Managing irritable bowel syndrome (IBS): Is microbiome modulation with a medical food the answer?

Managing irritable bowel syndrome (IBS): **Is microbiome modulation the answer?**

As our understanding of the human microbiome continues to grow, its connection to various health conditions becomes ever clearer, bringing exciting health management opportunities. This has immense potential for patients with irritable bowel syndrome (IBS), a common disorder of the digestive system characterized by chronic, recurrent abdominal pain and changes in bowel habits and bloating.[1,2] IBS significantly impacts the lives of those affected and presents a considerable cost burden for healthcare services.[3] Now, a growing body of evidence has demonstrated interesting links between the gut microbiome and IBS that could form the basis for better, more timely patient management, preventing an unnecessary erosion of quality of life.

Recent studies show distinct microbiota differences between those affected by IBS and those who aren't.[1,4,5] In addition, dysbiosis, an imbalance of the microbiome, can be identified in 73% of IBS patients, compared to 16% in healthy individuals.[1] Additionally, perturbed microbial metabolism has been shown to result in a greater production of hydrogen gas, indoles, phenols, and other compounds in those affected by IBS. These findings pave the way to identifying specific IBS biomarkers[1] that could enable more rapid, accurate diagnosis.

Likewise, determining the role of gut dysbiosis in IBS pathophysiology and symptom severity points towards potential management options. Reestablishing microbiome health could improve both the GI symptoms and the psychological comorbidities associated with IBS.[5] Here we take a deeper exploration into the microbiome and the potential for life-changing management for IBS patients.

IBS – A common concern and a major healthcare burden

IBS is a prevalent condition, particularly in developed countries where it is thought to affect at least 10 to 20% of the population.[3,6,7] Its onset is insidious, primarily affecting those under the age of 50 (after which the incidence drops by 25%), and it has a prevalence that is 67% higher in women compared with men.[2,8,9] In addition to the serious impact IBS has on the lives of patients, IBS also represents a major burden on healthcare services and society, particularly because current treatments can only help with symptom management. The healthcare cost in the U.S. alone exceeds $20 billion each year,[10] and the direct and indirect healthcare costs are comparable to other chronic diseases such as hypertension, asthma, and migraine.[3]

The need for new IBS management options

With the exact causes of IBS unknown, the condition is characterized and diagnosed by its symptoms: abdominal discomfort/pain, relief upon defecation, changes in stool pattern, altered bowel habits (diarrhea, constipation), bloating, dyspepsia, dysphagia, nausea, and pain.[1,10,11] It is often associated with other somatic comorbidities, mental health conditions (including depression and anxiety) and visceral hypersensitivity.[1,2,11]

A variety of environmental factors are known to influence IBS, including stress, environmental toxins, nutrient depletion in our foods, food hypersensitivity, poor water quality, chronic infections, antibiotic usage, increased use of antibacterial products, and dysbiotic gut microbiota.[1,11–17] As a chronic condition with symptoms that can come and go over periods of days, weeks, or months, IBS can seriously impact quality of life.[18]

In the absence of a cure, the first step in symptom management involves lifestyle and dietary modifications—most commonly, the adoption of low fermentable oligo-, di-, and monosaccharides, and polyols (FODMAPs) and gluten-free diets, plus regular exercise and psychological therapy.[5,10] Pharmacological interventions are used to target some specific symptoms of IBS; however, some of these medications may themselves result in serious adverse events.[19]

The role of the microbiome in human health

Humans are home to trillions of microbes—bacteria, archaea, viruses, fungi, and multicellular parasites[20]—which

play an important role in many of the physiological and pathophysiological processes that influence host health. Each of us has about 20,000 human genes in our 23 chromosome pairs. But, amazingly, researchers have discovered that our microbial genetic catalog ranges from 2 to 20 million microbial genes. So, at the genetic level, we are, at best, 1% human and 99% microbial. From this perspective, the genes of our microbiome essentially present a second genome which augments the activity of our own.[21,22]

An increasing amount of research demonstrates the importance of the microbiome in maintaining gut health, with these microbial communities playing a vital role in gastrointestinal homeodynamic balance.[23] The human gut is highly dynamic and undergoes temporal changes from birth to adulthood. In the first years of life, the microbiota grows and diversifies. It then stabilizes in adolescence, and, in adulthood, the composition often changes once more, becoming less diverse. Research suggests that the human gut is likely to be affected by environmental factors, including xenobiotics, stress, diet, and lifestyle. Furthermore, the gut microbiome itself is also likely to be a good predictor for metabolic variables and clinical phenotypes.

How does the microbiome offer solutions for IBS management?

