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Expert Perspectives on PPI Prescribing & Monitoring Patterns

Dr. Buch:

Proton pump inhibitors, or PPIs for short, are among the most commonly prescribed class of medication for acid-related disorders. But what are the long-term consequences of PPIs? And how have they changed the prescribing pattern among gastroenterologists?

Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. And joining me today to answer these and other key questions about PPIs is Dr. David Leiman, Assistant Professor of Medicine at Duke University School of Medicine and lead author of "Proton Pump Inhibitor Prescribing and Monitoring Pattern Among Gastroenterology Practitioners," which was published in the *Journal of Clinical Gastroenterology* in August 2022.

Dr. Leiman, welcome to the program.

Dr. Leiman:

Well thank you very much for the invitation to be here. It's a pleasure to be able to speak about our recent study and talk generally about the use of PPIs in clinical practice.

Dr. Buch:

Let's begin with some background, Dr. Leiman. What was the purpose of your study?

Dr. Leiman:

Well, we wanted to know how the accumulating information about PPI safety and potential risks has translated into practice patterns among gastroenterologists. Over the years, numerous studies have been published that describe a wide variety of potential side effects of PPI use, which include vitamin and micronutrient deficiencies, bone mineral density loss, kidney injury, pneumonia, enteric infections, dementia, diabetes, and more recently, infections from the SARS-CoV-2 virus. However, best practice recommendations are to use PPIs at the lowest effective dose for patients with appropriate indications, and that among this group, monitoring for side effects is actually not recommended despite that litany of potential risks.

Now there have been several studies that evaluated attitudes about PPIs among patients, as well as physicians, though this was broadly studied and not really focused on gastroenterologists specifically. So our study highlighted that GI clinicians, who are experts in the use of prescription of PPIs, are frequently ordering tests for patients in contrast to best practice recommendations. And while we do not ask specifically in our study which tests were done, or which risks they were monitoring for, we did observe a relationship in which physicians were more likely to stop PPIs or recommend stopping PPIs when both they and their patients expressed some concerns about risks.

Dr. Buch:

And in your study, you noted that 36 percent of respondents reported testing for PPI side effects at least once a year. So just to really re-emphasize the standard of care, should clinicians be checking bone mineral density or serum magnesium based solely on the fact that the patients are taking PPIs?

Dr. Leiman:

That's a good question, and the short answer to that is no, based on the best available evidence. Of course, these recommendations may change in the future, but for now, expert opinion is to not periodically check for things such as electrolyte abnormalities or changes in bone mineral density just because a patient is taking a PPI. If however, those patients are due for age-appropriate screening, then these tests might be part of that evaluation. Similarly, if there's a specific symptom that might suggest testing is needed, then of course it would be warranted in that context as well.

Dr. Buch:

Thank you for that. Now if we move on to our patients, how often do they stop their PPIs inappropriately?

Dr. Leiman:

It's difficult to know how frequently patients may be either intermittently holding or all together stopping their PPIs on their own initiative, especially because patients may be getting these medications over the counter. Now many of us in clinical practice can recall patients with previously well-controlled heartburn or other symptoms, such as gastroesophageal reflux disease or GERD, that had their PPIs stopped by other providers only to then see them present to the GI clinic worsening of those same symptoms, and in some instances, complications of their GERD such as erosive esophagitis. Likewise, a study published just several years ago reported on a national survey of patients and suggested that even among those with well-controlled GERD symptoms, that about 40 percent attempted to stop their PPIs and over 80 percent did so without consulting their clinicians.

Now this data suggests a message that, in my opinion erroneously emphasizes PPI risks over benefits, is making its way directly to patients with a potential for harm, but in some instances, it may be entirely appropriate to discontinue PPI therapy, especially if there's not a good indication for someone to have been on a PPI in the first place. And it may also be quite reasonable to trial coming off of acid suppression. In fact, a recent consensus conference statement published just earlier this year, suggested that patients with unproven reflux or GERD should be offered objective testing to assess whether or not long-term PPI is actually needed. And of course, patients should always be encouraged to use the lowest effective dose of PPI. Such a strategy is generally applicable in the practice of medicine but I think is useful in the context of PPI prescription as well. However, that same consensus guidance that I referenced earlier, also recommends that clinicians should emphasize the safety of PPIs for the treatment of reflux disease.

