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A Guide for Deprescribing Proton Pump Inhibitors

Dr. Buch:
Proton pump inhibitors, or PPIs for short, are among the 10 most widely prescribed medications, but PPI overuse has been associated with adverse events. So what is the best advice for de-prescribing PPIs?

Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. And joining us today is Dr. Laura Targownik, Associate Professor and Division Director for Gastroenterology at the University of Toronto. She's also the lead author of the AGA Clinical Practice Update on De-Prescribing of Proton Pump Inhibitors, which was published in *Gastroenterology* in April 2022.

Dr. Targownik, thanks for joining us today.

Dr. Targownik:
And thank you, Dr. Buch, for having me. It's a pleasure to be able to talk about PPIs and PPI de-prescribing with you.

Dr. Buch:
Now, Dr. Targownik, can you start by telling us why there is so much PPI overuse?

Dr. Targownik:
So I think the main reason for this, Dr. Buch, is that PPIs are very effective for certain GI conditions, so I think anybody who has reflux symptoms, particularly if it's due to actual acid reflux from the stomach to the esophagus, finds PPIs to be very effective. Any clinician who's prescribed a PPI has time and time again seen how effective they are for treating things like erosive esophagitis, in both for treating and preventing peptic ulcer disease, and so we know that there are some very specific clinical scenarios where these drugs work very well and where they are the best medications to treat those conditions.

One of the issues that we as physicians deal with is when we hear a patient's story, we don't always know exactly is this reflux? Is this peptic ulcer disease? Might this be something like functional dyspepsia where someone has stomach pain or discomfort even though there's not a structural problem that can be detected with the stomach? And so we think while this has some of the symptoms of reflux or has some of the symptoms of peptic ulcer disease, why not just try a PPI and see if it works? So there's a lot of empiric proton pump inhibitor use where we kind of just use it on speculation that this might be gastroesophageal reflux disease or peptic ulcer disease.

Now the other consideration is that because a lot of gastrointestinal symptoms are transient, is that sometimes someone will start a PPI and then 2 months later they feel better, but they probably would have felt better anyways because that's just the natural ebb and flow of gastrointestinal symptoms in a lot of situations, but the patient and the physician will often say, "Oh well, this must be because the PPI is working." And then that patient remains on a PPI for an extended period of time despite the reason that their symptoms got better having nothing to do with the PPI. So that's probably one of the main factors that probably drives PPI use.

Dr. Buch:
Thank you. And with that in mind, which patients should remain on PPIs?

Dr. Targownik:
For anyone who is either at risk for developing severe, recurrent symptoms or has an underlying condition that could increase the risk of long-term complications, it's important that those patients remain on proton pump inhibitors and that they are not stopped. And probably the most common ones that we would see in clinical practice would be a known diagnosis of Barrett's esophagus, having a known diagnosis of erosive esophagitis, meaning that you've had reflux disease that's been severe enough to cause damage to the esophageal lining, or if you have a history of having an ulcer and an ongoing risk factor for that ulcer developing, like an untreated H. pylori infection, or if you require aspirin or other nonsteroidal anti-inflammatory drugs for pain or for prevention of cardiac disease. Those kinds of patients should remain on a proton pump inhibitor long-term in nearly all circumstances.

Dr. Buch:
And can you share with us your work focusing on PPI use and osteoporosis?

Dr. Targownik:
I was one of the authors on one of the first works that demonstrated that PPI use had an association with fractures. And the study caught a lot of attention because it seemed to show an association between proton pump inhibitor use and the risk of fractures and that that risk seemed to go up the longer you were on a PPI. And so what we thought was can we actually show that PPIs caused osteoporosis? Because while it's easy to detect in a hospital database when people have fractures, not everybody gets tested for osteoporosis.

So we got the idea of why don't we identify people who are just about to start on a proton pump inhibitor and do a bone mineral density test right when we start as well as some other tests to look at bone structure and then check on them in a year later and see did any of these patients develop osteoporosis. And also, did we see any change in some of the markers of bone metabolism that happen in people using PPIs so that we see evidence in the blood that more calcium is leaking out of the bones or that certain enzymes that are associated with increased bone metabolism or the loss of bone matrix like the solid part of the bone? You know, are we seeing things that indicate that when you're on a PPI that those go up? And what we found was that people on PPIs did not have an increased rate of bone turnover; they did not have any change in their bone density.