Many studies have concluded that dysbiosis of the gut microbiota plays an important role in the pathogenesis of IBS,[5,6] and the Rome Foundation recently incorporated this view into its clinical guideline about the manipulation of the gut microbiota in IBS.[24] Distinct differences have been observed between the intestinal microbiota of IBS patients compared with healthy controls. In the latter, intestinal bacteria typically comprise Firmicutes (64%), Bacteroidetes (23%), Proteobacteria (8%), and Actinobacteria (3%).[1] However, in IBS patients, results have consistently shown increased amounts of Firmicutes and reduced amounts of Bacteroides.[6] In addition, it has been observed that the different subtypes of IBS have different gut microbiota composition—for example, a lower abundance of butyrate-producing bacteria in IBS-D and IBS-M.[1,6]

Further studies have explored the bidirectional pathways of the gut-brain-microbiota axis, establishing that signals from the brain can influence the sensory, motor, and secretory functions of the GI tract.[6] Conversely, dysbiosis of the gut microbiota can activate mucosal immunity, leading to a damaging of the epithelial layer, which functions as a protective barrier, and resulting in dysmotility and hypersensitivity in IBS patients.[6] Furthermore, with the intestinal barrier function also linked to brain and neurologic function, disruption to that barrier can also influence all the other body systems, including the central nervous system.[16]

It therefore makes sense that modulating the microbiome to reduce dysbiosis should offer a clinical benefit to IBS patients.

Studies show that probiotics combined with beneficial microorganisms already present in the GI tract, through several mechanisms, contribute to healthy gut balance and immune function—for example, by preventing pathogens from increasing intestinal permeability by improving mucosal barrier function.[25,26] Probiotics directly support both the innate and adaptive immune responses by beneficially modulating the inflammatory response and positively influencing the function of our immune cells—not only helping to educate the immune system during development but also maintaining healthy immune function throughout life. Likewise, prebiotics can also be used to enhance gut health[6,27-30] and reduce dysbiosis via microbiome modulation. [1,6]

Tools to enable microbiome modulation

Improving microbiome health (in terms of both the number and biodiversity of microbes present in the gut) has become an increasingly common approach to achieving a variety of health benefits—and this offers great potential for IBS, too. While there are a variety of methods (such as diet modification or fecal transplants), there is growing support for the use of medical food products that provide a quick and easy way of boosting the microbiome, replenishing it with certain bacteria, altering gut pH, providing barrier protection, and beneficially modulating the inflammatory response.

Such medical food prodcuts include:

Probiotic Medical Foods

Probiotics are viable microorganisms which, when administered in adequate amounts, have a beneficial effect on their host organism.[31] They are frequently administered via capsules, powders, or chewable tablets and most commonly contain *Bifidobacterium, Lactobacillus, Streptococcus thermophilus, Saccharomyces,* and/or *Bacillus* species. Probiotic products may contain either a single species or a mixture of different species. Their effects can be specific to the species and strains involved, and the same bacteria may behave differently and offer different benefits when used in combination.

When selecting a probiotic medical food to help with IBS management, choose a product that clearly states that

it contains live and active bacterial cultures and offers a combination of different species. Ensure that the specific species within the probiotic medical food are named together with their CFU counts and that they are those best suited to reducing the symptoms of IBS. Moreover, high-quality probiotics incorporate a gastric acid protection technology that prevents probiotics from dying in the stomach and ensures the optimal delivery of the probiotics to the intestine.

Prebiotic Medical Foods

Prebiotics are non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon that have the potential to improve health.[32] Furthermore, they are shown to positively modulate gut ecology by acting as carbon sources for primary and secondary fermentation pathways in the colon, supporting digestive health in many ways, including producing beneficial metabolites, increasing mineral absorption, decreasing protein fermentation, modulating inflammatory response, and improving gut barrier integrity.[33]

Prebiotics are commonly found in fruits and vegetables, particularly those containing complex carbohydrates. Common prebiotics include fructooligosaccharides (FOS), galactooligosaccharides (GOS), xylooligosaccharides (XOS), inulin, fructans, and partially hydrolyzed guar gum.[1,20,34] Prebiotics should not be absorbed in the upper gastrointestinal tract but should be easily and selectively fermentable by the beneficial intestinal microbiota.

Care should be taken, however, to identify the best prebiotic medical food for IBS management, as many prebiotics contain high amounts of high-FODMAP substances, in particular the oligosaccharides. As a result, while some individuals with GI sensitivities may be able to quickly digest the short-chain oligosaccharides, they may metabolize so fast as to result in uncomfortable symptoms such as gas, bloating, and diarrhea—especially if a person is new to prebiotic use. These same individuals often have reduced populations of beneficial bacteria in the gut, making the processing of long-chain fibers, including resistant starches, especially challenging. In contrast, prebiotics that are certified as low-FODMAP, such as partially hydrolyzed guar gum, make ideal prebiotics for those with IBS who want to support a healthy microbiome without the struggle of digesting complex fibers.

