American Journal of Biomedicine and Pharmacy
https://biojournals.us/index.php/AJBP
ISSN: 2997-7177

Disturbances of Normal Intestinal Microflora in Children and a Modern Approach to their Correction

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Received: 2024, 15, Feb
Accepted: 2025, 21, Mar
Published: 2025, 09, Apr

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Annotation: Although dysbacteriosis is a well-recognized clinical and laboratory syndrome, its interpretation can be problematic [17]. Therefore, in addition to the ability to correctly interpret the nature of the microbial landscape in real practice, the ability of the practicing pediatrician to analyze the premorbid background, the nature of nutrition and food tolerance, as well as to understand the nature of the general somatic problem in its specific clinical variants, is of great importance.

To date, it has been established that the human microflora has a very large biological potential, sufficient both to ensure the full protection of the host and to provide its metabolic support [6,12,18]. The indigenous microflora plays a very important role in the processes of digestion and metabolism. There is a lot of direct and indirect evidence that intestinal microorganisms, due to the production of various enzymes (proteases, amylases, lipases, etc.), enhance the hydrolysis of proteins, ferment carbohydrates, saponify fats, prevent bacterial decarboxylation of food histidine, and inhibit the increase in histamine levels [1,13]. A number of studies have provided convincing evidence of the amylase and caseinolytic activity of bifidobacteria and lactobacteria, their participation in the metabolism of bile acids, as a result of which the total pool of the latter is maintained during enterohepatic circulation [10].

Keywords: Dysbacteriosis, microflora pathology, pathogenesis, prognosis and treatment.

Introduction: According to modern concepts, microorganisms of the gastrointestinal tract interfere with cholesterol metabolism and are the most important metabolic and regulatory system that cooperates with the host organs and cells in maintaining the normal lipid composition of the blood [10]. When these processes are disrupted, the microbiota enhances the deconjugation of secondary hydrophobic hepatotoxic bile acids that disrupt the microcirculation in the intestinal wall, which leads to the accumulation of the entire pool of bile acids and, as a result, their removal from the enterohepatic circulation. The next stage is associated with a decrease in bile acid synthesis in hepatocytes, resulting in hypercholesterolemia, hypertriglyceridemia and dyslipoproteinemia [10]. It has been found that bifidobacteria limit the release of cholesterol from hepatocytes, while some strains of streptococci enhance the catabolism of cholesterol into bile acids [18].

Another important factor maintaining an optimal microbiota is the flow of bile into the duodenum (if the duodenum, gallbladder, bile ducts, and sphincter of Oddi are functioning normally). Recent advances in the study of bile formation and bile secretion have revealed that bile acids, the main surfactant components of bile, have bactericidal and bacteriostatic effects [21].

Of particular interest is the detoxification capacity of the indigenous intestinal microflora, which researchers are increasingly comparing with a similar function of the liver. These two organs participate in the processes of hepatic-intestinal recirculation of various organic and inorganic compounds. The main difference between the metabolism occurring in the intestine is that there are hydrolysis and reduction reactions, while in the liver, oxidation and synthesis with the formation of water-soluble products dominate. Xenobiotics undergo biotransformation under the influence of microbial fermentation with the formation of non-toxic products and isoforms and are rapidly eliminated from the body [18].

Research methods and materials: In dysbacteriosis of various origins, when the detoxification function of the digestive tract microflora decreases, pronounced functional disorders of the liver were detected, the metabolic indicators of which were directly related to the level and profile of volatile fatty acids in feces, as well as the value of anax. It is known that in conditions of dysbacteriosis, the synthesis of volatile fatty acids, which are the main components of the water-electrolyte, acid-base and energy balance of the human body, decreases. Today, various deviations in their content from the physiological norm, as well as changes in the spectra of isomers of acetic, propionic, valeric, caproic, butyric and valeric acids in the total pool of volatile fatty acids, are used as informative biochemical markers of structural and functional disorders of the test microflora. The list of pathological processes that occur as a result of the migration of intestinal microflora into the liver and extrahepatic biliary system and the continuation of increasing endotoxemia includes: non-alcoholic steatosis, steatohepatitis, nonspecific reactive hepatitis, intrahepatic intralobular hepatitis and hepatocellular cholestasis, dyskinetic diseases of the extrahepatic biliary tract [21]. There is reliable information about the occurrence of chronic functional liver failure in cholelithiasis, the cause of which is considered by researchers to be decompensated, difficult-to-correct dysbacteriosis of the colon. These studies have shown that the use of modern probiotics reliably restores the normal microbiocenosis of the colon, the activity of the reticuloendothelial system of the liver, and improves metabolic processes in it [10].

Results: In recent years, a connection has been established between the proliferation of intestinal bacteria and the development of exocrine pancreatic dysfunction. Experiments have shown that

the microflora of this biotope undoubtedly plays a role in maintaining the inflammatory response in the gland. Lipopolysaccharides and oligopeptides (endotoxins) of microorganisms exhibit the properties of strong antigens and stimulate the migration of cellular elements to the site of inflammation [19]. In this case, relative pancreatic insufficiency develops, which is manifested by a lack or decrease in enzyme activity (digestive disorders) and subsequently impaired absorption of essential nutrients (malabsorption).

