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The role of the gut microbiota and the use of new therapies in Irritable Bowel Syndrome

Rola mikrobioty jelitowej oraz stosowania nowych terapii w Zespole Jelita Drażliwego

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ABSTRACT

Introduction: Irritable bowel syndrome is a functional disorder of the gastrointestinal tract with a multifactorial nature of the disease. IBS affects 11% of the population, with the gut microbiota playing an important role in the pathophysiology.

Purpose: The aim of this article is to present the course of irritable bowel syndrome, the role of the gut microbiota in pathophysiology, and new therapeutic approaches, including probiotics, based on the current state of knowledge.

Conclusions: IBS is a syndrome whose exact pathophysiology is not fully understood. The state of the gut microbiota has a huge impact on the course of the disease, but also on the functioning of the whole body. New therapies currently in use, i.e. probiotics, are showing promising results, but more research is needed to find the golden mean to treat the disease.

Methods: Data for the article were retrieved using PubMed setting the time descriptors to 2013-2023.

Keywords: irritable bowel syndrome, gut microflora, probiotic, prebiotic, fmt, gut-brains axis, dysbiosis

INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic condition involving the small and large intestine [1,2]. According to the Rome IV criteria, the disease is defined as a syndrome with recurrent abdominal pain lasting at least 1 day per week over the past 3 months [3,4]. The most common symptoms include pain, which may be acute, spasmodic and, very importantly, never causes awakening in the abdominal region at night, mainly in the lower abdomen and left quadrant, and disturbances in bowel movements, i.e. constipation, diarrhoea and alternating constipation and diarrhoea, which may be accompanied by flatulence. In addition, there may be a change in the form of the stool - watery or semi-liquid, corresponding to type 6 or 7 according to the Bristol Stool Formation Scale (BSFS) [2,3,5]. The direct cause is not yet known. IBS is defined as a functional disorder of the gastrointestinal tract, of which the most significant pathophysiological factor is a dysregulation of the brain-gut axis. Other factors of significant importance in the pathophysiology of the disease include abnormal composition of the intestinal microbiota, abnormal functioning of the intestinal barrier, a history of gastrointestinal infections of viral or bacterial origin and, affecting normal intestinal motor and secretory function, increased activity of the sympathetic nervous system [1]. Importantly, diet is an important aspect contributing to the development and course of IBS. Nutrients

provided with food affect gastrointestinal motility, sensitivity and the intestinal microflora [3,5]. It is a very important fact that more than half of the patients see a correlation between the occurrence of gastrointestinal symptoms and the specific food consumed, further emphasising the importance of diet in irritable bowel syndrome. Inadequate diagnosis and the exclusion of too many nutrients from the diet can lead to significant nutritional deficiencies, which can contribute to worsening of the patient's condition and even the development of other conditions, so correct diagnosis under the supervision of a medical and dietetic specialist is important [3].

The multifactorial nature of the disease makes it significantly more difficult to find the most effective treatment. IBS affects approximately 11% of the human population, the average age of patients is 40 years and women are much more commonly affected. On average, 80% of patients have psychiatric disorders, i.e. depression and anxiety disorders [1]. Based on recent scientific research on IBS, the importance of the gut microflora in the pathophysiology is becoming increasingly apparent [3]. This has led to the need to invent new therapies to improve the patient's condition and possibly control the disease to some extent. The use of prebiotics, probiotics, synbiotics, as well as the transplantation of the gut microbiota (FMT), is intended to modify the pathologically altered bacterial microbiota [1,4].

GUT MICROBIOTA

The ecosystem that inhabits the human digestive tract is referred to as the microbiota. It is made up of billions of micro-organisms including bacteria, fungi, viruses and some eukaryotes that colonise the tract from birth. More than 1,500 species of microorganisms make up the gut microbiota [1,6]. Among the most numerous groups are the Bacteroidetes, Firmicutes, Proteobacteria, Fusobacteria and Acinobacteria. The type and number of specific microorganisms depends on the section of the gastrointestinal tract in which they reside [7]. Bacteroides is the most widespread genus. They are most abundant, as much as 70%, in the large intestine. In the intestine, almost 99% are anaerobic bacteria. It is estimated that the microbiota consists of approximately 10¹⁴ microorganisms [7,8]. Several factors are listed that may influence the composition and function of the intestinal microbiota, including genetic factors, diet, age, type of birth, as well as possible antibiotic therapy, use of non-steroidal anti-inflammatory drugs and past infections. Research shows that the development of the microbiota begins in the foetal period, but that the most important moment is the birth; depending on whether the birth was natural or by caesarean section, the composition may

differ. Breast milk feeding also influences changes in the composition of the microbiota and is very important in the development and functioning of the child's immune system [7].

In the human body, the physiological microbiota has a number of important functions that ensure proper functioning and the maintenance of homeostasis. It enables protection against potential gastrointestinal infections and produces antimicrobial substances [3,7]. It ensures proper regulation of metabolic pathways. Participates in the synthesis of bile acids and cholesterol. Participates in the digestion of carbohydrate chains, fatty acids and takes an active part in the synthesis of vitamins by the bacteria that make up the intestinal microflora - vitamin K, B1, B6, B12 and folic acid. It controls puberty and also strengthens the immune system. Recent studies emphasise the role of the microbiota in the brain-gut axis pathway, which influences mental and neurological functions, i.e. the development of cognitive functions, social interactions or behaviour in stressful situations. Microbiota-building bacteria can synthesise neurotransmitters min. serotonin and GABA [7,8,9].