Synbiotic Medical Foods

Synbiotics are food ingredients or medical foods that combine prebiotics with probiotics to offer a synergistic effect. Together, they may offer a more profound influence on GI function than that achieved with probiotics or prebiotics alone. With synbiotics, the prebiotic favors probiotic microorganisms, improving their survival and growth in the GI tract.[26] The prebiotic provides a food source for both the probiotic bacteria in the product and the beneficial bacteria present in the gut.

It is thought that, with the use of prebiotics, probiotic microorganisms gain better tolerance to a range of environmental conditions within the intestine, such as pH, oxygenation, and temperature.[26]

With such a large number of possible prebiotic and probiotic combinations, there is great promise in the application of synbiotic medical foods for modulating the microbiome.

When selecting a synbiotic for IBS management, it is important to consider both the probiotics and prebiotics contained in the medical food and to ensure that they align with the benefit sought. As mentioned above, for those with IBS, low-FODMAP prebiotics should be chosen.

Tools for IBS Management

- **Probiotic Medical Foods:** viable microorganisms which have a beneficial effect on their host organism
- **Prebiotic Medical Foods:** non-digestible food shown to positively modulate gut ecology and support digestive health in many ways
- **Synbiotic Medical Foods:** food ingredients or dietary ingredients that combine prebiotics with probiotics. These have a synergistic effect and may offer a more profound influence on GI function than probiotics or prebiotics alone.

Improving IBS with microbiome modulation

It is now clear that the composition of the gut microbiome is intrinsically linked to human health and has a considerable influence over a wide range of medical conditions, especially GI-related issues like IBS. Therefore, it makes sense that probiotic medical foods can be used as an intervention tool, where altering the microbiome composition can have a beneficial impact on medical conditions and alleviate the symptoms. For patients with IBS in particular, this can significantly improve the quality of life, as demonstrated in the studies below.

Many specialists now consider the use of probiotic medical foods to modulate the microbiome to be a good management option for IBS patients. Not only is there considerable research demonstrating their effectiveness in reducing GI symptom severity and improving quality of life, in terms of both emotional well-being and social functioning for certain IBS subtypes,[5,35] but probiotics also have a history of safe use.[36]

In several randomized control trials, IBS symptoms were alleviated following the use of probiotic strains including:

- After six weeks, both *L. acidophilus* and *B. lactis* reduced severe abdominal pain. Compared to the placebo, probiotics also improved abdominal distension (bloating), bowel habits, and quality of life. Those who took either probiotic also had more normally formed stools.[37]
- *L. plantarum* reduced abdominal pain and bloating in a four-week study. 38 Results of a 12-week study showed it reduced the severity of abdominal pain by 67%, diarrhea by 70%, and constipation by 79%. It's also worth noting that *L. plantarum* may help improve the quality of life in those with IBS. People who took this probiotic reported a 110% improvement in mental well-being after 12 weeks.[39]
- Adults diagnosed with functional constipation reported more regular bowel movements after taking the probiotic *B. animalis lactis* for 28 days, compared to those who took a placebo.[40]
- *Lactobacillus acidophilus* and *Bifidobacterium animalis* subsp. *lactis* have both been shown to improve abdominal pain and symptom severity, with a corresponding normalization of bowel habits in adults with IBS. Quality of life scores were significantly improved in participants taking *L. acidophilus*.[37]
- Use of *Lactobacillus plantarum* provided effective symptom relief (particularly of abdominal pain and bloating) in IBS patients.[38]
- After 12 weeks, adults with moderate to severe IBS-related pain who took the probiotic *L. acidophilus* reported significantly less abdominal pain compared to those who took a placebo.[41]
- Multispecies probiotics (*B. longum, B. bifidum, B. lactis, L. acidophilus, L. rhamnosus*, and *S. thermophilus*) proved effective in the global relief of IBS symptoms and induced the alterations of intestinal microbiota in those with IBS.[42]

The beneficial effect of probiotics in IBS extends across many genera, species, and strains, and the diversity and complexity of IBS may indicate that a multispecies probiotic combination could be more efficient than a single strain for IBS.[10]

IBS management – A potential new frontier

There are a lot of factors that influence IBS, but its causes remain undefined. Increasing evidence is building a picture that shows how the microbiome is closely linked to IBS. Importantly, some studies are now showing that modulation of the microbiome through the use of prebiotic, probiotic, and synbiotic medical foods has successfully alleviated IBS symptoms, and this offers a promising management option for IBS patients and, most importantly, for improving their quality of life.

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