococci, veillonella, gram-negative enterobacteria and others) that prevent the development of methemoglobinemia with high nitrate levels. This is especially important in young children with a high proportion of fetal hemoglobin.

Metabolic detoxification processes occur primarily with the participation of hydrolysis and reduction reactions, with biotransformation leading to the formation of non-toxic products and accelerated elimination.

Formation of microbiocenosis in children

The formation of a child's microbial biocenosis begins from the first stages of life. During childbirth, ingestion causes the entry of microflora into the mother's birth canal and colonization of the vaginal flora in the child's digestive system. Currently, recommendations have been developed for correcting the vaginal flora of a pregnant woman in the last trimester of pregnancy using the bacterial preparation Zhelemik, which is lyophilized live lactobacilli isolated from the vagina of healthy women. Colonization of the child's intestines with the mother's microflora prevents the development of dysbacteriosis in the newborn. After birth, the intestine is colonized by microbes of the mother, as well as personnel and the environment, which are mainly represented by aerobes and optionally anaerobes. If a child is latched to the breast within 12 to 24 hours after birth, then bifidoflora is detected in only half of the children; later latching of children results in the colonization of bifidobacteria only in every 3-4th child. Starting from the 4th day of life, lactobacilli, Escherichia, streptococci, and staphylococci are detected in the newborn's colon. It is noted that Escherichia coli and streptococci create conditions for the appearance and colonization of obligate anaerobes. By the end of the first week of life, the titer of lactobacilli, Escherichia, and bifidobacteria increases, and bacteroides, clostridia, and anaerobic cocci appear. The flora of a child in the first year of life is directly dependent on the nature of feeding. Children who receive natural feeding have the following types of bifidum bacteria: B. bifidum and B. breve, and those who are artificially fed have a biovar in B. longum. After one year of life, B. breve, B. adolscentis, B. longum, B. infantis become dominant. In adults, B. bifidum serovar a, B. adolscentis, and B. longum are more often present. Lactobacilli are determined in a higher titer during artificial feeding. Clostridia exceed the level of 106 CFU/g of test material when artificial mixtures are used. C. dificile and C. perfringens, which can produce enterotoxins, are often found in these children. Increased levels of clostridia may occur in older children when using an unbalanced diet with a significant increase in the content of meat products. In children receiving artificial feeding, bacteroides and veillonella appear more often and in higher titers. With an excessive amount of the latter, increased gas formation and the development of dyspeptic manifestations may be observed. The facultative anaerobic flora also depends on the nature of nutrition. Patients who are bottle-fed more often suffer from enteritis, which is caused by endogenous Escherichia, or Escherichia coli with altered properties (lactose-negative and hemolysin-producing). Other bacteria: Klebsiella, Proteus, Morganella, Enterobacter, Citrobacter, Serration are opportunistic; when the body's resistance decreases, they can acquire pathogenic properties, cause inflammation and diarrhea.

Non-pathogenic staphylococci (S. epidermidis) colonize the intestines of children from the first days of life. Sometimes staphylococci with pathogenic properties are present in small concentrations. However, the development of an infectious process is possible when nosocomial strains are transmitted from carriers to a child. These strains are resistant to antibacterial drugs and can cause severe inflammatory bowel disease and even a septic process. The role of streptococci in the formation of the optimal level of colonization resistance is quite large. With natural feeding, the level of streptococci remains constant, but with artificial feeding it can significantly exceed the norm. However, with a reduced amount of obligate microflora in children, the increased growth of enterococci contributes to the formation of an endogenous infectious process.

Thus, natural feeding of a child, begun immediately after birth, forms a more favorable flora of the digestive tract, which is capable of colonization resistance and ensures adequate digestive processes. Artificial feeding may be one of the reasons for changes in the child's microecology with the subsequent participation of endogenous flora in the formation of infectious, allergic, and immunopathological processes. Microorganisms colonize the lumen of the digestive tract, as well as the surface of the mucous membranes. In this regard, mucosal microflora and cavity microflora are divided. For a number of pathological conditions, it is very important to take into account the composition of each pool. Currently, methods for separate assessment of the flora of the digestive tract are being developed and implemented. Clinical manifestations of dysbiosis appear much later than microbiological changes. They are very nonspecific, but a number of symptoms are possible that are formed due to disruption of processes occurring with the participation of certain bacteria.