Dr. Buch:

When dealing with this kind of question, I've always told my patients, "Do not stop PPIs until you speak to me." For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. David Leiman about PPI prescription patterns among GI practitioners.

So, Dr. Leiman, for those still not clear about chronic PPI use, can you please tell us about the side effects?

Dr. Leiman:

Absolutely. Now we've discussed many of the putative risks already, but the most common side effects remain GI upset, things like diarrhea or constipation. There are common side effects though, that would be seen in many medications such as nausea and things like that, so these are not necessarily specific just to PPIs. Now there are some established risks of PPIs, but these are generally rare and what we would consider idiopathic reactions, such as an acute inflammatory condition of the kidney, which is called acute interstitial nephritis, or AIN. This is not something one would routinely screen for. Alternatively though, there are some data from a well-conducted randomized controlled trial that shows that there likely is a real small but increased risk for enteric infections among those on long-term PPIs.

So how does that practically translate in my clinic? What I do is caution patients about this risk, but review that the risk overall is low enough that it is usually outweighed by the benefit of PPI, again making sure that the patients are on the right medicine for the right reason. Now in some instances, if patients are on chronic acid suppression with PPIs and they know they have an upcoming trip somewhere where they may be in an area that's higher risk for waterborne illness or other GI illnesses, I suggest that perhaps during that brief time they hold their PPIs and then resume them safely when they return.

Dr. Buch:

And could you comment on clostridium difficile, please?

Dr. Leiman:

Yeah, so that's the main association that's been suggested by the randomized controlled trial that I just referenced. This is probably a real increased risk, but the overall difference in the study was, although significant, not a substantially large number of infections. So I would suggest that in appropriate patients who are on long-term PPI therapy, this is a risk that one should discuss with them, but in most instances the risk is going to be outweighed by the benefit.

Dr. Buch:

And as a segue to what we just discussed, who should be on chronic PPI therapy?

Dr. Leiman:

Well right now their best practice recommendations published by the American Gastroenterological Association, or AGA, that several years ago outlined the group who should be on chronic PPI, and among these are patients with complications of their gastroesophageal reflux disease, including those with Barrett's esophagus. Others with GERD who need PPIs for symptom control can safely maintain their PPI therapy, again emphasizing at the lowest effective dose. Further, patients with a high risk of GI bleeding, such as from peptic ulcers or patients who are on chronic anti-inflammatory medications like NSAIDs, can safely continue PPIs long-term. To that list I would also add patients who are taking PPIs for an allergic inflammatory condition of the esophagus, which is called eosinophilic esophagitis, or EOE. Many of these patients do very well on PPIs long-term, and I would suggest that that's an appropriate indication as well.

Dr. Buch:

Now, Dr. Leiman, is there a relationship between proton pump inhibitor use and the risk of developing COVID-19?

Dr. Leiman:

This remains an outstanding question, though there are data that have suggested this relationship does exist. Some early studies describe that PPI use was associated with worse clinical outcomes, and the main hypothesis there was that gastric acid suppression from PPIs might increase patients' susceptibility to viral infection, yet other studies have shown that another medication called famotidine, that also suppresses gastric acid may be protective. Newer data that have come out, have suggested that there may be a small increased risk for hospitalization among those on PPIs. And the authors felt that this was likely due to residual confounding or other unmeasured variables, and that ultimately, there was probably no relationship between SARS-CoV-2 infection or death among PPI users.

I would say that there really do remain quite a number of variables in this question, in this assessment of the risk, and relationship between COVID-19 and PPIs that are difficult to assess or control for right now. This includes the evolving nature of the pandemic, but ultimately, what I would argue is that the risk for any poor outcome from COVID is much more likely to stem from being unvaccinated than from taking PPIs as indicated and prescribed. And so if patients are on PPIs, they can feel comfortable with continuing them, particularly if they have discussed this with their clinicians.

Dr. Buch:

Well this has been an outstanding discussion about PPI prescription patterns. And I want to thank my guest, Dr. David Leiman, for sharing his insights. Dr. Leiman, it's been a pleasure speaking with you today.

Dr. Leiman:

Likewise. Thank you again so much for the opportunity to talk with you.

Dr. Buch:

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.