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### A Discussion on Dyspepsia: What We Need to Know

Dr. Buch:

This is Dr. Peter Buch, your host for ReachMD, *GI Insights*. Dyspepsia affects a large number of Americans, yet what exactly is dyspepsia? How can we distinguish dyspepsia from other diseases? And what is the difference between dyspepsia and functional dyspepsia? Here to answer these questions and more is Dr. Scott Gabbard, who is section head center of neuro-gastroenterology and motility at the Cleveland Clinic. Dr. Gabbard, thanks so much for joining us here today.

Dr. Gabbard:

Thank you so much for having me. It's a topic that's close to my heart or I'd say close to my stomach. So I love the opportunity to discuss this.

Dr. Buch:

There seems to be some confusion out there. How would you define dyspepsia? And what is the difference between dyspepsia and functional dyspepsia?

Dr. Gabbard:

Dyspepsia is really discomfort in the center of the upper abdomen, sort of over the area of the stomach and the first part of this small intestine, the duodenum. And dyspepsia is incredibly common. And studies estimate it's probably about 20 percent of the population, though most know most of the population doesn't seek treatment for it.

The vast majority of patients who present with dyspeptic symptoms, when you do an endoscopy on them, it ends up being normal. In those patients, the majority of them fit under the category of functional dyspepsia. And that makes up about three quarters of all patients who present to gastroenterology clinics with dyspeptic symptoms I mean, to put it simply, it's a disorder of the visceral nerves of the stomach. Visceral hypersensitivity plays a major role in this.

And the Rome Foundation has set forth diagnostic criteria for functional dyspepsia. And really you should have had symptoms for at least three months. And you can have one of two categories, either postprandial, so after meal fullness or bloating, and that's called postprandial distress syndrome. Or you can have epigastric pain, sort of burning, stabbing pain. And that can occur with meals, without meals.

Dr. Buch:

Thank you very much. So let's dive into the next question. When is an endoscopy appropriate to evaluate a patient for dyspepsia?

Dr. Gabbard:

You know, that's a really common question we get and somewhat controversial. I think in gastroenterology, it seems like we have reflexive thought that everyone who presents with discomfort needs a scope. We have to take a step back and ask ourselves, what does a scope get us? And I think, you know, everyone's fear is that we want to rule out cancer. We want to rule out malignancy. We want to rule out an ulcer. I think that now the current American College of Gastroenterology guidelines would say that if a patient is above the age of 60, very clearly they should go to an upper endoscopy to evaluate dyspepsia and make sure there's no malignancy. But even in a patient who's under the age of 60, even if they have alarm symptoms such as weight loss, vomiting; the American College of Gastroenterology doesn't suggest endoscopy to ensure no malignancy in that group because the rate of malignancy is so low, much less than 1 percent in patients under the age of 60. Now, you have to make exceptions. Certainly, if someone has signs of GI bleeding, if someone has dysphasia, certainly those are good reasons to get endoscopy if they have those symptoms in addition to dyspepsia. But I think for most adults under the age of 60 with dyspeptic symptoms, an upper endoscopy isn't indicated for excluding malignancy.

There are noninvasive tests for diagnosing H. pylori, which is the other major thing we want to rule out in someone with dyspeptic symptoms. And certainly there are noninvasive tests that are much cheaper than endoscopy, such as a stool antigen, which is very, very accurate, very high sensitivity specificity. Urea breath test, again, very accurate. So I think not everyone needs an endoscopy in 2021 for this.

Dr. Buch:

For those of you just joining us, this is Dr. Peter Buch. And joining me today is Dr. Scott Gabbard, who is discussing dyspepsia.

So is there a relationship between gastric emptying and functional dyspepsia?

Dr. Gabbard:

So I'm going to answer yes and no. And I think we have to go back and think about physiologically what happens in the stomach when you eat a meal. We get so many patients who have bloating and fullness immediately after finishing a meal or during a meal, and they get sent to my clinic and the referring physician says, rule out gastroparesis. In reality, there's probably something else going on. So when you eat a meal, the first step in digestion is at the very top part of the stomach called the fundus expands. So it relaxes and it opens up to accommodate the meal.