Composition of intestinal microflora

Bifidobacteria - gram-positive rods, strict anaerobes - in the colon of children make up about 95% of the bacterial population. Being saccharolytic microbes, they produce a large amount of acidic products. The resulting lactic and acetic acids enhance the absorption of calcium, iron, and vitamin D ions. Their production of lysozyme, bacteriocins, alcohols and high antagonistic activity towards pathogenic bacteria prevent the penetration of microbes into the upper gastrointestinal tract and other organs. Bifidobacteria have a high ability to synthesize amino acids, proteins, and many B vitamins, which are then absorbed in the intestine. Therefore, with persistent, severe dysfunction of bifidobacteria, a complex of protein-vitamin-mineral deficiency can develop. With a decrease in the level of bifidobacteria, translocation of opportunistic microbes into the upper intestine can cause their overgrowth with more severe manifestations of malabsorption syndrome. **Lactobacilli** include 44 species, but the main ones are L. acidophilus, L. casei, L. plantarum, L. fermentum. The suppression of putrefactive and pyogenic microbes and the antibacterial activity of lactobacilli are associated with the production of lactic acid, alcohol and lysozyme, products with high antibiotic activity, interferons, interleukin 1, and a number of others. The disappearance of lactobacilli leads to a shift in the reaction of the environment towards the alkaline side, sharply reducing the intestinal utilization of biologically active compounds. An interesting fact is that people following a strict vegetarian diet have very high levels of lactobacilli. The important role of eubacteria, which are anaerobic gram-positive non-spore-forming rods, in the transformation of cholesterol into coprostanol has been proven. In connection with this situation, a number of works by foreign researchers on the use of functional foods enriched with appropriate microorganisms to reduce cholesterol levels in patients require the attention of pediatricians. However, it should be remembered that eubacteria can participate in the development of inflammation of the oral cavity, the formation of purulent processes in the pleura and lungs, and infective endocarditis.

Clostridia also take part in the deconjugation of bile acids; many support colonization resistance and suppress the growth of pathogenic clostridia. Clostridium difficile and C. perfrogens are capable of producing enterotoxins. Microbial peptide toxins have a pro-inflammatory effect, cause neutrophil chemotaxis, secrete serine proteases and oxidants, and form chronic inflammation. With their participation, local and systemic sensitization with antigens of the enteral system and food sensitization occur. Thus, the development of pseudomembranous colitis caused by C. difficile is associated with the use of a number of antibiotics that suppress normal microflora and a sharp decrease in the number of non-toxigenic clostridia.

Bacteroides are still insufficiently studied representatives of microflora; their specific role in the breakdown of bile acids is known. Among them, B. fragilis has a number of factors that determine pathogenicity: the ability to secrete lactamase, enterotoxin, hyaluronidase, heparinase, fibrolysin, and neuraminidase. There are indications that 10% of cases of diarrhea are caused by enterotoxigenic strains of B. fragilis; diarrhea caused by bacteroids is especially common in preschool children. A number of species of fusobacteria are capable of secreting hemolysins, hemagglutinins and platelet aggregation factors. Therefore, in severe septicemia associated with the growth of fusobacteria, thromboembolism may occur, which has the corresponding clinical characteristics.

Veillonella are capable of reducing nitrates. When Veylonella multiply excessively in the intestines, increased gas formation is observed, and severe dyspeptic disorders may occur.

Some strains of Escherichia produce colicins, which inhibit the growth of enteropathogenic strains of Escherichia coli. These properties are primarily due to the mechanism of synthesis of secretory immunoglobulins in the intestine. Escherichia takes part in the synthesis of vitamin K, providing hemostatic processes. However, it is necessary to point out the ability to form hospital strains of Escherichia with multiple resistance to antibacterial agents, which is the cause of the development of hospital infection. Citrobacter, Enterobacter, Proteus, Klebsiella and others, with a decrease in the body's immunological resistance, can also lead to changes in intestinal function, the formation of inflammatory processes in various organs as a result of exposure to microbial peptide toxins.

Immune reactivity of the body

A wide variety of adverse effects on a child: stress, physical and psycho-emotional stress, unbalanced nutrition, environmental distress and many pathological conditions cause changes in the immune response and therefore can affect the qualitative and quantitative characteristics of normal intestinal flora. If intestinal dysbiosis develops in a sick child, clinical conditions may be detected that are associated with a decrease in colonization resistance, digestive disorders and trophic disorders, a violation of the detoxifying function of the intestinal microflora and changes in the immune response.

