

# THE PLACE AND ROLE OF PROBIOTICS IN THE TREATMENT OF IRRITABLE BOWEL SYNDROME

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**Abstract:** Irritable bowel syndrome (IBS) is considered the most common functional disease, being associated with a marked deterioration of the patients' quality of life. However, the pathophysiological basis of IBS is not fully elucidated. As the composition of the gut microbiota was noticed to undergo changes in IBS, the possible use of probiotics in IBS has been intensely debated lately. This paper proposes to review certain theoretical aspects related to probiotics and discuss some recent data regarding the efficiency of probiotics in the treatment of IBS.

Irritable bowel syndrome (IBS) is clinically characterized by chronic abdominal pain, transit disturbances and abdominal distension. It is considered the most frequent functional disease, encountered in about 11-20% of the adult population in the developed countries.(1) Despite its high prevalence, the pathophysiological substrate of the condition is not fully known yet, being probably multifactorial. Several factors are incriminated: hereditary and environmental, infectious, disturbances of intestinal motility, visceral hypersensitivity, psycho-emotional factors, as well as a dysfunction on the brain-gut axis.

As there is no curative therapy of IBS as yet, the objectives of the treatment are represented by the disappearance of symptoms and improvement of the patient's quality of life. For this purpose, a number of drugs are currently used: anticholinergic, anti-diarrheic, tricyclic antidepressants, laxatives, antagonists of serotonin receptors, antispasmodics or antibiotics. However, in many cases these treatments do not have the desired effects.

Given that in IBS, a change of the gut microbiota composition was noticed, its role in the pathophysiology of IBS has been increasingly emphasized recently. Consequently, the possible beneficial effect of probiotics in the improvement of IBS symptoms has become an interesting issue, though the opinions of the various authors differ.

This paper proposes to review certain theoretical aspects related to probiotics and discuss current data on the efficiency of probiotics in the treatment of IBS.

Probiotics are defined as "live microorganisms (most often bacteria) that are similar to certain beneficial microorganisms found in the human gut".(2) They have special properties that make them resistant to the action of the gastric juice and bile and can survive the competition with other intestinal microorganisms.(3)

They have been studied and used in a number of gastrointestinal diseases, among which colitis with *Clostridium difficile*, inflammatory bowel diseases, diarrhea associated with antibiotic therapy and the traveller's diarrhea.(4)

The alterations at the level of bowel microbiosis are considered to be involved in the etiopathogenesis of IBS, the

proof being the onset of IBS symptoms after an acute infectious diarrheic bout.(3,5,6,7,8,9) It has been suggested that the small intestinal bacterial overgrowth (SIBO) could play a role in the generation of symptoms such as abdominal distension, meteorism and flatulence. Various studies provide percentages for the presence of SIBO in IBS, which vary over a wide range: 4 – 84%.(3)

Gastrointestinal infections as well as antibiotic therapy may alter the composition of bowel microbiosis, a situation associated with the onset of IBS symptoms. Certain diet habits (such as consumption of yogurts or fermented foods), characteristic of geographical regions and traditions, may also alter the composition of bowel microbiosis in different individuals.(3)

Starting from these findings, various clinical trials have attempted to identify the role and place of probiotic treatment in IBS.

The mechanisms of action of probiotics at the level of the gastrointestinal wall are considered to be the following: (1) improvement of the mucosal permeability; (2) the suppression of the growth of pathogenic bacteria; (3) the beneficial effect for visceral hypersensitivity; and (4) immunomodulator effect.(10,11)

The most known probiotics are based on bacteria from the *Lactobacillus* and the *Bifidobacterium* species, or non-pathogenic strains of *E. Coli*, *Bacillus*, *Enterococcus*, *Streptococcus Thermophilus* and certain yeasts, such as *Saccharomyces boulardii*.(12)

A number of clinical trials have analyzed the effects of one single microorganism on the various symptoms and/or the IBS patient's quality of life.(14) In a study using *Bifidobacterium infantis* administered for 8 weeks in patients with IBS versus placebo, a significant improvement of abdominal pain, abdominal discomfort and meteorism was obtained in the group receiving the probiotic.(7)

Several studies have used mixtures of bacterial species. Thus, with a mixture of several species of *Lactobacillus* (*L. casei*, *L. plantarum*, *L. acidophilus* and *L. delbrueckii*), *Bifidobacterium* (*B. longum*, *B. breve* and *B. infantis*) and *Streptococcus thermophilus*, good results were obtained

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## CLINICAL ASPECTS

regarding the feeling of abdominal distension after 8 weeks of treatment, but without improvement of other IBS symptoms.(14) The same combination proved to be effective for abdominal distension in another study, versus placebo.(15)

An ample meta-analysis (16) on 19 clinical trials, including 1 650 patients with IBS, found that in 15 trials the IBS score was improved. The authors concluded that probiotics seemed to be efficient in IBS, but stated that the extent of the benefit and the identification of the most effective species and strains could not be documented.

McFarland et al (9) performed a meta-analysis on 20 randomized controlled clinical trials, extracting data on the effectiveness of probiotics in a total number of 1 404 patients. In the 20 clinical trials 23 patient groups receiving probiotics and placebo were compared; 18 studies compared one probiotic versus placebo, one study compared 2 probiotics with placebo, and one study compared 3 doses of the same probiotic with placebo. The studies used various probiotics, but only 2 probiotics were studied in several trials: *Lactobacillus rhamnosus GG* and *Bifidobacterium infantis*. Overall improvement of symptoms was reported by 75% of the studies, while less pain was reported by all the studies. According to the authors of the meta-analysis, these results represent preliminary evidence of the effectiveness of probiotics in IBS, but further studies are needed to confirm this.

Though there is a relatively high number of studies that used probiotics for the treatment of IBS, there are still questions regarding the optimal dose, their place in combined therapy, the specific action of each species, and their stability in the gastrointestinal tract during therapy. In order to find the answer to these questions ample, placebo-controlled studies are needed.(10)

Like in the case of most therapeutic alternatives used in IBS, it is unlikely that probiotics benefit all the patients with IBS.

A number of studies investigated the efficiency of probiotics by differentiating between the two subtypes of IBS: IBS with predominance of constipation (IBS-C) and with predominance of diarrhea (IBS-D), respectively. Thus, in a study on two patient groups (IBS-C and IBS-D) who took yogurt enriched with *Bifidobacterium lactis* and acacia fibers for 8 weeks, the overall improvement of symptoms obtained was significantly superior in the patients with IBS-C as compared to controls, while in the patients with IBS-D, only the transit disturbances symptoms improved.(17)

Given the low cost of probiotics, as well as their safety profile, their use may be taken into account for improving IBS symptoms. However, the aspects related to the quality and composition of the products existing on the market should not be overlooked. And it is important to choose the species proven to have the expected benefits.

Nevertheless, in the absence of consistent large cohort studies that provide solid proof of the effectiveness of probiotics in IBS, it would be unethical to rule out drug therapy, for which we have convincing evidence. It is very likely that the place of probiotics that are well endorsed by studies is beside one or more drug preparations currently used in the treatment of IBS.

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