So when a patient comes to my office and I ask them, you know, what happens when you eat a hamburger? And they say, I get full, I get bloated immediately. In my mind, I don't go to gastroparesis or delayed gastric emptying. In my mind, my first thought is, does this patient have a problem with fundic accommodation? Is their fundus not relaxing? And that's why they get that fullness, bloating, and discomfort after meals.

Certainly in clinical practice, you know, if someone is coming to me and they're having vomiting. You know, vomiting after meals or hours after meals, certainly getting a gastric emptying scan in that case to make sure they don't have gastroparesis, very, very reasonable. But for most patients who just complain of postprandial bloating, fullness, discomfort, I'm not sending those patients for a gastric emptying scan.

Dr. Buch:

Thank you for that. When addressing functional dyspepsia with patients, how do you characterize their condition when you're talking with the patients?

Dr. Gabbard:

So, you know, in functional dyspepsia, there are two major subtypes that I had discussed. And I sort of think of them as sort of bloating in one category and burning or stabbing in another category.

And certainly, there's the whole idea of the post inflammatory cascade causing visceral hypersensitivity. And what can happen for irritable bowel syndrome or for functional dyspepsia is you get some sort of acute inflammatory event, be it some sort of pathogen, a virus, bacteria causing, you know, the stomach flu, some sort of allergen. But you have some sort of acute inflammatory event that stimulates the immune system. So eosinophils, mast cells, lymphocytes get activated. And as part of the process, when they're activated, they're degranulating and releasing interleukin-5, 4, 13, among many others. Right? That stimulates the immune system, gets rid of whatever the acute inflammatory event is.

However, in about 10, 15 percent of the population, the downstream effect of this cascade is that it causes the nerves to fire when they're not supposed to. And you end up with hypersensitive nerves, be it in the stomach and functional dyspepsia or in the small intestine and colon when you're talking about irritable bowel syndrome. These are all, you know, nerve disorders or now the term is disorders of brain-gut interaction.

But that's the whole thought process behind how these often develop. And it's really a nerve problem. And so those patients, again, have the burning, stabbing. Patients can have both the postprandial distress, the bloating, fullness, and epigastric pain syndrome, the burning, stabbing. Patients can have both together. Patients can go from one to another. So they can go from being more of a bloating and fullness to more of a stabbing burning and back and forth.

Dr. Buch:

So the essence of what you're saying to the patients themselves, it's a real condition, it's not in your head.

Dr. Gabbard:

Oh, absolutely. You know, it's unfortunate that there is such stigma with what are known as functional gastrointestinal disorders. And I think a lot of experts are trying to get out of calling them functional disorders, and talking about more disorders of brain-gut interaction.

You know, when I talk to patients, I tell them the visceral nerves are mediated by so many different chemicals. But probably the most

important, at least in terms of clinical practice, is serotonin and norepinephrine. Serotonin, as we all know, is involved in anxiety and depression. But patients and many physicians are surprised to know that over 90 percent of the body's serotonin stores are generated in the GI tract by enterochromatin cells. And these chemicals modulate the way the nerves of the intestinal tract fire. So certainly, patients who have severe anxiety or depression, you know, I like to think of that as an amplifier, if you will, for the visceral inputs coming from the GI tract and going up to the brain. So certainly patients who have severe anxiety and depression may have severe functional dyspepsia or other GI, you know neurogastrointestinal disorders. And I don't tell patients it's all in their head. You know, these are clear problems with the visceral nerves. But certainly, anxiety and depression can be additive and make symptoms go from mild or moderate to quite severe.

Dr. Buch:

That was great. So part two of all of this, when addressing these functional dyspepsia patients, what therapies might you offer?

Dr. Gabbard:

So certainly, you know, any patient with functional dyspepsia, you've checked for H. pylori, and if you have it, I think in gastroenterology, we should get away from clarithromycin-based based triple therapy because the eradication rates are going down, and think of other therapies. Either, you know, quadruple therapy or levofloxacin-based triple therapy. But we should really be getting away from clarithromycin-based triple therapy for treating H. pylori.

