

Irritable Bowel Syndrome: Medical and Nutritional Therapies

Irritable bowel syndrome (IBS) is a functional disorder of the gastrointestinal (GI) tract characterized by abdominal pain/discomfort and altered bowel habits, e.g. diarrhea (IBS-D), constipation (IBS-C), or alternating periods of both (IBS-A). In western countries, approximately 10-15% of adults suffer from the disorder,¹ but only 10-30% of IBS patients seek medical care.² Because the etiology of IBS is multi-factorial and not entirely understood, IBS treatment typically focuses on symptom alleviation.

Medical Therapy

Due to the wide range of IBS symptoms, there are no unique pharmacologic targets for therapy, and it is necessary to include multiple therapeutic interventions in IBS treatment.³

Table 1. Symptom – Based Treatment of Irritable Bowel Syndrome

Pain Predominant	Diarrhea Predominant	Constipation Predominant
Antispasmodic Agents	Antidiarrheal Agents	Serotonin (5-HT ₄) Agonist
<ul style="list-style-type: none">• Dicycloverine (Bentyl)• Mebeverine	<ul style="list-style-type: none">• Loperamide (Imodium)• Cholestyramine (questran)	<ul style="list-style-type: none">• Tegaserod (Zelnorm)
Tricyclic Antidepressants	Serotonin (5-HT ₃) antagonist	C-2 chloride channel activator
<ul style="list-style-type: none">• Amitriptyline	<ul style="list-style-type: none">• Alosetron (Lotronex)• Ondansetron (Zofran)	<ul style="list-style-type: none">• Lubiprostone (Amitiza)
		Over-the-counter laxatives
		<ul style="list-style-type: none">• Bulk-forming laxatives• Stool softeners• Lubricant laxatives• Stimulant laxatives• Saline laxatives

Drugs are prescribed according to a symptom-based rationale (Table 1). For IBS patients with pain-predominant symptoms, antispasmodic agents and tricyclic antidepressants have shown benefit.⁴ Antispasmodic agents may reduce abdominal pain or bloating via anticholinergic effects and direct smooth muscle relaxation, whereas antidepressants ameliorate pain by a central antinociceptive effect. However, these drugs mainly provide short-term relief of abdominal pain; evidence for long-term use is not available.⁵

For patients with diarrhea-predominant symptoms, antidiarrheal agents, such as loperamide,

may decrease the frequency of bowel movements and increase water absorption. Also, in some patients with severe diarrhea, bile acids may lead to decreased water reuptake from the colon. As a bile acid sequestrant, questran may be used as a second line agent in the treatment of diarrhea-predominant IBS. In addition, a serotonin antagonist can be used to slow colon transit, but there is no benefit on abdominal pain. Alosetron has proven more effective than placebo at relieving global IBS symptoms in IBS patients with diarrhea. However, this agent was withdrawn from the market in 2000 because of serious post-marketing events, including severe constipation, ischemic colitis, and death. Since then, the FDA has approved the reintroduction of alosetron, under strict prescribing and patient guidelines, for female patients with IBS-D in which conventional treatments have failed.⁶ Ondansetron (Zofran) is another 5-HT₃ antagonist and it is currently used largely for the management of severe nausea and vomiting. It has been studied for use in IBS-D also.

For patients in whom constipation is the predominant manifestation of IBS, laxative consumption is usually recommended. Dietary fiber may be considered a laxative and will be discussed in detail in the nutrition section. Another avenue that is available to these patients is serotonin agonists, which may increase intestinal movement. Clinical trials have shown that Tegaserod is more effective than placebo at relieving global IBS symptoms in female IBS-C and IBS-A patients, but commonly cause diarrhea. In addition, there have been some cardiovascular adverse events; therefore, FDA has requested its withdrawal from the market. Finally, Lubiprostone, a C-2 chloride channel activator, is approved by the FDA for IBS-C in women. This medication stimulates secretion of chloride-rich fluid in GI epithelial cells, softening the stool and increasing mobility. Studies need to be conducted in men before this agent can be recommended for use in men.⁵

Nutritional Therapy

Drug therapy for IBS is constrained by its side effects and short-term use. Nutritional therapy does not have these limitations. The most widely studied nutritional interventions for IBS are fiber and probiotics.

