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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Managing Treatment-Resistant IBS-C: Strategies to Address Refractory Symptoms

Announcer:
You're listening to *GI Insights* on ReachMD, and this episode is sponsored by Ardelyx Incorporated. Here's your host, Dr. Brian McDonough.

Dr. McDonough:
This is *GI Insights* on ReachMD, and I'm Dr. Brian McDonough. Joining me to share strategies for managing treatment-resistant irritable bowel syndrome with constipation, or IBS-C for short, is Dr. Prashant Singh. He's an Assistant Professor at the University of Michigan Health, specializing in gastroenterology and internal medicine. Dr. Singh, thanks for being here.

Dr. Singh:
Absolutely. Thank you for having me.

Dr. McDonough:
Let's dive right in, Dr. Singh. When managing IBS-C, what clinical signs and patient-reported outcomes suggest an inadequate response to first-line therapy?

Dr. Singh:
If you want to use patient-reported outcomes, a good and easy one to measure with five questions is IBSS, or the IBS symptom severity scale. It has five questions and measures a patient's pain, bloating, dissatisfaction with bowel habits, and overall quality of life related to IBS. And a higher score means that they are generally more symptomatic, so we can do it pre and post, as sometimes we do in clinic. Or sometimes, patients can tell you how they are feeling with regards to pain, bloating, and bowel habits, and that's enough.

Dr. McDonough:
And as a quick follow up to that, when should primary care providers refer these patients to gastroenterology specialists?

Dr. Singh:
If they're not responding to first-line therapies, then it would be a good time to refer them to gastroenterologists. So if you have tried your antispasmodics, your over-the-counter laxatives, or maybe even one prescription laxative and patients are still very symptomatic and not experiencing adequate relief of their symptoms, then I would say that patient probably needs to come in and see a GI.

Dr. McDonough:
So, Dr. Singh, once we decide to move on to second-line treatment, what are the available options?

Dr. Singh:
So when we move on to the second-line options in the pharmacological therapies, the first class of medications is secretagogues. Secretagogues work by making the colon secrete water, thereby making the stool loose and making the transit a little faster. Some of the secretagogues in animal models have also been shown to improve barrier function and visceral hypersensitivity, which are key pathophysiologic features of IBS. And the three main secretagogues available to us that have been approved by FDA for this condition are lubiprostone, linaclotide, and plecanatide. They work on different receptors, but the end result is the same—you end up with more water in the colon.

And then the last medication is tenapanor, which is a sodium-hydrogen exchanger 3 inhibitor specific to the GI tract. And what it invariably does by blocking that receptor, which is very important for reabsorption of water, is prevent the reabsorption of water and

sodium. So there ends up being more water in the colon, which again, improves transits and stool consistency. And similar to the others, it has been shown to improve barrier function and visceral hypersensitivity as well in IBS.

Dr. McDonough:
And how can combination strategies play a role in our treatment approach?

Dr. Singh:
There are different ways to combine therapies. First, I would talk about combining pharmacological therapy with nonpharmacological therapy, and then I would talk about combining two pharmacological therapies.

So starting with combining pharmacological therapy with nonpharmacological therapy, the three main non-pharmacological therapies available for IBS are GI behavioral therapies, dietary therapies, and pelvic floor biofeedback. And they all have a place in IBS. We know that GI behavioral therapy, such as cognitive behavioral therapy, or CBT, and GI-specific hypnosis are very effective in improving IBS. They work for all IBS subtypes and are very effective in improving pain and bloating. So they can be a very useful tool to manage this hypersensitivity, GI-specific anxiety, and visceral hypervigilance. They can address a lot of ongoing symptoms if the patients are not responding to first-line therapies, and they can be easily combined with pharmacological therapy.