And so based on this, because we couldn't actually show that there was any obvious mechanism through which PPIs should cause fractures, it made it much less likely that PPIs were the thing that was responsible for that increased risk of fracture in those patients.

And since then, other studies have come out that have corroborated those findings to the point where I can confidently say that PPI use is probably not responsible for osteoporosis and probably not responsible for fractures but that people who are at risk for fractures because they're elderly or because they're frail, we know that those kinds of patients are often more likely to be inappropriately prescribed PPIs, and it is probably more just the fact that the person is at high risk for fracture and happens to get a PPI than the PPI actually causing the fracture.

Dr. Buch:
Very important information. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Laura Targownik about de-prescribing PPIs.

So, Dr. Targownik, what can you tell us about the association of PPI use with dementia, renal failure, and COVID-19?

Dr. Targownik:
One of the ways that we often find an important side effect of the drug is by looking for associations between the use of that drug and certain adverse events, so this is similar to the PPI story. Other researchers have shown that PPI use may be more common among people who eventually develop dementia or people who develop renal failure or people who have more severe COVID-19. And when you see these associations, it becomes incumbent on the research community to try to demonstrate is this just an association, is this just a coincidence, or is there an actual causal mechanism? And what we've generally found is that despite these associations being able to be demonstrated, we have been yet to be able to find a mechanism through which PPIs caused those effects.

So I do advise our physicians to take those findings with a grain of salt. It's very important for physicians, if they have a patient, let's

say, who has dementia or you feel might be at risk for developing dementia or any of those other complications, if that person needs a PPI for a legitimate indication, it's probably more harmful than beneficial to withhold a PPI from someone who has a definite indication. On the other hand, it also reminds clinicians that because a lot of the science is unsettled, that if there are situations where the need for a PPI is uncertain or where the need for a PPI has been disproven, that you shouldn't just prescribe them willy-nilly because there is the potential that they still might cause some harm if we definitively prove this in future studies.

Dr. Buch:
Caution is the key. With that being said, what's the best way to prevent rebound acid secretion when de-prescribing PPIs?

Dr. Targownik:
This concept of rebound acid secretion is a finding that some patients do report and has been shown in studies that when people who have been on a PPI, particularly those who have been on it for a long time, stop the medication suddenly, there can be a phenomenon by which the stomach goes through what's called a rebound hypersecretory phase, meaning that it's been trying to make acid for a long time, the PPIs have prevented the stomach from doing so, and then when the PPI is stopped, all the acid kind of rushes out at once, and this excess acid could potentially lead to increased reflux symptoms or increased stomach pain. And there have been studies that show that when people stop a PPI, that this does actually happen in some proportion of people.

And in terms of what can be done to prevent it, we don't have a lot of great evidence about a preferred strategy. So there have been some studies that have looked at whether it's better to stop the PPI slowly versus stopping the PPI abruptly, and it didn't show any definite improvement. Having said that, if I have someone who I'm anticipating wanting to stop their PPIs, I do caution them about these symptoms. I do tell them those symptoms tend to be short-lived. If they do find that the symptoms are very bad, it might indicate that they actually had a reason to be on the PPI, and those are the kind of patients in whom you should start them back on their PPI. But I do advise them that they may have some mild to moderate symptoms for, you know, maybe a week or so after stopping the PPI and that they have a true need for PPI therapy over the long-term.

Dr. Buch:
We've certainly covered a lot of ground today, Dr. Targownik. But before we conclude, are there any other thoughts you would like to share with our audience?

Dr. Targownik:
We really want to make sure that for people who have definite indications for PPI use, that we don't unnecessarily withhold an effective medication from people in whom this medication can control their symptoms, decrease their risk of future complications, and improve their quality of life. On the other hand, it does remind the clinician that for those situations where a patient is on a PPI for unclear indications or where it's clear that this was started a long time ago and that it's not actually treating the symptom that you started it for, it's just a reminder of one more reason why it's important to consider de-prescribing those patients.

Dr. Buch:
Well that brings us to the end of today's program. I want to thank my guest, Dr. Laura Targownik, for helping us better understand the new guidelines on de-prescribing PPIs. Dr. Targownik, it was a pleasure having you on the program today.

Dr. Targownik:
Thank you, and the pleasure is all mine, Dr. Buch.

Dr. Buch:
Thank you. 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.