

ADVANCES IN IBS

Current Developments in the Treatment of Irritable Bowel Syndrome

Section Editor: William D. Chey, MD

Highlights of the Updated Evidence-Based IBS Treatment Monograph



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G&H Why was an update to the monograph on the management of irritable bowel syndrome necessary?

EQ An update to the monograph on the management of irritable bowel syndrome (IBS) was necessary because quite a few developments have occurred in this field since 2014, when the previous monograph was published. The most obvious changes were related to diets and several of the newer pharmacologic agents.

G&H What was the methodology for including studies in this update?

EQ The American College of Gastroenterology Task Force (of which I am a member) conducted a systematic review, meaning we abided by the current guidelines for the performance of systematic reviews and meta-analyses. A detailed literature search was performed in every major database using predefined search criteria that we believed might be relevant to the field of IBS. All terms relating to IBS and every possible therapy were used as the basis for these searches. The literature derived from these searches was then scrutinized, and studies that met the inclusion criteria (eg, randomized, controlled trials; parallel design; lasted for ≥ 1 week) were then examined in detail, and data were extracted for the meta-analysis. The updated monograph was then published in the June 2018 issue of *The American Journal of Gastroenterology*

and is available at <https://www.nature.com/articles/s41395-018-0084-x>.

G&H How is an evidence-based monograph different than a guideline?

EQ The 2 publications are quite different. A guideline basically instructs physicians on how to treat a patient, starting with specific treatments before moving on to a different treatment or method. An evidence-based monograph is a systematic and detailed review of the available literature, or, in this case, the new literature since the publication of the last monograph. The Task Force evaluated the evidence for individual treatment categories and assessed how well the methods stack up. Importantly, the monograph does not directly compare treatments, as there are few, if any, published studies that have performed head-to-head comparisons of 2 or more IBS treatments. Physicians can use the information from the monograph to guide how they treat patients, but it is not intended as a guideline.

G&H What are the key changes in the updated monograph?

EQ Exercise and diet therapies emerged as one of the newest categories since the release of the last monograph, and is one that the Task Force looked at in the most detail. In the intervening years, there have been numerous studies

performed on the roles of diet and dietary manipulation in IBS. Three fairly firm conclusions were made following the review of these studies: (1) the low-fermentable oligosaccharide, disaccharide, monosaccharide, and polyol (FODMAP) diet seems to be effective for overall IBS symptom improvement; (2) a gluten-free diet is not effective for symptom improvement; and (3) conducting tests to detect various types of allergies or intolerances in order to base a diet on those results does not appear to be effective. Of these 3 conclusions, the most impressive data that came out of the research was the evidence for the low-FODMAP diet. Not only were there more studies on this diet, but the results were fairly consistent and favorable, at least for the short-term management of IBS.

G&H What strength of recommendation was given to exercise and diet therapies?

EQ Exercise and diet therapies received weak recommendations due to the lack of high-quality evidence. It is clear that exercise is better than a sedentary lifestyle in terms of general health, and there is some encouraging evidence to suggest that exercise might help patients with IBS. However, there are few studies on this topic, and the number of patients involved is small. Thus, despite the evidence suggesting the benefits of exercise in patients with IBS, there are currently not enough data to be absolutely conclusive. Similarly, dietary studies are challenging to conduct; as there is no adequate placebo, it is difficult to perform a truly double-blind, randomized, controlled trial of a diet in any disease condition, including in IBS, and to recruit the large numbers of patients needed to garner proper results. In terms of study design and performance, the quality of a diet study is not at the same level of a drug study. The Task Force concluded that although there was evidence for the low-FODMAP diet, it was not enough to allow a strong recommendation.

G&H What does the monograph recommend regarding prebiotics, synbiotics, and probiotics?

EQ We did not find evidence supporting the idea that prebiotics and synbiotics were effective in IBS management, and, thus, we do not recommend their use. In contrast, studies demonstrated that probiotics did improve global gastrointestinal symptoms, as well as the individual symptoms of bloating and flatulence in patients with IBS. However, determining which probiotic is best was difficult. There were very few, if any, head-to-head studies, and the quality as well as the multitude of studies focusing on individual probiotic strains made recommending the optimal probiotic or probiotic cocktail challenging.

