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THE INFLUENCE OF PREBIOTIC AND PROBIOTIC ON THE SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO)

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ABSTRACT

Background: SIBO is a significant and growing problem in the XXI century. Patients suffer from symptoms that inconvenience their everyday life. Despite numerous trials existing SIBO treatment does not fully alleviate patients' symptoms. Prebiotics and probiotics have proved and widely recognized benefits for gut health, which could be influential for SIBO treatment and for more severe disorders like cirrhosis.
Aim: This narrative review synthesizes evidence on the influence of prebiotics and probiotics on human health, especially in SIBO.
Material and methods: A search of relevant research databases was conducted to identify eligible papers.
Results: Many studies showed that supplementation of prebiotics and probiotics may alleviate the prevalence and severity of SIBO symptoms. Correlation of those therapeutic agents, especially probiotics with antibiotics like rifaximin may bring additional benefits. However, further multi-center studies are required.
Conclusions: Prebiotics and probiotics may be an important factor in the SIBO therapeutic path.

KEYWORDS

SIBO, Probiotics, Prebiotics, Saccharomyces, Bifidobacterium, Lactobacillus

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1.Introduction

Small intestinal bacterial overgrowth (SIBO) is a condition characterized by the excessive growth of bacteria species, which are usually present in the colon, in the small intestine. This process determines the production of gases such as hydrogen or methane through carbohydrate fermentation. Under physiological conditions gastric acid and the intestine motility prevent bacterial overgrowth. Many disorders or abnormalities can increase the risk of developing SIBO, such as obesity, high-fat diets or diabetes-mellitus (1) (2). The diagnosis of SIBO can be made when over 10^3 CFU/mL are found in the aspirate (3). Symptoms are non-specific and present as bloating, belching, diarrhea, abdominal pain or fatigue (4). The standard therapeutic path consists of antibiotics such as metronidazole or rifaximin, however recent studies have shown new ways for managing this disease (5). This article mentions the potential role of prebiotics and probiotics. The definition set up by The International Scientific Association for Probiotics and Prebiotics states that "prebiotics are substrates that are selectively utilized by host microorganisms conferring a health benefit" (6). Prebiotic compounds should meet the following criteria be non-absorbable in human gastrointestinal system, they cannot be hydrolyzed by host enzymes, and they should allow for the growth of physiological bacterial flora (7).

Probiotics are yeast or bacteria which are profitable for the host's organism when used in prescribed dosages. Many of which are able to produce hydrogen peroxide or other antibacterial compounds, which allows for non-physiological overgrowth restriction (8). Many studies and clinical practices demonstrate that probiotics may ameliorate antibiotic-associated diarrhea or other gastrointestinal conditions. They also influence the immune system by differentiation regulation of lymphocytes T and anti-inflammatory agents (9).

2. Research materials methods

This systematic review aimed at summarizing the most meaningful and current information on the topic of prebiotics and probiotics implementation as a therapeutic method in SIBO. The research was carried out using search phrases in PubMed. Those phrases included: "SIBO prebiotics" and "SIBO probiotics".

3. Results

3.1 Prebiotics

Galactooligosaccharides (GOS) are among the most common prebiotics. GOS molecules are composed of chains containing two to five galactose residues linked to an N-terminal glucose, which form a lactose unit at their end as a terminal disaccharide. They reach the large intestine unchanged, where they are fermented by gut flora bacteria (10) (11).

A randomized, double-blind, multicenter study was conducted to determine the effect of GOS supplementation on gut microbiota and lactose tolerance. To this end, gut microbiota was analyzed before supplementation, 36 days after the start of supplementation, and 30 days after its completion. It was demonstrated that increasing GOS intake has a beneficial effect on the gut microbiota, particularly Lactobacillus acidophilus and bacteria from the Bifidobacteriaceae family. When comparing the fecal microbiome obtained before and after the end of supplementation, an increase in bifidobacteria was observed in 90% of the study participants. After reintroducing dairy products into the diet and discontinuing GOS supplementation, the gut microbiota in the study group was reanalyzed, revealing an increase in lactose-fermenting Roseburia species. Furthermore, a correlation was demonstrated between beneficial changes in the gut microbiota and clinical improvement in lactose tolerance. In summary, GOS supplementation resulted in a bifidogenic response in 90% of the study participants. A reduction in the severity of at least one symptom was observed in 71% of patients. At the same time, patients who did not achieve a bifidogenic response still experienced symptomatic improvement. These results suggest that GOS supplementation may be a significant factor in improving the quality of life for patients with SIBO (11).

