

# Probiotics in Irritable Bowel Syndrome

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Irritable bowel syndrome (IBS) is one of the most frequent gastrointestinal problems (10–20% of the adult population). IBS is characterized by abdominal pain, excessive flatulence, bloating and an altered intestinal motility pattern for which no structural abnormalities can be found [1]. The diagnosis is made clinically by exclusion of an organic disease using the Rome III criteria.

The main theories to explain the pathophysiology of IBS include alteration in the visceral perception, intestinal microbiota, motility, gut epithelium and immune function. It seems that a dysregulated interaction between the intestinal bacteria, the gut barrier and the intestinal immune system play a role [2]. Patients with IBS have a different composition of intestinal bacteria compared to healthy controls [3]. A nonspecific microscopic inflammation with increased mast cells and neutrophils were found in mucosal biopsies [4]. There are speculations that IBS symptoms may result from cytokine or mediator secretion by these inflammatory cells. Increased production of proinflammatory and decreased production of anti-inflammatory cytokines were in fact demonstrated [5, 6]. In addition, a low-grade inflammatory infiltration and activation of mast cells in proximity to nerves in the colonic mucosa were found and may be involved in the pathogenesis of pain episodes.

These new views in the pathogenesis of IBS changed the treatment approach to influence the composition of the gut microbiota and to stop the inflammatory process and to interfere in the dysregulated intestinal immune system. Among several treatment options, the use of pro-

biotics seemed to be promising. Probiotics are living organisms which, when ingested in certain numbers, exert health benefits beyond inherent basic nutrition [7]. It is well known that specific bacteria strains have numerous positive effects in the gastrointestinal tract. Probiotics reduce the adherence of pathogen bacteria on the epithelial cells and thus the ability of pathogen bacterial translocations. Probiotics can control the growth of pathogen bacteria by stimulating the secretion of bacteriocins and defensins, modulate signal transduction (e.g. NF- $\kappa$ B) and influence the innate/adaptive immune system (e.g. IgA secretion). Therefore, the beneficial effects of probiotics in IBS could be explained by increasing the mass of beneficial bacteria in the large bowel, decreasing a bacterial overgrowth in the small bowel and reversing the imbalance between the pro- and anti-inflammatory cytokines. Recently it was also demonstrated that some lactobacilli strains may modulate intestinal pain attacks by inducing the expression of  $\mu$ -opioid and cannabinoid receptors in the intestinal epithelial cells [8].

For IBS treatment many good clinical studies using mainly lactobacilli and bifidobacteria alone or in combination were published. Nineteen randomized controlled trials with 1,650 patients were recently analyzed in a systemic review [9]. In 10 randomized controlled trials (918 patients) the outcome was analyzed as a dichotomous variable and showed that probiotics were significantly better than placebo. Fifteen randomized controlled trials (1,351 patients) assessed improvement in IBS score as a continuous outcome and again showed a significant ben-

efit for probiotics. There was a significant heterogeneity for both calculations. This review demonstrated only a trend for lactobacilli and bifidobacteria but a significant improvement for different probiotic combinations.

In general, it appears that probiotics are effective in IBS. However, looking on single trials, it seems that probiotics are more effective on single symptoms than on the entire IBS. The specificity of probiotics was demonstrated by O'Mahony et al. [5]. *Lactobacillus salivarius* or *Bifidobacterium infantis* in malted milk drinks were compared, but only *B. infantis* was able to alleviate IBS symptoms. This was associated with a normalization of the ratio of an anti-inflammatory to a proinflammatory cytokine ratio (IL-10/IL-12), suggesting an immune-modulating role for *B. infantis*.

Several studies with *B. lactis* DN-173010 in patients with IBS or abdominal discomfort were published. This strain is interesting. In addition to the known probiotic effects, there is acceleration in slow colonic transit [10–12]. In a double-blind, controlled trial with 267 constipated-predominant IBS patients, Guyonnet et al. [13] found a significant effect on discomfort using the health-related quality of life score. In the subgroup of constipated pa-

tients, also the stool frequency improved significantly. These results were confirmed in 2 large trials including 360 and 253 women with IBS-like symptoms. In both studies, a significant improvement on global symptoms [14, 15] and bloating [14] was demonstrated.

In conclusion, the concept of using probiotics in IBS patients is interesting and it appears that certain probiotics strains are efficacious on several symptoms. Overall, the results from all the published studies are difficult to compare because of variation in the design, probiotics strains used, doses administered and formulation. There is still a need for further studies to determine the most effective species and strain, the right doses and to clarify whether a combination is better than a single strain.

### Disclosure Statement

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