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Updated AGA Guidelines: Managing IBS with Diarrhea

Dr. Buch:
Welcome to GI Insights on ReachMD. I'm your host, Dr. Peter Buch. And joining us for an encore presentation to discuss the AGA Clinical Practice Guideline article about the pharmacological management of irritable bowel syndrome with diarrhea that was published in Gastroenterology 2022, is Dr. Eamonn Quigley. Dr. Quigley is the David M. Underwood Chair of Medicine in Digestive Disorders, Professor of Medicine at the Academic Institute, and Director of the Lynda and David M. Underwood Center for Digestive Disorders at Houston Methodist Weill Cornell Medical College.

Dr. Quigley, welcome back to the program.

Dr. Quigley:
Thank you very much. Great to be with you again.

Dr. Buch:
So, Dr. Quigley, the updated recommendations include the use of eluxadoline. What has been your experience with this medicine?

Dr. Quigley:
To be absolutely honest, it's been limited. Eluxadoline is an interesting product. It has shown statistically significant benefits to patients with IBS with diarrhea, but I think the clinical impact, if you look at the data, is not overwhelming. But having said that, that's true for a lot of drugs that are used to treat irritable bowel syndrome. I think a lot of the reluctance by physicians to use eluxadoline has centered around the issue of some rare but apparently quite adverse events, in particular with pancreatitis and sphincter of Oddi dysfunction. I think that has inappropriately scared a lot of people off from using it, and this may be an overreaction, but I think that has somewhat limited its use in clinical practice.

Dr. Buch:
Another update is the use of rifaximin. Please comment on how you use this medication.

Dr. Quigley:
That's a very interesting question, Dr. Buch. The idea to use rifaximin came out of literature from a number of years ago that suggested small intestinal bacterial overgrowth was quite prevalent among people with irritable bowel syndrome. In my opinion, that remains a controversial issue. But regardless, when examined in high-quality clinical trials, it was shown that in patients with non-constipated IBS, rifaximin was significantly beneficial in terms of relief of IBS symptoms and not just bloating but overall IBS symptoms. What's very interesting about that data is that in these studies, not only did rifaximin produce a short-term benefit, but for some of these patients, a two week course of rifaximin produced quite longstanding relief of symptoms, which is extremely interesting.

Now the problem again with rifaximin comes down to the question of reimbursement. If the patient has IBS with diarrhea, then I think reimbursement is not an issue, but in other areas reimbursement has been a problem. So I think rifaximin is worth a try in the patient with IBS with diarrhea. A certain proportion will respond. You'll know very quickly whether they do respond or not, and if they do respond, they may get lasting benefit. The question arises then, can you use it again? In fact, there have been studies which show that if you get a benefit once and retreat the patient, they will actually get the benefit again. So I think rifaximin has earned a place in the management of patients with IBS with diarrhea. The question remains for me, as somebody with an interest in the microbiome, as to how exactly it works and what we should be doing in the long term.

Dr. Buch:
And also when we're talking about rifaximin, other questions always come to mind for practitioners— do we use it first among

therapies? Do we use it last? How do you use it in your practice?

Dr. Quigley:
That's a very good question. By the time I see a patient with IBS with diarrhea, they have probably tried first-line therapies like a stool binder or a fiber supplement. They maybe used loperamide, which is another antidiarrheal. They probably used antispasmodics. So at that stage, rifaximin would loom fairly large in terms of the options for treatment. I think in primary care, I would still go with simpler approaches first before going on to rifaximin.

Dr. Buch:
One last updated treatment recommendation I'd like to discuss with you, Dr. Quigley, is alosetron. Why has this been added back to the treatment algorithm?

Dr. Quigley:
This is a very interesting story. So alosetron was first approved for the treatment of irritable bowel syndrome with diarrhea in women a good number of years ago, maybe as long as 15 or 20 years ago, and it was effective. However, there soon emerged reports of patients getting severe constipation and even ending up with surgical consequences, and because of the effect of the alosetron, it was actually withdrawn from the market. It was subsequently reintroduced under a very limited FDA supervised program, and that's been liberalized a little bit.

In my own opinion, alosetron is a good drug. It has very good efficacy in patients with IBS with diarrhea, and I think if you're careful in terms of patient selection, it actually is quite a safe drug. So I think that's the reason it's been brought back. And the other interesting thing about alosetron is when you look at the literature, it's actually one of the relatively few drugs which has long-term data. In other words, not only does it have data showing efficacy in the short term, for example eight to 12 weeks, but it actually has data over several months showing continued efficacy. One limitation to alosetron is that, it remains approved for women with IBS with diarrhea only. And of course, when men have IBS, they tend to have more diarrhea type IBS phenotype, which is a problem.

