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Proton Pump Inhibitors: Overused or Necessary?

Dr. Buch:

Proton pump inhibitors, or PPIs for short, are among the most frequently prescribed medications in the world, but in many instances they may actually be unnecessary. On today's program we'll take a look at the overuse of this medicine and potential risks.

Welcome to *GI Insights* on ReachMD. I'm your host Dr. Peter Buch, and joining me to share his perspective on PPIs is Dr. Alexander Perelman. Dr. Perelman is a board-certified gastroenterologist at Vanguard Gastroenterology in New York.

Dr. Perelman, welcome to the program.

Dr. Perelman:

Thank you, Dr. Buch. I appreciate you having me on. I look forward to our chat.

Dr. Buch:

So to get us started, why do you think PPIs are overused?

Dr. Perelman:

I think part of it is because we, as both clinicians, and I think in part because the general public, feel that it's a relatively safe medication. And so it's available over the counter, and often times, when we have nonspecific GI symptoms, it's very common that folks will go to the pharmacy aisle, they'll ask the pharmacist, they'll find the 24-hour heartburn relief, and it turns out that it actually ends up being a PPI; they end up in a GI office. And we sort of follow the old classification system of GERD, and that's the Canadian definition, which is "Well, you have some symptoms. Let's try a PPI. Let's see if you respond."

Dr. Buch:

Based on your experience, which patients should be on long-term PPIs?

Dr. Perelman:

That's a great question. I think that's a little bit of a loaded question and I think in part because when we think about the person who got started on a PPI on their own, the person who got started on a PPI by a primary care clinician or a person who got started on a PPI by one of us, meaning a gastroenterologist or a GI mid-level provider, the indication may be because of this nonspecific symptom, but then we have to think about where the end game is. And so the end game for people who definitely have known significant gastroesophageal reflux disease that has resulted in things like Barrett's esophagus, that person should be on a long-term PPI. In a person who has advanced erosive reflux disease, so that means LA grade C or D—or in the old grading system, grade 3 or 4—that person has evidence and reason to be on long-term PPI. Then there's the subset of folks that we don't often think about from a GI set of things, but it's actually a lot of work that Neena Abraham has done, which is cardio GI. So the folks who have an indication to be on chronic NSAIDs and usually on chronic aspirin medications and they have had a history of gastric ulcer disease or prior GI bleeding, those people should be on a long-term PPI to help suppress the likelihood of recurrent bleeding and catastrophic events.

Dr. Buch:

Let's now move on to eosinophilic esophagitis. What role do PPIs play in the management of this disease?

Dr. Perelman:

So that's a great question, and that sort of harkens back to the history of eosinophilic esophagitis. It's a relatively new disease. So thinking back 30 years when we were just starting to recognize this entity, there was this notion of eosinophilic esophagitis responsive to PPIs, and then there's the not responsive to PPIs. So our thinking about this has changed in the last I'd say five or so years, and so now the thought process is PPIs do have a space in treating eosinophilic esophagitis, but the mechanism that we're trying to use here is a little bit different. So when we think about PPIs, we're thinking about decreasing acid production in the stomach, and that's the sort of average use indication. Now in terms of eosinophilic esophagitis, the thought process is actually independent of the acid effects, and it's actually intended to target something called eotaxin-3, and this is a chemokine, or a fancy way of saying a signaling cascade, that's activated in people with EoE, and the PPIs can help dampen that down and diminish the actual presence of eosinophils in the esophagus. Now that doesn't happen in every person with eosinophilic esophagitis, and so the data are somewhere in the ballpark of 42 to 60-ish percent of people with eosinophilic esophagitis that will have what we call histologic response to PPIs.

Dr. Buch:

Thank you. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Alexander Perelman about the use and misuse of PPIs.

So now let's get into this. What are the risks of using chronic PPIs?

Dr. Perelman:

Well, that depends who you ask. If you ask the FDA versus if you ask the folks who are putting out some papers that are a little bit more aggressive, we'll see different approaches. Now realistically, if you look at the package insert and you look at the things that we've said to the FDA, there are common, basic, adverse events that we expect when we start people on PPIs, and those can be something as frequent as a headache, some change in constipation or diarrhea or some bloating or flatulence. And that's not a common thing, and those things have a tendency to go away once we stop the medication. Then there's been a lot of hype, and the hype is rooted in the fact that the associations are scary. And that's been things like chronic kidney disease. That's been things like dementia. There's been things like bone density issues and even cardiac events. And that was addressed very nicely in some literature, but we still have low-quality data to support these potential risks. And so for now, with the data being poor, we still want to make sure we're doing a risk/benefit analysis and then the benefit of the medication outweighing the risk.

There's been a really nice guideline that just recently came out from the American College of Gastroenterology, and that's the guideline for the updates for the management of gastroesophageal reflux disease. And I have this beautiful table they put together looking at these long-term risks of PPI and really showing the hazard ratios and odds ratios here are tiny, and the only evidence that we have that we can say is robust enough for us to actually hang our hat on is there is a little bit of a true increase in GI infections that happen. And the thought there is the bacteriocidal effect of the gastric acid is diminished because there's less gastric acid while everything else is more of an association, correlation, or even just a theoretic physiologic risk.

Dr. Buch:

And specifically *Clostridium difficile*, could you just comment on that?

