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Moving in on Gastroparesis Treatment Strategies

Dr. Buch:
Gastroparesis affects approximately five million people in the United States alone, and there are more than 50 recognized causes. In recent years, however, it's been shown that simply accelerating gastric emptying may not improve symptoms, and the overlap of functional dyspepsia and gastroparesis has further clouded our understanding of this condition, which is why today we'll be working to help clear up some of that confusion.

Welcome to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and here to help us find the pearls of gastroparesis treatment is Dr. Amir Masoud, who's the Medical Co-director of the Hartford HealthCare Neurogastroenterology & Motility Center.

Dr. Masoud, welcome to the program.

Dr. Masoud:
Thank you. Thank you so much for having me.

Dr. Buch:
So Dr. Masoud, let's start off with testing. What are the alternatives to a four-hour gastric emptying test?

Dr. Masoud:
So for the assessment of gastric transit time in general, there are three main modalities that we use. The most commonly used one and that's most recognized is the four-hour gastric emptying test, which is a nuclear med study which involves eating a test meal followed by serial images over four hours. The newer alternatives are breath testing. It's a radioisotope breath test, which is a similar protocol that requires breath test samples to be collected within a four-hour period. And then finally, the newest kid on the block is something called SmartPill, which is a whole-gut transit study, which among other parts of the gastrointestinal tract, can measure the gastric emptying time.

Dr. Buch:
So when we think about those tests, what are the advantages and disadvantages of each one?

Dr. Masoud:
I think the gastric emptying test, the conventional nuclear, medicine test is the most widely kind of recognized and accepted one. Interestingly, the other modalities have actually been compared to that, so that has always been held as the kind of gold standard or yardstick against which everything else is measured, so that seems to be the easiest to interpret, the easiest to get. I mean, most centers have the ability to do a gastric emptying test, a four-hour gastric emptying test. However, obviously convenience is a factor, right? So for our gastric emptying test, you have to come into the hospital, and you have to wait around, and there's all that associated inconvenience, but with a breath test there's the potential to pretty much do it at home. I mean, you could have send-away kits that you can do at home and do the collections yourself, and then mail it in. There are some commercially available kits that allow for that. And then finally, as far as SmartPill goes, the main advantage—and particularly for me as a motility specialist—is the ability to gauge the other parts of the gastrointestinal tract as far as transit time goes. So often gastroparesis, when we're talking about dysmotility, isn't an isolated problem. Sometimes it can be in conjunction with small bowel dysmotility or even colonic inertia, and sometimes it's very, very important for us to gauge those things in tandem.

Dr. Buch:
And how do you use metoclopramide in your practice?

Dr. Masoud:
I tend not to use it because of the complications from it. And at the center and at my previous practice, we've always had an IND from the FDA to be able to prescribe domperidone, which is basically the same thing as metoclopramide minus the central side effects since it doesn't pass the blood-brain barrier. The alternatives which are quite efficacious are azithromycin, which is a better alternative than erythromycin, which is poorly tolerated, and then the newer kid on the block which, unfortunately, is only approved in this country for constipation, is Motegrity, which we've been actually using for years for gastroparesis as well.

Dr. Buch:
That's great. Can clinicians anywhere get domperidone from foreign countries?

Dr. Masoud:
I think to be able to prescribe it under the rules and regulations—in air quotes—you really do need a special kind of license, so to speak, from the FDA, you know, an IND at the very least and all of our patients are enrolled under that in a clinical trial to allow us to prescribe domperidone, which is actually formulated in a compounding pharmacy specific for each patient.

Dr. Buch:
And talking about domperidone, can you tell us what the complications of domperidone use might be?

Dr. Masoud:
Yeah, domperidone, unfortunately, never really got a fair shake here in the United States. The main complication with domperidone and the one that we're very careful to look for is cardiac arrhythmia, and it's mainly related to something called QT prolongation, and as part of our IND and a part of our protocol IND, we are able to or we have to actually get baseline EKGs and serial EKGs and any time there's a dose change get an EKG to assess for QT prolongation, and there are cutoffs. So if your QT is, you know, high normal, we may not be able to prescribe it. All of this kind of came about when they first introduced the medication domperidone, which was in intravenous form, and patients who had received a rapid injection or infusion of domperidone developed these life-threatening cardiac arrhythmias, and that's what kind of put the kybosh, so to speak, on domperidone in the United States, but it's used very commonly outside of the United States for gastroparesis, other gastrointestinal disorders, and here it is primarily used off label for lactation, as an aside.

