

ADVANCES IN IBS

Current Developments in the Treatment of Irritable Bowel Syndrome

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Update on Irritable Bowel Syndrome Guidelines



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G&H Why is a guideline update on the management of irritable bowel syndrome necessary?

BL Over the last few years, the field of irritable bowel syndrome (IBS) has experienced many changes with significant advances in terms of novel diagnostic tests and new information regarding diet and medications. Several gastroenterology societies have released, or are in the process of updating, guidelines on the management of IBS. The British Society of Gastroenterology published its guideline in 2017, which, although helpful, is not widely used by clinicians in North America. The American Gastroenterological Association is currently updating its guideline, which is expected to be published in 2021. The American College of Gastroenterology (ACG) released a comprehensive monograph in 2014, with an updated version published in 2018. However, the newest ACG IBS Clinical Practice Guideline is different from the guidelines that have been previously published. In addition to expert opinion and a summary of review articles, the updated guideline uses Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology, which is the strictest set of guidelines to provide the best level of evidence to clinicians. With all of the changes in

the field, it felt appropriate to assess the quality of evidence and the strength of recommendations.

G&H How was the new ACG guideline developed?

BL This guideline, which was a collaborative group effort involving experts in the field of IBS, was developed for clinicians. My colleagues and I reviewed the literature and identified 25 clinically important questions that we felt would be most valuable to clinicians. Nine of those questions focused on diagnostic testing, and 16 questions focused on therapeutic testing. Using GRADE methodology, we then provided guidance on the strength of the data (eg, strong or conditional recommendation) as well as the quality of the evidence, which is ranked high, moderate, low, or very low.

G&H What is the current status of diagnostic testing for patients with IBS? What strength of recommendation is given to these tests?

BL One change from past guidelines that was made based on the Rome IV criteria is that it is now acknowledged that limited diagnostic testing, including a complete blood

count and a C-reactive protein (CRP) test, is reasonable. Diagnostic testing generally depends on the subtype of IBS, and the biggest change in this area concerns diarrhea-predominant IBS (IBS-D). Based on data from the literature and on individual studies and systematic reviews, clinicians now recognize that it is appropriate to check for celiac disease in patients with IBS and diarrhea. Serologic tests, such as serum immunoglobulin A and serum tissue transglutaminase antibody, may identify approximately 2% to 3% of patients who have celiac disease, either instead of or in addition to their presumed IBS. The average prevalence rate of celiac disease in the United States is approximately 0.5%; thus, serologic testing for celiac disease is recommended in patients with IBS-D. It is also recommended to check CRP levels and fecal lactoferrin in patients with IBS and diarrhea symptoms. One of the concerns of patients and clinicians is whether symptoms of IBS-D are truly from IBS or whether they might be inflammatory bowel disease (IBD). There are very good data from a number of studies showing that if a patient's CRP level is quite low (<0.5 mg/L), it is highly unlikely he or she will have IBD. In addition, fecal lactoferrin has a very high sensitivity and specificity for excluding IBD. CRP and fecal lactoferrin are 2 tests that are easily performed, inexpensive, and can distinguish IBS from IBD. Using the GRADE methodology, both routine testing for celiac disease and checking for CRP and fecal calprotectin receive a strong recommendation with a moderate quality of evidence. The data supporting checking fecal lactoferrin were of lesser quality, and this method received a strong recommendation but with a very low quality of evidence.

G&H What are the current recommendations for diet and lifestyle changes?

BL Dietary interventions have advanced significantly over the years in ways that allow clinicians to review data carefully. A decade ago, a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) was not well known. However, patients now come in prepared and routinely talking about the nuances of a low-FODMAP diet and comparing certain recommendations from one website to others that they have read and reviewed. Clinicians recognize that a low-FODMAP diet does improve symptoms in many, but not all, IBS patients, as has been demonstrated by a systematic review and meta-analysis. In contrast, many clinicians recommend (and many patients choose) a low-gluten diet, but the worldwide evidence for this diet is actually not very good. In fact, there have only been 2 randomized, controlled trials that could be evaluated, and they were published in *The American Journal of Gastroenterology* in 2018.

Lifestyle changes are more challenging, as additional data are needed to confirm typical recommendations. For example, clinicians frequently suggest exercise and better sleep, as there are some data showing that these factors

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improve IBS symptoms. However, there is not enough information to analyze the impact of these changes using GRADE guidelines.