Dr. Buch:
Now switching gears a bit, do you ever use SSRIs or SNRIs in patients with irritable bowel syndrome?

Dr. Quigley:
Indeed, I do. Now as you know, tricyclic antidepressants have been used for many years, and I do use them a lot in patients with IBS, but you really should not be using them in patients with IBS with constipation because they would make the constipation worse. However, in patients with IBS with diarrhea, tricyclics are a good option because they have an anticholinergic and therefore an antidiarrheal effect. SSRIs and SNRIs in general tend to be better in the other spectrum in the patients with constipation, but they are effective in patients with IBS in general.

Now one of the questions that always arises is, who should you select to use these agents? Should you limit it to people with comorbid anxiety or depression? Certainly, they are a group in which these agents would be very appropriate, but we really do not have good data to suggest exactly who will respond to these. As I mentioned, I've been using tricyclics for many years in patients with IBS with diarrhea, and I still don't know how to select the optimal patient for these medications. What I tend to find is that they either work dramatically, or they have no effect whatsoever. And the other thing that tends to occur with tricyclics, more than SSRIs, is that some of these patients are very sensitive to side effects such as dry mouth or somnolence, which is very interesting. So even with very low doses of tricyclic, like 10 mg of amitriptyline, these individuals can develop side effects. Why this occurs, I don't know, but it's an interesting phenomenon.

I think as gastroenterologists, we tend to have some reluctance to use what we will call psychoactive medications because of our lack of comfort with dealing with depression and anxiety, which is an effect of our training. But I think we need to be more proactive in terms of selecting these drugs and using them in appropriate individuals if we can start knowing exactly who's the best person to use them in.

Dr. Buch:
For those just tuning in, you're listening to GI Insights on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Eamonn Quigley about the AGA guidelines on managing irritable bowel syndrome with diarrhea.

So, Dr. Quigley, given everything we've discussed so far, can you comment on the limitations of medications in the treatment of IBS?

Dr. Quigley:
Yes. Unfortunately, virtually all pharmacological approaches to irritable bowel syndrome have limited efficacy. They have efficacy and they have evidence to support their use, and we could go through all the drugs if we had time but the efficacy is usually limited. Now, that doesn't mean to say that these are not good drugs or effective drugs. The problem is that IBS is a heterogeneous disorder, and within IBS, I believe are lurking a variety of clinical phenotypes, which we still don't have adequately sorted out such as some of whom

may be responders to particular agents and some of whom may not; and of course they all get lumped together, and we get kind of a mish-mash with a modest response.

So I think we still have a long way to go to sort all of this out, but there is work ongoing to look at a variety of biomarkers, which might help us to develop a more personalized approach in the management of irritable bowel syndrome and not one based simply on whether they have constipation or diarrhea, which is all we have at the moment.

Dr. Buch:
With that in mind, is a low-FODMAP diet more effective than antispasmodics for treatment of irritable bowel?

Dr. Quigley:
Low-FODMAP diet has now been established as an important approach to the management of irritable bowel syndrome. There are limited studies comparing it with other diets or even with other approaches, but as of yet, we don't have the breadth of the studies which would allow us to place it in competition with other pharmacological agents. So I would say a low-FODMAP diet is an important, basic component of the management of IBS, whether you add drugs on top of that is another question. Right now, we don't have enough data to make direct comparisons.

Dr. Buch:
And before we conclude this discussion on managing irritable bowel with diarrhea, are there any other thoughts you would like to share with our audience?

Dr. Quigley:
The fact that we have new drugs and we have evidence to support drugs is very encouraging, but I still think we are quite a bit off fundamental approaches to the management of irritable bowel syndrome with diarrhea. And we mustn’t forget the importance of the brain part of the brain-gut access, which I think we lost sight of recently because of a lot of focus on microbiome, on immune responses, and other host responses.

Dr. Buch:
Thank you. This was an outstanding discussion on therapy options for irritable bowel syndrome with diarrhea. And I want to thank my guest, Dr. Eamonn Quigley, for sharing his insights. Dr. Quigley, it was a pleasure having you back on the program.

Dr. Quigley:
Great to be with you again today.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights where you can Be Part of the Knowledge.

Thanks for listening and see you next time.