Dr. Perelman:

Yes. So that's been the one that we're sort of seeing the most out of, and that's the one that actually has a reasonable odds ratio of about 2.3 compared to a general population now taking PPIs, and so that's the population we sometimes think twice about, especially if it's a person who has had prior episodes of CDI. That's the people that we may want to come off the medication. But again, if there's a significant need, if there's a benefit that outweighs the risk, then we still favor using that.

Dr. Buch:

Thank you. And this is a question that everybody is asking: Does the use of PPIs increase the possibility of acquiring COVID-19?

Dr. Perelman:

So that's an interesting question. I think the literature I've looked at in the past has been very, very inconclusive. I think in the early phases of the COVID pandemic, we actually did have a couple of papers come out, and they showed some associations with severe COVID presentations and some even increased mortality in the hospital setting, but again, I think that goes back to this association output because there were doses that were higher that seemed to not have that same effect and doses that were lower that seemed to have that effect, so it really wasn't clear. And at present, based on the data that I've seen, I would say, no, it does not increase the likelihood of you getting COVID-19.

Now one nuance that I think is important to suss out, and this is more conjecture than actual data, is the fact that obesity is a risk factor for severe COVID disease, and obesity on its own is a risk factor for gastroesophageal reflux disease. And so I'm wondering if in folks who happen to be coming into the hospital setting with COVID because it's going to be more severe in the obese population, they're also potentially on these medications if we're just looking at another association rather than causative event.

Dr. Buch:

That's good food for thought, and I don't know that there's any literature out there quite yet at this point. Thank you. Let's turn our attention to some practical pointers. How do you treat a patient on chronic PPI therapy who is having difficulty weaning off the medication?

Dr. Perelman:

I think the first question that we have to always ask this patient is, "how did they end up on chronic PPI therapy?" Often the case is really that they started it themselves; they had some mild improvement; it's still not enough improvement, which leads them down the pathway of they went to their primary care physician, who kept them on medication, potentially increased the dose; they still didn't get better, and they end up in our office. So the big part of that question is do they actually have gastroesophageal reflux disease, and do they fall into that category of a person who needs to be on long-term acid suppression?

And so we could talk a little bit about that, which really is going to be seeing if we can take them off the medication, see if we have the same symptoms or no change. If they have not had an endoscopy in the past, I think it's reasonable to do an upper endoscopy to evaluate for things like erosive reflux disease, and if they have no clear evidence of actual pathologic acid exposure on the procedure itself, even thinking about doing wireless pH monitoring or catheter-based pH monitoring to see if they have pathologic acid reflux.

Now if we have gone down this pathway and we're at a point to say, you know what, they have some mild reflux that should have run its course and it's just they're having a hard time coming off therapy, I think there is no good data to say that one approach is better than the other. I almost think of it as the same way as when we talk about steroid tapering, right? You get 10 doctors in a room; you're going to get 10 different regimens to wean them off steroids. And I think that holds true for PPIs.

I can tell you my personal preference and my approach to this, which is to get folks down to the standard available dose with the medications that they have, and often I do favor reaching for something like esomeprazole because I do think that the potency of it, of the ones available, is actually on the higher side, so the esomeprazole and rabeprazole being the two of the more potent ones that we have available. And so what I'll often do is I'll have folks do a 4- to 6-week course. If they responded well to therapy, I will then decrease until we can be on 20 mg once daily. And if they continue to do well, I will then, after 1 to 2 weeks, wean them down to every other day at that dose. I will have them take Pepcid usually for breakthrough symptoms. And breakthrough symptoms have a tendency to happen a little bit later than in the first week of weaning. If they are good after 1 to 2 weeks, I go to every 3 days for 1 to 2 weeks, and then I have them discontinue.

I think an alternative approach also exists, which I've tried in past in folks who have struggled to wean off, is switching to things like pantoprazole, which has got a lower potency in terms of acid suppression but also has an availability of lower dosage, and so you could go a little bit slower that way as well.

Dr. Buch:

That's great. So Dr. Perelman, before we close, are there any final thoughts that you'd like to share with our audience today?

Dr. Perelman:

Yes, absolutely. So I think one of the biggest things I think is important to understand, there's lifestyle risk factors that contribute to gastroesophageal reflux disease. And so oftentimes people will prefer to reach for a medication that's going to correct the underlying process, but that's not really going to happen in things like gastroesophageal reflux if we don't address the lifestyle things that led us there. So oftentimes in folks who are a little bit on the heavier side, there is some benefit in weight loss.

I think the other thing that's often underutilized is actually diaphragmatic breathing. So Magnus Halland had a really wonderful paper in *The Red Journal* that showed postprandial reflux episodes and symptoms significantly decreased in folks who practiced diaphragmatic breathing for about 5 to 10 minutes after meals that were known to cause reflux. And so I think a lot of folks have still not implemented this in practice, but the risk is minimal, and the benefit can be fantastic for patients. I often recommend it, and I actually suggest that Michigan State University has a really nice 4-minute video to teach patients how to do it, so much so I actually include it in my notes.

Dr. Buch:

That's great. I really appreciate your wonderful insights today. Dr. Perelman, thank you so very much. It was a pleasure having you on the program.

Dr. Perelman:

Thank you, Dr. Buch. I had a great time. I look forward to hopefully doing this again sometime.

Dr. Buch:

I'm looking forward it to myself. 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.