Thus, intestinal dysbacteriosis significantly alters the digestive processes at the level of the lumen of the gastrointestinal tract and is accompanied by a multicomponent syndrome of digestive disorders (maldigestion / malabsorption).

To confirm the presence of functional insufficiency of the pancreas, stomach, gallbladder associated with dysbacteriosis, it is necessary to analyze the data of coprological research, which has not lost its relevance to this day and is the standard, most physiological method [16]. Unfortunately, in real practice, coprology is often ignored or its results are misinterpreted. The doctor should pay attention to the following pathognomonic diagnostic signs: steatorrhea - neutral fat in the coprofiltrats (type 1 steatorrhea), fatty acids, soaps (type 2 steatorrhea), a combination of the above (type 3 steatorrhea), a large number of muscle fibers - a large number of - in coprofiltrats. grains.

In dysbacteriosis accompanied by fermentative dyspepsia, the amount of feces increases significantly, the nature of the feces is mucous, foamy, the reaction is sharply acidic, muscle fibers, soap and fatty acids are detected in the feces, the amount of excreted organic acids increases. A strong positive result for the detection of starch, digestible and indigestible fiber and iodophilic flora.

A different coprological picture is observed with dysbacteriosis, accompanied by putrefactive dyspepsia. In this case, the amount of feces increases, its alkaline reaction is noted, an unpleasant, putrid odor, the nature of the feces is liquid, there are many transverse striated muscle fibers and connective tissue, the reaction to starch, undigested fiber, iodophilic flora and mucus is positive. The amount of ammonia excreted increases sharply (10-14 conventional units).

In dysbacteriosis, which is clinically manifested by inflammation of the intestinal mucosa and is accompanied by constipation, the amount of feces decreases, the nature is decomposed with undigested food residues, the reaction is alkaline, mucus is detected, a large number of leukocytes, intestinal epithelial cells are present.

The pathological symptoms of digestive insufficiency are usually not short-lived and cannot be eliminated without additional therapy. Therefore, the need for the appointment of digestive enzyme preparations is obvious.

Discussion: Despite the fact that the doctor now has a large number of pancreatic enzyme preparations in his arsenal, it is not always possible to ensure adequate restoration of the lumen's digestibility. Treatment of maldigestion / malabsorption syndrome in dysbacteriosis and functional disorders of the biliary tract has its own characteristics that must be taken into account when prescribing digestive enzymes. In the pathogenesis of the syndrome of indigestion, not a primary violation of proteolysis and lipid hydrolysis prevails, but a violation of the solubility of food fats as a result of an imbalance in the motor activity of the gastrointestinal tract, a decrease or violation of the secretion of bile acids and bicarbonates. Preparations containing bile are required. Bile acids enhance pancreatic secretion and choleresis, stimulate the motility of the gallbladder and intestines, thereby increasing the osmotic pressure of the intestinal contents [21]. Under conditions of microbial contamination of the intestine, their deconjugation occurs, which in some cases contributes to the activation of cAMP enterocytes with the subsequent development of osmotic and secretory diarrhea. Therefore, the clinical effect of these drugs is manifested in patients with concomitant functional disorders of the biliary tract, such as

constipation.

At the same time, digestive enzymes containing bile acid components should be used with caution in patients with chronic hepatitis or cirrhosis of the liver, since bile acids enter the liver via the enterohepatic route, where they are metabolized, as well as in duodenal ulcers and chronic gastroduodenitis, where duodenal reflux is common. In this regard, in our opinion, preference should be given to modern microgranulated pancreatic enzyme forms with high specific lipase activity, resistance to the action of gastric juice, and a short dissolution time of the enteric coating of minimicrospheres that quickly release active enzymes in the small intestine [16].

Creon® 10000 is one of the most advanced polyenzyme preparations of the latest generation, suitable for replacement therapy and therefore widely used in pediatrics. It contains standardized pancreatin obtained from the pancreas of pigs. The highly active monospecific combination of enzymes in the preparation is almost identical in its activity to the enzymes synthesized by the human pancreas. Based on the pharmacokinetic properties of Creon® 10000, minimicrospheres with a pH-sensitive shell are “bioavailable” in the proximal parts of the small intestine.

A detailed meta-analysis of clinical trials of Creon® 10000 allows us to reliably assess the high therapeutic potential of the polyenzyme preparation in the complex treatment of acute and chronic inflammatory diseases of the digestive organs associated with dysbacteriosis in children of all ages. It has been reliably proven that pancreatin minimicrospheres significantly improve the quality of replacement therapy for digestive diseases, as a result of which steatorrhea is reduced or completely eliminated.

The advantage of Creon® 10000 is its use in young children; in this case, the minimicrospheres are poured from the capsule and, after calculating the required amount, the child is given a drink with water or juice (but not with alkaline liquids) during meals. For older children, the capsules should be swallowed whole, without breaking or chewing. Since the enteric coating of Creon® 10000 consists of hydroxypropyl methylcellulose, the drug has a high safety profile.