Diagnosis and assessment of the severity of intestinal dysbiosis

Depending on the severity of clinical manifestations and the characteristics of microbiological changes, 3 degrees of dysbiosis are distinguished: compensated, subcompensated and decompensated. However, there is no single point of view in assessing the degree of dysbiosis, since different clinical and laboratory criteria are often used. Clinical manifestations of intestinal dysbiosis are largely determined by the localization of changes. Dysbiosis of the small intestine is a syndrome of excessive bacterial growth (contamination), often characterized by diarrhea and the formation of a syndrome of impaired intestinal absorption with a wide variety of abnormalities in homeostasis. Colon dysbiosis may not have clinical manifestations. In some cases, a connection between constipation and microflora disorders is described. A serious disease may develop - pseudomembranous colitis.

Laboratory diagnosis of dysbiosis is most often based on microbiological analysis of feces. ***Microbiological criteria include a decrease in bifidolactobacteria, a decrease or increase in Escherichia, the appearance of strains with altered properties, an increase in the number of cocci, detection of opportunistic gram-negative bacilli, as well as fungi and clostridia more than 103 CFU/l. Various combinations of these shifts are possible in analyses.***

Currently, gas-liquid chromatography is also used. The chromatographic method allows you to evaluate chemical compounds associated with the life of normal microflora.

Assessment of scatology reveals fermentative and putrefactive dyspepsia, disturbances in the breakdown and absorption of food ingredients. In some cases, it is advisable to determine the LPS-O antigen and the level of enterotoxins.

Microflora correction

Treatment programs for restoring damaged microflora should be built taking into account possible factors leading to its change. Having a wide range of different drugs in his arsenal, to select specific drugs, the doctor must analyze individual changes in the child's body, taking into account the premorbid background, age, nature of feeding, allergic reactions, previous intestinal infections, as well as drugs used to treat the underlying disease.

Nutrition

Adequate, age-appropriate, balanced nutrition with normal functioning of organs and systems prevents the development of dysbiosis. With changes in microflora, nutritional correction is necessary taking into account motility, secretory changes in the gastrointestinal tract, enzymatic activity of the digestive tract and additional administration of vitamin and mineral complexes. Currently, so-called functional nutrition is becoming widespread. In functional nutrition, prepared food products are consumed, to which biological products, antioxidants, carotenoids, enzymes and other substrates are added. For young children, adapted mixtures enriched with representatives of microflora are widely used - (Malyutka), (Biolact adapted), (Bifidok), (Bifilin), (Bifidolact), (Bifilife), (Vitalakt) and a number of others. In many cases, the use of a dry mixture (Lactofidus) containing bifidobacteria and streptococci (NAN) with bifidobacteria is justified. To care for children in the neonatal period, functional nutrition has been developed in the form of lyophilized breast milk enriched with Bifidobacterium bifidum.

Dietary fiber is of great importance for correcting intestinal microflora. They are natural enterosorbents and affect the composition of microbial communities. Microbial flora uses dietary fiber as a substrate for life, but it should be remembered that the products of their metabolism can have both physiological and toxic effects.

Dietary fiber (pectins, lignins, cellulose, hemicellulose) is found in large quantities in bran, seaweed, apples, carrots, red rowan and other vegetables and fruits; entering the colon, they are exposed to glucosidases. Glucose is a substrate for many anaerobic bacteria. The role of other metabolites that are formed is also great, among them lactic acid and other short-chain monocarboxylic acids, which inhibit pathogenic flora and are a substrate for the restoration of the intestinal epithelium. Propionic acid regulates microcirculation of the colon through vascular sphincters, butyrate is involved in the proliferation and differentiation of the intestinal epithelium. Dietary fiber significantly reduces the level of endogenous histamine and other biological amines, which cause allergic manifestations in diseases of the digestive system. Lactulose preparations have proven themselves well. Normase is widely used to treat dysbiosis. The drug is highly effective in the presence of constipation and an allergic component.

Enzyme preparations

To improve the breakdown and absorption of food ingredients, enzyme preparations based on pancreatin can be used, and in difficult cases, micro-tabletted enzymes that can prevent putrefactive processes. Recently, combination drugs Wobenzym and Flagenzyme have been used with good effect. They are especially effective in the complex treatment of intestinal dysbiosis, accompanied by impaired intestinal absorption and allergic manifestations in children.