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. Amir Masoud about gastroparesis treatment.

Now Dr. Masoud, should we consider gastric peroral endoscopic myotomy in refractory gastroparesis?

Dr. Masoud:
G-POEM is a very, I would say, interesting and potentially exciting therapy for some patients. I think we have to be very, very selective. The studies that have come out over the past five years or so have kind of been all over the place. There have been some that have shown efficacy with a G-POEM, others that have not, and I think it all comes down to patient selection. We sometimes have a very simplistic view of the gastrointestinal system, and I think we have looked at POEM, peroral endoscopic myotomy, for achalasia as a very well-known and successful therapy for that disorder and thought "Well, if you can cut one sphincter, why can't you cut the other?"

The nuance here is that the pylorus is not like the LES. The LES, when you cut it on one side, it tends to stay open whereas the pylorus is very different. There are tonic, phasic contractions. There are all sorts of things that happen, and there's an interplay between the pylorus and the antrum that is underrecognized, and I think that simply doing a unilateral or one-sided cut doesn't really work. Studies have suggested that increasing the surface area is what we should look at as far as the opening goes. Other studies have suggested distensibility, which is a measure using something called EndoFLIP to see how tight the sphincter is, but that really hasn't panned out. So I think right now the jury is still out. I have to say for, in my case, I tend not to push for G-POEM unless I feel that the problem is related to the pylorus and there is preserved antral function. If the stomach is able to squeeze, we just have a closed door; then I tend to think, okay, maybe G-POEM would work here.

Dr. Buch:
That's very helpful. And similarly, under what circumstances should we consider gastric electrical stimulation for refractory gastroparesis?

Dr. Masoud:
Yes, that's probably my number one gastroparesis referral is for an enteral or a gastric stimulator, and I think that while the basic mechanism makes sense from basically a mechanistic standpoint, it really hasn't panned out when we've looked at it in a systematic fashion, so I think in general, again it comes down to patient selection. So if every single patient who came in through the door got a gastric stimulator, you'd have more patients who don't benefit than those who do. However, there are some data to suggest that

patients with diabetic gastroparesis benefit better from a gastric pacemaker, and most importantly, patients whose symptoms are deemed related to gastric emptying. So if you have gastroparesis and you have, as you alluded to earlier, a functional manifestation such as pain, 24/7 nausea, you're not going to benefit from enhancing gastric emptying even if we're able to demonstrate it, and studies have shown that demonstrably enhancing gastric emptying does not help with these atypical symptoms, but if you're somebody who eats, feels full very fast, gets nauseated, throws up and feels better, that seems to be more related to the speed with which the stomach empties. Therefore, perhaps, enhancing that may improve your symptoms, and I think those are the patients that would benefit from these measures.

Dr. Buch:
Before we conclude, are there any other insights you would like to share with our audience today?

Dr. Masoud:
The main thing I'd like to say is you can have gastroparesis and have your symptoms. I think a lot of times gastroparesis may just be a bystander. You know, we know that the stomach doesn't empty at the same rate no matter what we eat, so if I eat a big plate of spaghetti versus if I eat a large bowl of something very heavy and creamy versus a salad, everything changes the way that the stomach empties because it's not a timer that goes off and says, "Okay, now I have to be empty." So I think we have a little bit of a simplistic view towards gastroparesis in general, and I think we're misdiagnosing a lot of patients by calling them gastroparesis when this can be, you know, "functional."

The last thing I'd also like to leave people with is sometimes there's a significant overlap with constipation. So we know that patients with severe constipation can have a secondary slowing of the gastro proximal foregut basically, and having a delayed gastric emptying test in somebody who has very severe refractory constipation is something I actually ignore. I say, "Well, I'm going to treat your constipation first, get your bowels moving a little bit more regularly; then we'll talk about seeing if the stomach is still a problem" because we know that the gastrointestinal tract, each part of it, is not functioning in isolation. They all communicate with each other. It's all kind of through feedback mechanisms, and a slow end of the line leads to a slow start of the line, so I think it's very important to think of the patient as a whole and not take symptoms nor tests in isolation.

Dr. Buch:
Those are all great takeaways. And I want to thank Dr. Amir Masoud for a great discussion. Dr. Masoud, it was a pleasure having you on the program today.

Dr. Masoud:
Thank you. The pleasure was all mine.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GI-Insights, where you can Be Part of the Knowledge. Thanks for listening and see you next time.