The second way is dietary therapy, where the most evidence is for low-FODMAP diet. This diet has been shown to work for all IBS subtypes—including IBS-C—and mainly works by improving pain and bloating. It is not very effective in improving stool consistency, but again, it's very effective in improving pain and bloating and can be combined with the pharmacological therapies I just mentioned.

And the third therapy I just talked about is pelvic floor biofeedback. So that is generally used to treat dyssynergia, and we know there is a huge overlap between IBS-C patient and pelvic floor dyssynergia. A good proportion of our patients who don't respond to first-line therapies are not responding because they have pelvic floor dyssynergia where the puborectalis muscle, which is supposed to relax when you try to defecate, is not relaxing. In some patients, it is actually contracting, so that's counterintuitive, and it doesn't help them. So the guidelines now suggest that if a patient with constipation—including IBS-C—is not responding to first-line therapies, we test them for dyssynergia using anorectal manometry and defecography and offer pelvic floor biofeedback if that testing shows that they indeed have dyssynergia. And again, combining pharmacological therapy with biofeedback can be very effective in managing IBS-C.

Of course, the other way is to just combine different classes of medicine. Sometimes, I would combine an osmotic laxative like polythene glycol, magnesium oxide, or other magnesium supplements with secretagogues or tenapanor. Or sometimes you can combine stimulant laxatives with them. So that can also work. And sometimes I combine neuromodulators like tricyclic antidepressants or SNRIs, which are very effective in improving pain, with these agents to manage pain. So there are various ways of managing IBS.

Dr. McDonough:
For those just tuning in, you're listening to GI Insights on ReachMD. I'm Dr. Brian McDonough and I'm speaking with Dr. Prashant Singh about managing IBS-C when first-line therapies are ineffective.

Now, even with multiple lines of therapies, patients may still experience refractory symptoms. So when and how should we escalate their treatment?

Dr. Singh:
Before I jump to escalating therapy, if you have tried a couple of first-line therapies and patients are still symptomatic, making sure the diagnosis is right is very important. Make sure they have a colonoscopy if they are age-appropriate, or if they have any alarm symptoms, make sure that we're not missing anything, and this is indeed IBS-C. This would be the first step. We have just talked about dyssynergia, and that needs to be investigated.

And let's say we are sure that IBS-C is the diagnosis, and we are ready to escalate. The next decision is, looking at it from the patient perspective, what is their predominant symptom? If their predominant symptom right now is pain and bloating, then I would act a little differently rather than if they are still constipated. If you still are not going for three or four days, then I would first try to make sure their bowel movements are more regular, and there are multiple ways you can do that. There is, as I just said, osmotic laxatives—which are not very good for pain and bloating—for example, polythene glycol, magnesium oxide, and other magnesium products. They're not very effective in improving pain and bloating, but they can improve stool frequency and stool consistency. So if that is the goal, you can use them. And sometimes we use them very often with secretagogues, like the linaclotide, the plecanatide, the lubiprostone. You can combine these two as well. Or even with tenapanor. You can combine osmotic laxatives with secretagogues, for example, or sometimes stimulant laxatives with secretagogues if you need to, to improve stool frequency and consistency.

Dr. McDonough:
Well, we've certainly covered a lot today, Dr. Singh. Before we close, do you have any key takeaways you'd like to share?

Dr. Singh:
First, once you have diagnosed somebody with IBS and they're not responding to first-line, feel comfortable using FDA-approved drugs for IBS, which would be secretagogues and tenapanor. And then second would be the combination strategies probably needed for a lot of our patients. So attacking IBS from a lifestyle standpoint, a dietary standpoint, and a behavioral therapy standpoint and using them in conjunction with pharmacological therapy is probably our best bet to provide adequate relief for most of our patients.

Dr. McDonough:
With those insights in mind, I want to thank my guest, Dr. Prashant Singh, for joining me to discuss how we can address treatment resistant IBS-C. Dr. Singh, it was great having you on the program.

Dr. Singh:
Thank you. Thank you for having me.

Announcer:
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