G&H What important changes or recommendations were made regarding pharmacologic therapies?

BL Several major updates have occurred in this area since the publication of the 2014 and 2018 ACG guidelines. Rifaximin (Xifaxan, Salix), which was not mentioned in the 2014 guidelines because the data were still being evaluated, now has a strong recommendation for the treatment of IBS-D symptoms. Secretagogues such as plecanatide (Trulance, Salix) and linaclotide (Linzess, AbbVie/Ironwood Pharmaceuticals) now have high rankings. Plecanatide, which is a guanylate cyclase activator, was not available several years ago, nor was it mentioned in the 2018 update to any great degree. Clinicians now recognize that these therapies can be very effective at treating symptoms. Another important change from the 2014 and 2018 guidelines is the reintroduction of tegaserod (Zelnorm, Alfasigma USA), a 5-hydroxytryptamine-4 agonist that is recommended for women 65 years of age or younger (and with ≤ 1 cardiovascular risk factors) with symptoms of constipation-predominant IBS who have failed secretagogue therapy. A key characteristic of IBS is abdominal pain, and clinicians have come a long way in understanding and learning how to treat that. The use of neuromodulators (in particular, the use of tricyclic antidepressants) is now recommended for the treatment of abdominal pain.

G&H Are there any treatment strategies that require stronger evidence before they can be recommended?

BL Absolutely. In instances where there are not enough data, recommendations *against* the use of certain treatments are just as important as recommendations *for* the use of medications or diets. For example, the new guideline does not recommend the use of smooth-muscle antispasmodics to treat IBS symptoms because the data are so limited. In fact, hyoscyamine, which is used to treat many patients with IBS, has never been tested in an IBS study. Additionally, probiotics are now widely used for a number of different conditions; however, based on a very large, systematic review and meta-analysis published in *The American Journal of Gastroenterology* in 2018, the data are very weak, and the routine use of probiotics is not recommended for patients with IBS symptoms.

G&H Are there any recent advances in the use of fecal microbiota transplantation that are included in the updated guideline?

BL Fecal microbiota transplantation (FMT) is a very controversial area, and we recognize that FMT can be incredibly helpful for patients with recurrent *Clostridioides difficile* colitis. The procedure is generally safe, effective, and very well-tolerated by patients. Recognizing that the gut microbiome is important for symptom generation in many IBS patients, it seems logical that modulating the gut microbiome by performing a fecal transplant could improve IBS symptoms. However, our recommendation is that FMT should not be performed at this time routinely for IBS patients. This was a strong recommendation that is based on the evidence to date, which is very mixed. Thus, further research is needed in this area.

G&H Does the new guideline note any other important changes in IBS management?

BL Yes. The guideline does not routinely recommend the use of bile acid sequestrants to treat global IBS and diarrhea symptoms. There is a lot of information coming out about the role of bile acid malabsorption in patients with chronic diarrhea or IBS-D. Some new tests, such as serum C4, can be used as a surrogate marker to measure bile acid malabsorption. However, while bile acid sequestrants may improve diarrhea symptoms, they do

not improve global IBS symptoms, which is why they are not recommended. It is also important to highlight new information regarding gut-directed psychotherapies such as cognitive behavioral therapy or hypnotherapy, the use of which is recommended to treat global IBS symptoms. Of note, gut-directed psychotherapies generally tend to work better when used either with dietary therapy or with some type of neuromodulator for the treatment of visceral pain.

G&H What are the most important areas for future research in IBS management?

BL Probably the most important area is the treatment of visceral pain. Chronic abdominal or visceral pain is the leading, most bothersome symptom in patients with IBS. Although neuromodulators, certain secretagogues (eg, linaclotide), and other agents improve pain, they are not perfect. Therefore, future research should target the better treatment of pain. Another exciting area of research is the role of intestinal permeability and intestinal microscopic inflammation in the generation of IBS symptoms. Some really interesting studies will be coming out in the next few years discussing those concepts.

Disclosures

Dr Lacy participates in scientific advisory boards for Salix, Arena, Allakos, and Ironwood; is a consultant to Viver; and is on the Board of Trustees of the American College of Gastroenterology and the Rome Committee.

Suggested Reading

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