Studies have shown that SIBO and lactose intolerance co-occur in 72% of patients, suggesting that GOS supplementation may have beneficial effects in patients with SIBO. However, it should be noted that bacteria like Bacteroides and Lactobacillus are disaccharide-fermenting bacteria, which may exacerbate some of the symptoms of SIBO, such as bloating (12). The effect of GOS on intestinal function in mice of various ages was also investigated. It was found that GOS supplementation in animals affects more than just the composition of the gut microbiota. In addition to an observed increase in the abundance of Bacteroides and Lactobacillus, a reduction in age-related increased intestinal permeability was also observed. In older mice, an increase in both the density and volume of mucus was observed (2×2 ANOVA, $P < 0.005$). Histopathological examination of the colonic wall revealed an increase in the number of mucin-producing cells, which explains this effect (13).

Inulin, a natural fructan classified as soluble dietary fiber, is a prebiotic that, like GOS, is resistant to digestive enzymes in the upper gastrointestinal tract. In the intestines, it is fermented by gut bacteria, which lowers the pH of the intestinal contents. Inulin stimulates the growth of bacteria such as Bifidobacterium, Lactobacillus, and Bacteroides. Both the fermentation of inulin itself and the increase in the number of fermenting bacteria may exacerbate symptoms in patients with active SIBO. However, inulin supplementation should be considered in patients with SIBO following eradication, as well as in the final stage of treatment, when the goal is to restore microbiota. Further research is needed on the effect of inulin on the gut microbiota in patients with SIBO (14).

Prebiotics are mostly dietary fibers that beneficially alter the composition and activity of gastrointestinal bacteria, providing health benefits to the host (15).Commonly, they are used with probiotics to increase their effect. SIBO treatment consists of antibiotics; the addition of prebiotics could promote the growth of non-pathogenic bacteria. However, studies on the impact of prebiotics alone in SIBO treatment are limited and contradictory. These studies usually show a positive impact of probiotics and prebiotics in treatment by reducing symptoms (16).

Research on human models showed significant improvement in SIBO symptoms, as observed by the Bristol Scale and Rome III criteria before and after 6 months of the experiment. Moreover, probiotics showed notably better results than prebiotics in the treatment, suggesting a probable supportive role in SIBO treatment (17).

Partially hydrolyzed guar gum (PHGG) is a water-soluble dietary fiber that comes from the endosperm of Cyamopsis tetragonolobus L. seeds. It is made up of galactose and mannose and has prebiotic effects. Studies in humans have found that PHGG can help with diarrhea. In one 12-week clinical trial, people took a PHGG sachet each day. Stool consistency, as measured by the Bristol Stool Scale, improved more in the PHGG group than in the placebo group. People taking PHGG also reported better quality of life, as measured by the SF-8 questionnaire. PHGG has demonstrated success in treating osmotic diarrhea, which is prevalent in small intestinal bacterial overgrowth (SIBO), and may therefore contribute to the management and symptom reduction of this condition (18).

3.2 Probiotics

In one clinical randomized study that used six strains of probiotics - Bifidobacterium bifidum, Bifidobacterium lactis, Bifidobacterium longum, Lactobacillus acidophilus, Lactobacillus rhamnosus, and Streptococcus thermophilus - it was found that in the group receiving probiotic supplementation, SIBO symptoms resolved (24% vs. 0%, $P<0.05$) or reduced in many of the participants and the intestinal microbiota showed an increase in the populations of B. lactis, L. rhamnosus, and L. acidophilus. In contrast, this effect was not observed in participants in the group receiving placebo; and the composition of the gut microbiota remained the same. The clinical trial included participants with chronic hepatic disease to determine whether probiotics are effective in such patients with small intestinal bacterial overgrowth. Liver function did not change in any of the groups (19) (20).

Another clinical trial investigating the effects of probiotics combined with prebiotics involved the participation of pregnant women with hypothyroidism and small intestinal bacterial overgrowth. It contains probiotic preparation consisting of Bifidobacterium infantis, Lactobacillus acidophilus, Enterococcus faecalis, and Bacillus cereus and polysaccharide fiber powder used as a prebiotic. Use of this therapy in female patients resulted in a significant reduction in positive results from the pure methane test after 21 days of treatment. The number of positive results was reduced by 46.4% following the implementation of treatment. It also decreased the average concentration of methane and hydrogen in exhaled breath, which are diagnostic tests for SIBO. In addition, the use of a probiotic combined with a prebiotic in patients with clinical hypothyroidism during pregnancy resulted in a reduction in thyroid stimulating hormone (TSH) levels to the range of reference values. The next positive effect was a reduction in the absorption and production of low-density lipoprotein (LDL) cholesterol and total cholesterol (TC) this is due to the increased number of Bifidobacterium and Lactobacillus in the gut microbiota following treatment, as these bacteria support the production of short-chain fatty acids (SCFAs), which activate PPAR receptors as ligands (21) (22).