Fiber

Fiber is a term used to refer to compounds that are resistant to digestion and absorption in the small intestine, allowing them to reach the large intestine with complete or partial fermentation.⁷ Based on water solubility, fiber can be divided into soluble and insoluble fiber. Soluble fiber tends to produce a viscous mass that delays small intestine absorption. It is fermented by colonic bacteria to a greater extent than insoluble fiber and is widely used as a bulking agent. Examples of soluble fibers include psyllium, calcium polycabophil, and partially hydrolyzed guar gum. Most insoluble fiber, in contrast, is poorly fermented. They increase the size and bulk of the stool.⁸ Wheat and corn brans are types of insoluble fiber.

There have been many clinical trials that have evaluated the use of fiber in IBS. However, the quality of most studies is not high. Limitations of these trials include small sample size, short treatment duration, strong placebo effect, lack of standardized inclusion criteria, lack of clarity regarding patient classification, and large variations in the outcomes measured (abdominal pain/discomfort, bowel movement difficulty, composite score of overall IBS symptoms, quality of life, etc).⁸ Despite the quality issues of these trials, the overall conclusion is that fiber does not significantly improve global IBS symptoms compared to placebo. Soluble fiber demonstrated a tendency to ameliorate global IBS symptoms, causing occasional bloating and pain, whereas insoluble fiber worsened the symptoms.^{9,10} While these findings suggest that fiber may not be appropriate for IBS treatment per se, data has shown its benefit in relieving constipation. Some scientists have recommended starting with low amounts of fiber and gradually increasing intake up to 20-30 grams/day to avoid bloating and gas.^{2,11}

Probiotics

The WHO/FAO definition for probiotics is "[l]ive microorganisms, which when administered in adequate amounts, confer a health benefit on the host."¹² Examples include lactic acid bacteria and bifidobacteria, which are widely used in yogurts and other dairy products.

There are several potential reasons that probiotics have beneficial effects. 1) They compete with pathogens by binding to the intestinal epithelium. 2) They can change cytokine profiles from pro-inflammatory to anti-inflammatory. 3) They ferment fiber, producing

nutrients for the gut and altering gut motility. 4) They up-regulate the secretion of mucin, which has lubricant and surface protective properties that help to maintain gut integrity.¹³⁻¹⁵ There are a large number of beneficial bacteria from which to choose probiotic strains. To be used in food or nutrition supplements, the bacteria are selected based on certain criteria; they must have a human origin, be nonpathogenic, be resistant to human intestinal acid and bile, be resistant to technologic processes, and be able to adhere to, colonize, and be metabolically active in the GI tract.¹⁶ Several reviews and meta-analyses have concluded that probiotics could have a role in improving some symptoms of IBS. However, there are many variables that impact the interpretation of results, such as species, strain, dose, formulation, treatment duration, and outcome measurement.¹⁷⁻²¹ Therefore, it is difficult to derive an optimal strategy for using probiotics in IBS patients. A recent 2009 review evaluated 16 randomized, placebo controlled trials and found that only *Bifidobacterium infantis* 35624 achieves significant improvement in abdominal pain/discomfort and/or bowel movement difficulty. There was inadequate data to comment on other probiotics due to problematic study designs.¹³ Two clinical trials have examined *B.infantis* 35624 and IBS.^{22,23} In the first study, it was found that when 10 billion live *B.infantis* 35624 were provided in a malted milk drink consumed each day for 8 weeks, symptom scores for abdominal pain/discomfort, bloating or distention, and bowel movement difficulty improved significantly. This improvement was associated with normalization of IL-10/IL-12 level. In the subsequent 4-week trial, they confirmed this finding in women subjects, and investigated an encapsulated formulation of three different doses. The optimal dose was found to be 10 million live *B.infantis* 35624.

