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

Breaking Down Bile Acid Diarrhea: Top Diagnostic & Treatment Strategies

Dr. Buch:
This is *GI Insights* on ReachMD, and I'm your host, Dr. Peter Buch. Bile acid diarrhea is a frequent, treatable cause of chronic diarrhea. But it's difficult to diagnose. So joining me to share how we can better recognize this disease is Dr. Michael Camilleri. Dr. Camilleri is a Professor of Medicine, Pharmacology, and Physiology at the Mayo Clinic. He's a leader in the field of gastroenterology and his honors would fill several of these programs. Welcome to the program, Dr. Camilleri.

Dr. Camilleri:
Thank you for having me.

Dr. Buch:
It's a pleasure. Let's get right into it. Why is bile acid diarrhea so important.

Dr. Camilleri:
So it's been estimated that about a third of the patients with functional diarrhea or irritable bowel syndrome with diarrhea actually have bile acid malabsorption or bile acid diarrhea. And I believe it's important because we're now able to make a specific diagnosis and we can give specific treatments for these patients with chronic diarrhea. And this specific treatment consists of bile acid sequestrants.

We also know from a recent study that even among adolescents with chronic diarrhea, almost one in every five will have evidence of bile acid diarrhea based on the very simple blood tests.

The other reason why bile acid diarrhea is important is that we also see patients who have some other gastrointestinal disease like an ileal-resection or Crohn's disease of the ileum or chronic pancreatitis, celiac disease, malabsorption syndromes that can be associated with the passage of bile acids into the colon and there they cause the diarrhea. So several reasons why many of the patients that we see in clinical practice in gastroenterology but also in primary care medicine could have bile acid diarrhea as the cause of their chronic diarrhea.

Dr. Buch:
Thank you. Dr. Camilleri, what have been the obstacles in recognizing this disease?

Dr. Camilleri:
I would say that the main obstacle has been the absence of a diagnostic test until relatively recently. So in other countries, there is a nuclear medicine test which has been validated and used to measure the loss of bile acids. But this has never been approved in the United States.

More recently, two diagnostic tests have been developed. One is based on a blood test taken in the fasting state before 9:00 in the morning, and that measures the substance called 7alphaC4, c for Charlie-4, so that's a screening blood test. And then there's a more formal diagnostic test, which is a 48-hour excretion of bile acids while the patient is ingesting 100 g fat diet. So just as we doctors or gastroenterologists in the past may have done a fecal fat excretion measurement to diagnose fat malabsorption, on that same stool sample, you can measure both the fat and the bile acid excretion and by doing so, then have probably what is the most accurate and most predictive diagnostic test for bile acid diarrhea.

Dr. Buch:
Can we clarify that a little bit, Dr. Camilleri? Are these tests available in a general community hospital? Or do these have to be sent out to the Mayo Clinic?

Dr. Camilleri:
These are tests that are available at reference laboratories. So Mayo Clinic happens to be one of those reference laboratories that offers both of those tests. However, there are other reference laboratories that also offer the C4 blood test. So I think it's it'll be relevant to find out which reference laboratory is available in different parts of the country to see where the test can be done.

Dr. Buch:
So when we're treating irritable bowel, we have various algorithms that we approach irritable bowel in the treatment. When should be consider bile acid diarrhea as the true source of irritable bowel syndrome?

Dr. Camilleri:
So we've been studying this here at Mayo Clinic for at least the last twelve years. Clinical experience has taught me that there are three clinical clues that make me suspect bile acid diarrhea. First, has the patient had a prior cholecystectomy? We know that some patients will develop bile acid diarrhea after cholecystectomy. Second, is there a sub-optimal response in the patient whose been treated with a medication like loperamide or diphenoxylate, which is Lomotil. And the third clue, in fact, is if the patient has body mass index of greater than 30, that is they are at least class 1 obese, and they also have functional diarrhea or chronic diarrhea, there is the possibility that they have bile acid diarrhea. So in our clinical practice, those are the three markers that we've identified as potential clues to suspect bile acid diarrhea.

Dr. Buch:
Thank you so much. I think those clues will be very, very helpful to our audience.

For those just joining us, this is *GI Insights* on ReachMD. I'm Dr. Peter Buch and here with me today is Dr. Michael Camilleri who is discussing bile acid diarrhea.

