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### A Look at the Treatment Landscape for Gastroparesis

#### Dr. Buch:

Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. Joining us today to help us better understand treatment of gastroparesis is Dr. Madhu Grover. Dr. Grover is an Associate Professor of Medicine at the Mayo Clinic and develops and conducts clinical trials on gastroparesis. Dr. Grover is also the lead author of "Gastroparesis: a turning point in understanding and treatment," published in *Gut* in 2019.

Welcome back to the program, Dr. Grover.

#### Dr. Grover:

Thanks, Dr. Buch.

#### Dr. Buch:

So, Dr. Grover, let's focus on the treatment of gastroparesis today. Do you use metoclopramide in your practice?

#### Dr. Grover:

Yeah, I do use metoclopramide. As you know, and it's a bit unfortunate, that this is still the only, you know, FDA-approved option we have to treat gastroparesis. I particularly use it for shorter durations of time, less than 12 weeks, which is also the guidance from FDA, because longer durations, more than 12 weeks, and, using it in folks over 65 years of age, some of these characteristics have been associated with increased risk of tardive dyskinesia, which is an involuntary movement disorder, which also happens with some of the other psychotropic drugs as well. So I do use it. I try to use it in lower doses over shorter durations of time because it does seem to help and just also because we don't have a lot of other therapeutic options.

#### Dr. Buch:

And that's a perfect segue into the next question. What can you tell us about your experience with domperidone and prucalopride?

#### Dr. Grover:

Yeah, so domperidone, it is also used. There was a recent study looking at experience from UK, and it's rather much heavily used, treatment option in UK as well as in Canada, whereas Reglan is more commonly used in the U.S. So, as we think about domperidone, I use it less often as compared to metoclopramide, more so because of some of the logistical, you know, challenges with, you know, getting the drug, but it's effective. One has to be careful about side effects, such as QTc prolongation. Thankfully, it doesn't cause some of the tardive dyskinesia-type side effects. And generally speaking, in the handful rather smaller subset of patients I have used domperidone, I haven't had encountered some of those QT prolongation type side effects. So, I think if you're monitoring your patient closely, they are under good supervision and good care, it's a perfectly reasonable option to consider.

#### Dr. Buch:

And for those physicians out there who are considering using domperidone, of course you're going to do an EKG before you give the medication. How frequently do you do an EKG after you started medicine?

#### Dr. Grover:

Yeah, so it depends. If their initial QTc is normal, they don't have a lot of other drugs that can modify QT. I would do it every 2 to 3 months, but I would caution them. As you know, a lot of other concomitant medications can have that effect as well. So, again, I think more than the frequency of doing EKGs, it's important that they're under good follow-up and good care of a primary care physician who's monitoring and who's aware of that effect on the potential over long term.

**Dr. Buch:**

What are your thoughts about endoscopic procedures like pyloromyotomy for gastroparesis?

**Dr. Grover:**

Yeah. So this is an area again of a lot of interest, I would say just over the last couple of years. So just going back, there is a history to us trying to treat gastroparesis using pyloric interventions. So, for those who need a little bit of a refresher on the gastric function, so pylorus is this last part of the stomach before things are emptied into the duodenum, and historically, it's been thought that at least a subset of patients with gastroparesis are unable to empty because they have a pyloric spasm or their pylorus is too tight to allow emptying of those contents. So dating back in the day and even until now, there are some practitioners who frequently or at least once would try a Botox injection in the pylorus to see if you know, relieving that pyloric spasm would help with the symptoms in gastroparetic patients. So, when we started doing these injections early on in uncontrolled or sort of open-label fashion, we saw that some of our patients were improving, but unfortunately, as you know, evidence grew and as we started getting randomized clinical controlled trials, we didn't see a clear superiority of Botox over placebo. So, you know, that's sort of history behind trying to intervene on the pylorus.

There have been other strategies like pyloric dilation using a balloon, but more recently, you know, you know, particularly endoscopy community started, doing, G-POEM, which is essentially a third space endoscopy. This is fashioned after surgery is done in the esophagus for achalasia, which is another disorder at that gastroesophageal junction where the lower esophagus doesn't relax very well. So we knew from our experience doing these myotomies for esophagus that it does help with the symptoms. So an extrapolation of that became what about if we were to enter into the pyloric channel underneath the mucosa and tried to really cut that pyloric ring or pyloric muscle, not cut it all the way but cut it enough so that that pylorus isn't any more restrictive. So that has led to a lot of studies recently, I would say over 10 to 15 studies, both open label as well as more recently some randomized controlled trials, and what's clear is that in a subset of patients it works. Okay? And now the difficult part comes where we are trying to define who is that subset and what are the clinical features, what are their physiological parameters, if there are any, and how can we educate ourselves better in trying to define that population that benefits from the gastric pyloric endoscopic myotomy.

There was a randomized trial which actually showed that at 12 months, close to 55 percent, 60 percent patients felt better. In about half of those patients the gastric emptying had actually normalized, which is phenomenal if you think about how deep that unmet need is in this area of gastroparesis. Folks are now trying to do sophisticated measurements of the pyloric channel using things like EndoFLIP, which is sort of trying to understand with a balloon the distensibility of the pylorus and trying to see if any of these things will predict, but I think much more needs to be done using things like EndoFLIP or high-resolution gastroduodenal manometry catheter that really gives you sophisticated information of what's happening in that part of the gut to really try to understand what's the subset of patients who are most likely to benefit, because I would like our audience to understand that doing it indiscriminately on every gastroparetic is also not the answer. In fact, we have seen some of the patients developing rapid gastric emptying after a G-POEM, which can also be very troublesome for patients and, and cause a lot of symptoms. So I think we want to we want to learn more about it, we want to use it, but we want to use it in the most ideal fashion so that we have the right patients undergoing that procedure.

**Dr. Buch:**

So caution sign ahead before thinking about pyloromyotomy. So, before we close, do you have any final thoughts or takeaways on gastroparesis you would like to share with our audience today?

**Dr. Grover:**

Yeah. No, I would just like to say we obviously are trying as a scientific community and some of us in the tertiary clinical centers how to understand this disease even further. There is a lot of exciting and emerging research in us trying to further improve our gastric emptying measurements, whether just the static images at several time points are enough or we need more dynamic understanding using things like MRIs and so on and so forth to understand gastric function. So I think a lot more needs to be done.

That said, I think we are at an exciting juncture where we are learning a ton about its pathophysiology and, as I said, how we can disease modify rather than just treat symptoms on a short-term basis, how can we do things that really get to the root cause of the problem. And I think we are learning as we learned, as it took us about 10 to 15 years to learn this much about gastroparesis, I think we are also at an exciting juncture where we are learning much more about dyspepsia. So, functional dyspepsia, as you know the term indicates, it's functional in nature, or we don't understand why it's happening, but I think within that functional dyspepsia category, there would be a subset of patients that are more in that gastroparesis-like spectrum, and there might be others that are driven by other causes.

So I think a lot more needs to be done. I think our patients deserve better treatments and more options, and we are very sensitive of that need and doing our best to think more carefully about the drugs as well as about the endoscopic procedures.

**Dr. Buch:**

With those closing thoughts in mind, I want to thank my guest, Dr. Madhu Grover, for sharing his insights on gastroparesis.

Dr. Grover, it was a pleasure having you on the program.

**Dr. Grover:**

Thank you, Dr. Buch. It was a pleasure to talk to you, and I hope our audience will get something meaningful out of this.

**Dr. Buch:**

They absolutely will. For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit [ReachMD.com/GIInsights](https://ReachMD.com/GIInsights) where you can be Part of the Knowledge. Thanks for listening.