In general, any patient now that you treat with pylori, you should test them at least four weeks after completing therapy to make sure they've eradicated H. pylori. But provided the patient either had a negative H. pylori test or they eradicated H. pylori, yet still have symptoms, then there are a few other options.

And I think certainly proton pump inhibitors are very commonly used for this. However, I would say that for many patients they will have continued symptoms despite proton pump inhibitors. So the patient has failed standard dose proton pump inhibitor for four weeks, in general, I would consider them to be a PPI failure. In my practice, I don't switch from one PPI to another to another. So if the patient has failed PPI standard dose for four weeks, I give up on PPI, and I say this is probably not going to be PPI responsive.

So then we talk about other therapies. And I like to break them down into either neuromodulators. So modulating the chemicals that I discussed like serotonin, norepinephrine, or sort of adjunctive therapies. You know, and these are the therapies using some herbal supplements have been shown to help. And other things like behavioral therapy or acupuncture can certainly help.

So for the postprandial distress, the bloating and fullness, the neuromodulators I like best is buspirone, which is a serotonin. It's a 5-HT<sub>1A</sub> agonist. And it actually has been shown in studies to help augment the fundus in accommodation. So it helps the fundus relax. And it's been shown to help with the fullness, the bloating with meals, very well tolerated at a dose of 10 milligrams, about 15, 30 minutes before meals.

For the patients who have stabbing or burning, that epigastric pain syndrome, I typically use low-dose tricyclic antidepressant like amitriptyline. It's been shown in an NIH study to help, especially with the epigastric pain syndrome subset. I start at 10 milligrams and I'll increase the dose by 10 milligrams every two to four weeks. If patients have a low tolerance for tricyclics, I will switch nortriptyline, which has less anticholinergic effect and is better tolerated, though it's a little weaker than amitriptyline. The last neuromodulator I want to point out, as many patients have weight loss, and the one medicine that has been shown to help with dyspepsia, you know, bloating, fullness, and weight loss is mirtazapine. Mirtazapine at 15 mg at night has been shown to help with dyspepsia symptoms and also have been shown to help patients regain weight, which can be quite helpful for these patients.

Dr. Buch:

Thank you. That was very comprehensive, appreciate that. Before we conclude, are there any thoughts you wish to share with our audience?

Dr. Gabbard:

No, I think that the major thing that I want to get out is to spread the word on functional dyspepsia. And don't label these patients as having GERD. You know, if a patient has heartburn, so burning, you know, in the center of the chest, you know that is GERD. But if a patient comes to you, and they're really complaining about epigastric bloating, fullness, or epigastric pain, you know, make the diagnosis. Use the Rome IV criteria, make a confident diagnosis, and talk to your patients about what functional dyspepsia is.

You know, I was fortunate enough to have been taught by one of the world experts in these disorders and at least to simplify it as best as possible, you know, I tell patients you have a nerve disorder. I understand that it's much more complicated than that. But when you're sitting down and talking to a patient, I think it's very helpful to just say you have a nerve disorder of the stomach and duodenum, functional dyspepsia.

Make a confident diagnosis, discuss what functional dyspepsia is with your patients. And then once a patient understands they can buy in, then they will actually be able to gain benefit from using, you know, a neuromodulators like a tricyclic. So many times, I get patients who are sent to me from multiple states away. Their doctor has put them on a low-dose tricyclic antidepressant, patient comes to me and says 'doc put me on an antidepressant. He or she thinks I'm crazy. I didn't take it.' I just go through my explanation. I put them on the exact same medicine and they leave incredibly happy and we help them.

So a little bit is the medicine. But I think more of what I do is just explaining what a functional gastrointestinal disorder is. So that's my last plea to get out to the audience.

Dr. Buch:

Very meaningful. Unfortunately, we're out of time for today. I want to thank Dr. Scott Gabbard very much for sharing his insights.

Dr. Gabbard:

Thank you, Dr. Buch. Had a great time. Appreciate it.

Dr. Buch:

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