According to some studies, small intestinal bacterial overgrowth has been observed in some obese patients following bariatric surgery. The study involved patients who had undergone Roux-en-Y gastric bypass surgery; in the group receiving a probiotic containing Lactobacillus acidophilus and Bifidobacterium lactis (5 billion CFU/strain), a reduction in the incidence of bloating was observed. In addition to reducing SIBO symptoms, the use of probiotics in postoperative patients had a beneficial effect on the absorption of vitamins

and microelements. However, this did not reduce the incidence of SIBO in either group. SIBO occurred with similar frequency in the group taking the probiotic and the group receiving the placebo (23) (24).

A study was conducted on patients one year after undergoing Roux-en-Y gastric bypass surgery who had experienced gastrointestinal disorders. The study used probiotics containing Lactobacillus acidophilus, Bifidobacterium lactis, Lactobacillus rhamnosus, Bifidobacterium longum, Lactobacillus plantarum, Bifidobacterium bifidum, and Lactobacillus gasseri. In both the probiotic group and the placebo group, no effect on the occurrence of SIBO was observed based on hydrogen breath test results, nor were there any changes in general gastrointestinal symptoms (25).

Another study examined the effect of Bifidobacterium infantis 35624 on the lactulose breath test for SIBO. The level of methane in exhaled air was higher after supplementation, with double the number of participants reaching the criteria for a positive test result, suggesting an effect on the test outcome. In contrast, the level of hydrogen in exhaled air remained similar (26) (27).

Saccharomyces boulardii is the most commonly studied and used probiotic. Its beneficial influence is widely known and consists of better rehabilitation when implemented in treatment process of antibiotic-associated diarrhea or H.pylori (28) (29). Saccharomyces boulardii may be a promising therapeutic strategy in patients affected by multiple sclerosis who often present with symptoms such as bloating, faecal incontinence or constipation, which resemble SIBO. This strain is not affected by the usage of antibiotics, and it does not spread antibiotic resistance across bacterial agents (28).

Aforementioned yest species seems to be most beneficial when implemented during rifaximin treatment. Researchers conducted the trial where patients with SIBO associated with PPI usage received rifaximin with or without a probiotic. After four weeks the eradication of SIBO was completed, however in the follow-up period SIBO reoccurred in 21.8% in the probiotic group compared to the 41.5% reoccurrence rate in the group who had only received rifaximin (30). In another trial the administration of Saccharomyces boulardii alongside with rifaximin and neomycin did not result in significant changes during the follow-up breath test. On the other hand, the frequency of symptoms reported by participants was downregulated (31). Patients with systemic sclerosis and SIBO may benefit from supplementation with this yeast strain. Saccharomyces used in monotherapy or in combination with metronidazole resulted in a measurable effect. The SIBO occurrence rate diminished by 33% and 55%, respectively. Furthermore, the symptoms of SIBO were down regulated as well (32). Efremova et al. observed twenty patients with cirrhosis and SIBO and supplemented them with Saccharomyces boulardii for three months. At the end of this follow-up the presence of SIBO was downregulated by 80%. What is more, the risk of occurrence of cirrhosis complications such as ascites and hepatic encephalopathy decreases (33).

4.Conclusions

Probiotics and prebiotics may offer beneficial outcomes when used in patients with gastrointestinal problems such as SIBO. Prebiotics including GOS or inulin may act in a synergistic manner with probiotics as its substrates to growth. Some studies report an improvement in symptom occurrence after implementation of that combination. On the other hand, some trials report that inulin should be supplemented under strict rules due to the fact that in some patients with SIBO symptoms may be intensified. Probiotics are widely studied and seem to give benefits in many disorders such as cirrhosis, obesity that in some patients coexists with SIBO. The analyzed material suggests that supplementing with yeast and bacterial strains, including Saccharomyces or Lactobacillus, can diminish not only the symptoms of SIBO but also the risk of complications, for example, in cases of cirrhosis. However, due to the lack of changes in the hydrogen tests after the treatment further multi-center trials are required.

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