Besides Align, several other probiotic supplements are available and listed in Table 2. Some contain a single strain of probiotics, such as Culturelle (*Lactobacillus* GG) and Sustenex (*Bacillus coagulans*), while others contain mixtures of probiotics, with or without prebiotics (e.g. inulin, FOS, acacia gum). Prebiotics are nondigestible food ingredients that improve host health by selectively stimulating the growth and/or activity of certain bacteria in the colon.²⁴ The potential benefit for IBS is that prebiotic fermentation may produce short chain fatty acids (SCFA), which have the following physiological effects: 1) SCFAs enhance

water and electrolyte absorption, useful in treating diarrhea; 2) SCFAs lower the pH in the colon, inhibiting pathogen growth; and 3) SCFAs are a nutrient source for colonocytes.²⁵ However, when tested in IBS trials, conclusions were similar to those for fiber. Prebiotics are beneficial for relieving constipation, but results for IBS are questionable. Some studies showed no benefit; others demonstrated improvement in IBS symptoms, but lacked control or blinding. Similarly, symbiotics (combinations of probiotics and prebiotics) lacked efficacy or were tested using an uncontrolled design.⁹

Table 2. Table of probiotics products for IBS treatment in the market

Product	Company	Functional Ingredients	Claims	Directions and Cost/month
Align	P&G	<i>Bifidobacterium infantis</i> 35624 (Bifantis(R))	clinically proven to protect against episodes of abdominal day; discomfort, constipation, diarrhea, urgency, and gas and bloating; #1 gastroenterologist recommended probiotics	one capsule per day; \$30/month
Culturelle	Amerifit Brands, Inc	<i>Lactobacillus</i> GG 10 billion cell + inulin 245mg/capsule	Reduce uncomfortable gas and bloating; prevent and shorten the duration of occasional diarrhea; promote regularity. #1 pharmacist recommended probiotics	One capsule per day; \$23/month
Sustenex	Ganeden Biotech, Inc	GanedenBC30 (<i>Bacillus coagulans</i>) 2 billion viable cells + calcium 140mg/capsule	Delivers 10 x more cells than yogurt, maintains the immune system, supports digestive health	One capsule per day, \$14/month
Phillips' colon health Probiotic supplement	Bayer HealthCare LLC	Proprietary Blend: 1.5 billion cells (L.acidophilus, B.bifidum, B.longum)/capsule	Replenishes good bacteria to promote overall digestive health; helps naturally promote regularity; supports a healthy immune system	One capsule per day, \$12/month
Acidophilus Probiotic complex	General Nutrition Corporation	Probiotic Complex Blend: 1.5 billion organisms (at the time of manufacture), L.acidophilus , B.bifidum, L.helveticus, L.lactis sp. Lactis, L,rhamnosus, L.salivarius, S.thermophilus	Promotes healthy digestion and natural resistance	One -two capsule per day, \$3-6/month

Boots probiotic and Prebiotic capsules	Boots Pharmaceutic als Inc.	L.Acidophilus 35mg (containing 3bn live cells); B.Lactis (containing 1bn live cells) FOS; Acacia Gum	One-two capsule per day, \$8-16/month
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Conclusion

Because IBS is treated on the basis of symptoms, there is no “one-size-fits-all” therapy. Medications are administered based on whether the patient’s experience is dominated by pain, diarrhea, or constipation. Nutritional therapies such as fiber and pre-/probiotics can be used to augment medical treatment, but findings regarding efficacy vary. Until the etiology of IBS is better understood, it does not seem likely that treatment will improve. (For information regarding the basis of IBS, see the ANHI pearl on IBS Diagnosis and Pathology.)

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