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Postoperative Crohn's Disease: Detecting Bile Acid Diarrhea

Dr. Buch:

You're listening to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch, and joining us to discuss testing for bile acid diarrhea in patients with postoperative Crohn's disease is Dr. Robert Battat. Dr. Battat is the Director of the Center for Clinical and Translational Research for Inflammatory Bowel Disease at the University of Montreal. He's also the lead author of "Advances in the Comprehensive Management of Postoperative Crohn's Disease," which appeared in *Clinical Gastroenterology and Hepatology*, which was published in July 2022.

Welcome to the program, Dr. Battat.

Dr. Battat:

Thanks for having me.

Dr. Buch:

Let's dive right into one of the cofounders in diagnosing and treating postoperative Crohn's disease, bile acid diarrhea. Dr. Battat, how can the community-based clinician diagnose bile acid diarrhea?

Dr. Battat:

In the United States, there are two commercially available blood tests for bile acid diarrhea. Traditionally, or in the literature there's something called the SeHCAT test, which is, you know, a test where a patient has to, you know, receive a radio-labeled material; they go for, you know, two days of visits and imaging to see the passage of the bile acids. It's not actually available in the United States, so it's really only available in Europe. What is typically done in the United States is there's therapeutic trials. Right? So, in the right clinical context, giving a medicine such as cholestyramine or your bile acid sequestrants as well, sometimes can have diagnostic accuracy.

The issue with doing therapeutic trials is that, you know, if you have a disease and the doctor says, "Well, just try this medicine, but we don't actually have any objective proof that you have the disease," well, if you have any issue with that medicine, like it causes bloating or, you know, you don't like the idea of being on a medicine, very quickly the compliance is going to tail off, and so there's a lot of people who don't like the idea of taking a lifelong medicine for a condition that they actually haven't been formally diagnosed with.

So, with that in mind, there's been a few entities that have looked into developing blood tests, the Mayo Clinic provides one. The other one is done by there's a laboratory in San Diego that does it as well and the blood test is called C4. What it is is that as you lose bile acids in the stool. So, when someone has bile acid malabsorption, you're not absorbing bile acids in the terminal ileum, and so the bile acids get lost in the stool, so you're losing bile acids from your pool, and when you're losing bile acids from your pool, your liver produces more bile acids to compensate for the losses. And so, one of the precursors in that pathway of producing bile acids is called C4. It's a stable molecule that you can measure in the blood. So, when you lose more bile acids because you're producing more by the liver, the C4 test value goes higher. So, there are commercially available assays, and depending on patient insurance and whatnot, it can be covered.

Dr. Buch:

Just as a segue to that, what is the cost of that C4 test?

Dr. Battat:

It depends. You know, I'm not sure how much Mayo charges for that and depending on insurance or whatnot. I know in San Diego, it's a one-time test, and I have seen that the cost is ranged in the, depending on insurance and coverage, between the \$100–300 range. This is typically not a test that is done serially or repeatedly. It's typically a one-time thing. But nonetheless, I think it's the problem that cost

can become a barrier, and so it would be interesting to see more widespread availability to be able to lower the cost of these things.

Dr. Buch:

For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and joining me to talk about testing for bile acid diarrhea in patients with postoperative Crohn's disease is Dr. Robert Battat.

Now Dr. Battat, if we continue looking at the C4 test, can you tell us about its accuracy in diagnosing bile acid diarrhea?

Dr. Battat:

So the accuracy is quite good across both assays that are available in the U.S. they have been kind of cross-validated through different ways, but, essentially, you know, in patients who have an elevated C4, amongst patients who have diarrhea, and then elevated C4, above which there was over 80 percent actually had, you know, objective signs through other markers of bile acid, malabsorption, and vice versa, if you had less than as, you know, the normal limit, upper limit of normal for that test, so i.e. a normal value, it was less than 5 percent, actually had any, you know, objective evidence of bile acid malabsorption. And then there's been tests, you know, to show that, you know, stool measurements of bile acids are high when the value of this test is high. And actually, the cutoff value for both assays, are very, very close numerically to one another, so it ranges from about 48–55, ng/L.

Dr. Buch:

Great. And I can already see some of my colleagues asking this question: Are there any conditions that we need to know about that can cause false-positive results for that C4?

Dr. Battat:

There's a whole, list of theoretical confounders: the time of day, liver disease, amongst other things, and really the truth is that in practice those haven't really panned out. I would say the, the biggest thing to look out for is that in patients, there's a subgroup of patients with bile acid so if you take out enough small intestine, like a lot of small intestines, typically more than 100 centimeters, but every patient is different. You get a lot of bile acid malabsorption to the point where you're losing so much bile acids that your liver can't produce enough to make up for your losses, so your bile acid pool decreases. When your bile acid pool decreases, the bile acids can't perform their function, so their function of bile acids or one of main functions is to help absorb fats, so when you have a large ileal resection and a lot of bile acid loss, you get fat malabsorption.

And why I'm bringing this up is because those patients will also have typically very high C4 values, and in those patients, if you administer a bile acid sequestrant, well you're actually worsening the absorption of bile acids, and so you'll actually worsen your steatorrhea, and patients will get more symptoms. Typically, though, you know, you can tell based on a clinical profile, say patient has a limited ileal resection not greater than 100, they don't have typical symptoms of steatorrhea and their C4 is elevated, but it's not, you know, 10 times the upper limit of normal. In those contexts, you would use it accordingly, but if there are, you know, these risk factors for short bowel syndrome, essentially, there you just want to be careful for adding a bile acid sequestrant.

Dr. Buch:

With those final thoughts in mind, I want to thank my guest, Dr. Robert Battat, for sharing his insights on testing for bile acid diarrhea in patients with postoperative Crohn's disease. Dr. Battat, thanks for joining us.

Dr. Battat:

Thank you so much.

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.