So let's go and do a deeper dive into this, Dr. Camilleri. What if we just empirically give colestyramine to treat suspected bile acid diarrhea rather than going through the testing?

Dr. Camilleri:
So that certainly is an option. But I think there are probably three reasons why I would recommend that getting the diagnosis is preferable to just an empirical trial. The first is that a study we did here in our clinical practice suggested that if we actually do just an empirical trial of bile acid sequestrants like colestyramine, the likelihood that the patients will respond is about 25%. In contrast, if the patient had a definite diagnosis proven by either the blood test or the stool test, then the likelihood of responding to a bile acid sequestrant is closer to 75%. So that's the first point.

The second major point is when I used to give an empirical clinical trial of particularly colestyramine, often patients had difficulty with compliance of the medication. So we didn't know exactly what would be the right dose to test; would it be 4 g per day or 16 g per day to test whether there is a presumptive diagnosis of bile acid diarrhea? And I, I'll never forget the time when a patient to whom I had prescribed 4 g, four times a day contacted me within a week and said, "Have you ever tried taking this yourself? I can't take this." So in other words, compliance is a very significant issue when we're doing a therapeutic trial with colestyramine.

Dr. Buch:
Thank you very much on that one. When might we use obeticholic acid to treat bile acid diarrhea?

Dr. Camilleri:
So obeticholic acid is a medication that actually stimulates the production of a substance of a hormone called fibroblast growth factor 19, which goes through the portal circulation, it stimulated in the ileal epithelial cells. The hormone is goes to the liver through the portal circulation and reduces the synthesis of bile acids by the liver. So, it would be, theoretically, a good idea. But let's keep in mind that obeticholic acid has been tested in one clinical trial and proved to be quite efficacious. But it's not approved for this indication by the FDA. The only approved indication for obeticholic acid is actually primary biliary cholangitis.

Dr. Buch:
Before we conclude, Dr. Camilleri, is there anything else you would like to share with our audience today?

Dr. Camilleri:
So two or three things, if I may. The first is that we are simplifying the diagnosis such that instead of having to collect a 48-hour stool sample, we can now have evidence that by doing that fasting blood test, and by taking a random single stool sample and estimating the amount of primary bile acids like colic acid and ketodeoxycholic acid in that one single stool sample, and if they amount of the primary bile acids is greater than 10%, and if the serum 7alphaC4 is greater than 52 ng/mL, we know that has as much diagnostic capacity for proving diarrhea, proving increased fecal weight, as when we do a 48-hour stool collection. So the first point is we are simplifying the

diagnosis and we are hoping that that simplified combined blood and stool test will be available relatively soon. Again, it will be launched by Mayo medical laboratories.

The second point, I think is a more general point. And that is that over time, we have been trying to identify the dysfunctions in patients with functional GI disorders. So conditions like irritable bowel with constipation. We now recognize that there are reasons why the patients have constipation. The pelvic floor may not be working well. The colon transit may be slow. And similarly, here in the context of diarrhea, we can identify the patients who have too much bile acid getting into the colon.

The reason I'm really excited about this is that by identifying what we call 'actionable bile markers,' we can give much more specific treatment to the patients. So if the patient has an evacuation disorder, pelvic floor retraining with bio-feedback is indicated. If they have slow colonic transit, then a medication that speeds up colonic transit would be indicated for the constipation.

And conversely, we just talked today about bile acid diarrhea and the opportunity to with bind those bile acids with a sequestrant or in the future, use medications such as the one we discussed, obeticholic acid to reduce the amount of synthesized bile acids and therefore reduce the likelihood that the bile acids would cause the diarrhea.

So those are the two main things that I'd like to leave you with. The first is the simplification of the diagnosis and the second is the availability of actionable biomarkers, which will allow us to be much more specific and directed and precise in our treatment.

Dr. Buch:
The future is here, now. I want to thank our guest, Dr. Michael Camilleri, for joining me to share diagnostic and treatment strategies. Dr. Camilleri, it was great having you on the program.

Dr. Camilleri:
Thank you for including me.

Dr. Buch:
For ReachMD, this is Dr. Peter Buch. To access this episode, as well as others from this series, visit ReachMD.com/GIInsights, where you can Be Part of the Knowledge. Thanks for listening and see you next time.