The dose is selected individually, calculated on the basis of lipase with an initial dose of 1000 U per 1 kg of body weight and depends, firstly, on the severity of clinical and laboratory indicators of the exocrine function of the pancreas, and secondly, on the diet prescribed to the child. It is necessary to take into account the fat content of food products, as well as the fact that acidic nutrients (with pH < 5.5) lead to the destruction of the pH-sensitive shell of minimicrospheres that protect them from the effects of gastric juice; it is necessary to abandon foods rich in fiber, as it reduces the activity of enzymes.

In the absence of effect, the dose of the drug is gradually increased according to clinical signs and objective indicators (body weight, height, degree of fat absorption, etc.). Enzyme therapy courses are intermittent: 2-3 courses of 2 weeks with a 2-week break, taking into account adequate diet therapy, until the coprogram stabilizes.

Pre- and probiotic preparations are currently used to normalize the intestinal microflora. Modern medical science defines probiotics as viable organisms and/or substances of microbial or other origin that, when administered naturally, have a beneficial effect on the physiological functions, biochemical and behavioral responses of the host organism by optimizing the microbiological state [22-29].

Many microorganisms have been studied that can be used in everyday medical practice as part of pharmaceutical preparations and functional food products, but today only a few of them are officially recognized. The main criterion here is the probiotic effect, proven in double-blind, placebo-controlled studies. Such reliable data were obtained for B. bifidum, Lactobacillus acidophilus, Lactobacillus GG, Lactobacillus fermentum, Strepto (Entero) coccus faecium SF68, S. thermophilus, Saccharomyces boulardii. The listed microorganisms are included in many drugs presented on the pharmaceutical market.

Accumulated clinical observations show that probiotics entering the intestine change not only its composition, but also its microflora [11,26-29]. It has been established that many probiotic bacteria protect the body in two main ways: by forming a barrier that prevents the attachment of pathogenic microorganisms to the intestinal mucosa and by modulating the body's defenses [2]. Both of these actions are achieved by direct antagonism of bacteria or by increasing the effectiveness of the immune response. Stimulation of the nonspecific immune system is assessed on the basis of the phagocytic activity of natural killer cells and the induction of various cytokines, and the response of the specific immune system is assessed on the basis of the content of immunoglobulins, the concentration of B- and T-lymphocytes and some cytokines [6]. Both systems are stimulated by various probiotics, such as L. casei [2,26]. The results of published studies have shown the fact of stimulation of local immunity, that is, an increase in the level of Ig A in coprofilate in children during the period of taking a mixture containing B. lactis.

Another well-documented effect of probiotics is to improve lactose digestion in people with impaired lactose digestion and absorption. Several studies have shown that live lactase-producing bacteria, such as Str. thermophilus, L. bulgaricus, etc., improve lactose digestion and absorption [3,7,29,39-41].

Certain requirements have been developed for bacterial biological preparations, which correspond to the following: microorganisms must be normal representatives of the human microflora with a clear taxonomic identification; have a positive effect on the host organism, confirmed in clinical studies; be free from pathogenicity and toxicity; have the ability to modify immunological reactivity; with prolonged use, do not cause side effects and remain in the digestive tract until the maximum positive effect is achieved [22-23].

Conclusion: Correction of dysbacteriosis with probiotics is based on a strictly individual plan based on the results of the colon microbiocenosis.

Among prebiotics, lactulose (Duphalac), which belongs to the class of oligosaccharides and the subclass of disaccharides, deserves special attention, that is, its molecule consists of galactose and fructose residues [8, 37]. It is not broken down and absorbed in the small intestine and remains intact until it reaches the colon, where it undergoes bacterial fermentation, serving as a source of energy and a nutrient substrate for bifido- and lactobacteria [40]. The development of these bacteria against the background of optimal pH in the colonic contents leads to an increase in their population. The final products of lactulose metabolism are low molecular weight organic acids - lactic, formic and volatile fatty acids (acetic, butyric, propionic). The latter, firstly, are a quick source of energy for colonocytes, and secondly, have an osmotic effect and a corresponding laxative effect that occurs 24-48 hours after taking the drug. Lactulose does not affect the electrolyte composition of the blood and does not cause electrolyte loss through the gastrointestinal tract, which is of great importance for newborns and infants prone to the development of exsiccosis. Lactulose inhibits the activity of pH-dependent 7-α-hydroxylase, reduces the amount of bile acids in the colon and reduces the lithogenicity of the liver. The use of lactulose and its analogues can be combined with the use of antibiotics - in this case, the prebiotic serves as a means of preventing dysbacteriosis. The metabolism of lactulose in the intestine does not lead to the formation of toxic products, so its long-term use is not only completely harmless, but also helps to maintain or restore intestinal function.

Thus, an important direction in restoring impaired gastrointestinal digestion in intestinal dysbacteriosis is the administration of pancreatic enzymes with simultaneous correction by modern pre- and probiotics.

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