G&H How does the monograph address the use of antibiotics?

EQ Several new studies on antibiotics were published since the release of the previous monograph, and they were consistent with prior studies in suggesting that rifaximin (Xifaxan, Salix) was effective in reducing global gastrointestinal symptoms and bloating in patients with diarrhea-predominant IBS. However, rifaximin is not indicated in patients with constipation-predominant IBS.

G&H What strength of recommendation was given to prosecretory agents for the management of IBS?

EQ Three prosecretory agents are available: linaclotide (Linzess, Allergan/Ironwood Pharmaceuticals), lubiprostone (Amitiza, Takeda), and plecanatide (Trulance, Synergy Pharmaceuticals), with plecanatide being the most recently approved agent. All 3 of these agents had convincing data to support their use in patients with constipation-predominant IBS, and were supported by several high-quality, randomized, controlled trials. Therefore, these agents received a strong recommendation for use in managing IBS.

G&H Beyond the medications discussed in the monograph, are there any treatments on the horizon of which gastroenterologists should be aware?

EQ Yes, there are a number of drugs currently under development. Tenapanor, a prosecretory agent, has promising results from phase 3 studies for the treatment of constipation-predominant IBS. This drug works in a different manner than the 3 prosecretory agents mentioned previously, but the basic effect is similar. Additional studies are being conducted on a variety of other agents, which are directed at pain, diarrhea, or constipation. More data can be expected within the next few years.

G&H How do you anticipate the management of IBS changing over the next decade?

EQ The biggest change thus far has involved diet. Patients have been telling their physicians for a long time that their symptoms are aggravated by eating, thinking perhaps that allergies could be a cause. While I do not think there is a big role for allergy in IBS, there is a role for food intolerance. As such, the movement toward looking at patients' diets in more detail is a major shift in the management of IBS.

I expect to hear more in the area of the microbiome in the coming years. IBS management will look to changes in the microbiome, whether it is altered by probiotics or antibiotics, or through additional research with prebiotics or synbiotics. My hope is that gastroenterologists will have some guidance, such as from baseline microbiome testing, that will enable them to select patients who might respond best to a prebiotic, a probiotic, or an antibiotic.

A related issue is the role of the gut-brain axis (also referred to as the microbiome-gut-brain axis) in IBS. Although new data were not available for the update to the monograph, the Task Force remains interested in and convinced by the role of antidepressants in IBS. We also were impressed by data on other psychological therapies, such as behavioral therapy, relaxation therapy, and hypnotherapy. This is another area that I hope we will see expand in the coming years.

Another group of compounds that I am looking forward to having data on is drugs that influence bile salt absorption. Drugs that inhibit bile salt absorption, such as elobixibat, appear promising for patients with constipation-predominant IBS, although no new data have been published for a number of years. Similarly, drugs that chelate bile salts and reduce their intraluminal concentration might be helpful for patients with diarrhea-predominant IBS.

Pain and bloating continue to be a management challenge, and research into modulating pain receptors and pathways is ongoing and should lead to new agents.

G&H What are the priorities of research?

EQ More large-scale studies are needed that focus on diet in IBS. Research into the role of the microbiome in IBS would also be beneficial: Is it predictive of outcome?

Is it predictive of responsive therapy? The other area in which progress is needed is the management of pain in IBS, as good agents for managing diarrhea and constipation already exist.

Dr Quigley has served as a consultant and/or on the advisory board for Alimentary Health, Allergan, Biocodex, Commonwealth Laboratories, 4D Pharma, Menarini, Rhythm, Salix, Shire, Synergy Pharmaceuticals, and Vibrant; has served as a speaker for Allergan, Biocodex, Pharmasierra, and Sanofi; has received research support from 4D Pharma, Allergan, Rhythm, Theravance, and Vibrant; and has been a nonexecutive director, shareholder, and patent holder for Alimentary Health.

Suggested Reading

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