Enterosorbents

The use of enterosorbents is especially important in conditions of increasing multiresistance of microbes to antibacterial agents. Sorbents have high sorption activity towards exo- and endotoxins, bacterial metabolites, bile acids, as well as bacteria and viruses themselves. Sorbents based on granular activated carbons are used: carbolene, microsorb P, activated carbon SKN, enterosorbent SKN, carbolong and a number of others. Enterosorbent smecta, which is a microplate of silicon and aluminum dioctahedron, has also found its use in pediatric practice. This drug improves the properties of gastrointestinal mucus, increases the resistance of the mucous membrane, and has a cytoprotective effect. New sorbents - SUMS1 and algisorb (calcium alginate) are used with good therapeutic effect; they quickly remove various metabolites and normalize microflora. SUMS1 is a carbon-mineral sorbent in the form of granules and powder. Algisorb is made from seaweed - kelp, does not affect the metabolism of calcium, potassium, iron, microelements, so it can be used for a long time. It restores many adaptation mechanisms well.

Bacterial preparations

Bacterial preparations based on living microorganisms, representatives of normal microflora - probiotics - have become widespread (see table). Currently, a new concept has emerged - biotherapeutic agents (BTA), which are preparations of microorganisms based on strains of lactobifidobacteria. Bifidumbacterin, lactobacterin, fermented milk bifidumbacterin belong to the BTA category. These drugs are characterized by the ability to survive in an acidic environment, effectively attach to epithelial cells, colonize the mucous membrane, produce antimicrobial substances, stimulate the immune system, prevent excessive growth and reproduction of pathogenic microorganisms, and restore normal microflora.

A number of preparations contain a combination of microorganisms: bificol (bifido-colibacteria), bifiform (bifidum-enterococcus), bifocyte (bifidum-lactobacteria), linex (three strains of lactobacilli), fermented milk bifilact. There are also complex preparations: bifidumbacterin-forte (with stone sorbent), bifiliz (with lysozyme), Nutrolin B (with B vitamins), kipacid (with immunoglobulin). Currently, recombinant drugs (subalin) are appearing. There are different points of view on the use of bacterial preparations containing aerobic spore-forming bacteria - bactisubtil, sporobacterin, etc. There are indications that the artificial introduction of these bacteria into the intestine in large quantities and the excessive proliferation of bacilli in an uncharacteristic ecological niche, accompanied by the spread of bacilli outside the intestine, against the background of a decrease in the amount of obligate flora, can increase the degree of dysbiotic disorders and worsen the patient’s condition. B. cereus synthesize hemolysins that can destroy red blood cells. The drug sporobacterin contains bacilli that produce proteolytic enzymes and fibrinolysins. Due to their high proteolytic activity, the strains contained in sporobacterin penetrate through the mucous membrane into the blood, lymph, and reach the lymph nodes, spleen, and liver. Essentially, these strains have properties characteristic of pathogenic microorganisms. We can agree with the opinion of a number of authors that the widespread use of these drugs is poorly justified and there should be strict indications for their use.

Currently, if commercial bacterial preparations are ineffective due to their poor survival rate in the patient's intestines, autostrains of bifidobacteria and lactobacilli can be used. They can retain their activity for a long time in a lyophilized state or in a refrigerator at a temperature of -20°C. Correction of microflora using autostrains is especially recommended in patients requiring the use of cytostatics, glucocorticoids, antibiotics, and radiation therapy. The use of donor strains of bifidobacteria and lactobacilli from the mother for the child 2 hours after cesarean section has been developed in order to prevent pathological colonization of the intestine and the formation of normal microflora.

Probiotic preparations are also used, consisting of food additives that selectively stimulate the growth of normal flora. Lysozyme, lactulose, and hilak-forte are widely used. In cases of dysbacteriosis of the 2-3rd degree, it is necessary to prescribe agents with selective antibacterial activity. Various phages are often effective in treating dysbiosis. Currently, staphylococcal, Klebsiella, pyobacteriophage, intestibacteriophage, Pseudomonas aeruginosa and other phages are used.

In some cases, with low sensitivity to phages, antibacterial drugs can be used: furazolidone, chlorophyllipt, metronidazole, nifuroxazide, intetrix, as well as antibiotics and a group of antifungal agents, among the latter should be ketoconazole, fluconazole, natamycin. Complex therapy may include immunomodulatory agents, including vitamins, cell membrane stabilizers, and microelements.

The result of treatment depends on the effectiveness of therapy for the underlying disease, the adequacy of the choice of a set of drugs, taking into account not only microbiological changes, but also the characteristics of the child's body.

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