Disruption of the existing symbiosis between the intestinal microflora and the human organism can adversely affect normal function. A condition in which the composition or function of the microorganisms that make up the microbiota is disrupted is termed dysbiosis [7]. This process can be the cause of the development of numerous diseases. It has an important role in, among others, inflammatory bowel disease, irritable bowel syndrome, liver disease, diabetes, allergic diseases and neurodegenerative diseases [9,10]. The impact on the pathogenesis of such numerous and diverse disease entities underlines how important a constant, unchanged state of the intestinal microflora is in the normal functioning of the entire human organism. According to current knowledge, the composition of the microbiota can change over the course of a person's life as a result of diet, medication and hygiene levels [7,8].

NEW THERAPIES

In recent years, it has become very popular to research and develop new therapeutic strategies to modify and rebalance the intestinal ecosystem. Methods include: the use of probiotics, prebiotics and synbiotics, the transplantation of faecal microflora and antibiotics whose effect is limited to the gastrointestinal tract [7,8].

Probiotics

Probiotics are defined by the WHO as live micro-organisms that, when supplied in appropriate amounts and composition, confer health benefits to the host [1]. They are considered safe in controlled use and are tolerant of the gastrointestinal environment where they can fully exist [3,11,12]. There is evidence of the effect of probiotics in IBS patients on gastrointestinal motility, visceral hypersensitivity, intestinal microflora function and the intestinal barrier [6]. The most commonly used probiotic species include *Lactobacillus* and *Bifidobacteria*. Depending on the form and clinical conditions, they can be supplied as a medicine, dietary supplement or with food, e.g. in yoghurts, kefir and dairy products. Probiotic bacteria lower the pH of the gut, synthesise vitamins, produce short-chain fatty acids (SCFAs) and have the ability to metabolise certain carcinogens. They produce bacteriocins and other inhibitory substances that show potent activity against pathogenic microorganisms [12,13]. They stimulate an immune response. The use of an appropriate dose and selection of suitable bacterial strains allows probiotics to be used as therapeutic agents to modify the composition of the intestinal microflora and restore the balance that has been disturbed in the process of dysbiosis. The use of probiotics finds application in the treatment of irritable bowel syndrome, diarrhoea, obesity and diabetes [6,14]. Some studies suggest their use as an alternative treatment for neurological and psychiatric diseases. Probiotics are considered safe, well tolerated and generally effective which supports their use [13].

Based on one study, *Bacillus coagulans* was found to be the most promising species in IBS patients with the aim of relieving symptoms including abdominal pain, bloating and general fatigue when compared with other probiotics [11]. Another study reported a beneficial effect with multi-strain preparations where the duration of use was at least eight weeks [12].

Regardless of the fact that the effect of probiotics has been proven and very widespread in therapeutic action, there are some aspects that limit their performance in clinical use more widely. This means that there is a need to improve the composition as well as the function of the bacteria and to conduct numerous clinical trials to control the action of the probiotics used. Thanks to the thriving development of genetic engineering, it is possible to create a new generation of probiotics that will include highly selected strains that can perform well-defined functions in the gastrointestinal tract, which will have a positive impact in the therapy process [6,15].

Prebiotics

Prebiotics are substrates that are selectively utilised by host micro-organisms causing specific changes in the composition and function of the intestinal microflora. Their function is to benefit the host by stimulating the growth of specific bacteria in the gastrointestinal tract, thereby improving body health. Resistant to digestive enzymes, they are absorbed in the upper digestive tract and are used by beneficial intestinal microflora species for growth. These are mainly short-chain carbohydrates, flavanols included in cocoa, and prebiotics can also be found in onions, asparagus and garlic. These substances lead to the inhibition of the growth of pathogenic microorganisms, lower the pH, increase the resistance of the host mucosa and improve the integrity of the intestinal barrier. The most commonly studied prebiotics include fructooligosaccharides (FOS), a so-called beneficial dietary fibre that relieves constipation, and isomaltooligosaccharides (IMO), which regulates immune function [6,15].

Synbiotics

When probiotics are mixed with prebiotics, they are referred to as synbiotics. Their purpose is to improve health in humans. Synbiotic products are those in which probiotic bacteria selectively use prebiotics for growth. They are used, for example, in the treatment of ulcerative colitis or to reduce the risk of developing colorectal cancer [3,6].

Faecal microbiota transplantation (FMT)

The process involves transplanting faecal micro-organisms from a fully healthy person with no daily contact with pathogens, e.g. working in a hospital, into the gastrointestinal tract of a patient who requires restoration of the normal community and function of the intestinal microflora. There is sufficient evidence in favour of the use of FMT to demonstrate its high efficacy and therapeutic effect for people with bowel disease. It is commonly used in patients with irritable bowel syndrome, inflammatory bowel disease, insulin resistance, diarrhoea and also in metabolic syndromes. Unfortunately, despite good reviews, there is a risk of many adverse effects. It has been proven that the microbiota of the transplant patient resembles that of the donor [6,7].

CONCLUSION

Irritable bowel syndrome is one of the more common functional disorders of the gastrointestinal tract. It manifests as recurrent abdominal pain, discomfort and bloating accompanied by bowel movements without a direct underlying cause. From multicentre clinical studies, it is known that disorders of various mechanisms within the brain-gut axis, altered gastrointestinal motility and visceral hypersensitivity are the underlying causes. In addition, many scholars are of the opinion that disturbances in the gut microbiota play a key role in the pathogenesis of IBS. However, the unequivocal cause of the disease is not known, so no permanent cure is possible and symptoms often recur. The most important part of treatment is maintaining a good relationship between doctor and patient, which creates an atmosphere of mutual trust and a sense of security. Treatment of irritable bowel syndrome includes general management, lifestyle changes, dietary modifications, pharmacology and psychological care. New therapeutic approaches are known, such as probiotics or FMT, but these processes are not yet fully understood and many years of clinical research are needed to be able to apply these therapies competently and help patients to have the highest possible quality of life with this disease.

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