Use, Misuse, and Rational Use of Proton Pump Inhibitors

Ramesh Satarkar*

Ever since their introduction in 1989, proton pump inhibitors (PPIs) have gained a significant place in prescriptions across all specialties. The market size of PPIs is estimated to be 3.45 billion USD and is expected to grow at a 5.50% compound annual growth rate (CAGR) to become 5.89 billion USD by 2034.[1] The rise in use is partly because of increased prevalence and awareness of diseases like gastroesophageal reflux disease (GERD), but also because of the overuse of these medicines for "slippery" indications. Of late, there has been a lot of awareness about overuse of PPIs, and many gastroenterological societies have issued guidelines toward their rational use.[2–5]

Indications for Use of Proton Pump Inhibitors

Short-term PPI use indications (up to 8 weeks):

- *Helicobacter pylori* eradication.
- First episode of dyspeptic symptoms in young patients, without warning symptoms like weight loss and gastrointestinal bleeding.
- Empiric therapy of uncomplicated GERD, diagnosed clinically in young patients.
- Low-grade esophagitis, LA grade A or B on endoscopy.

Long-term PPI use indications (>8 weeks):

- High-grade esophagitis, LA grade C or D.
- Barrett's esophagus.
- Zollinger–Ellison syndrome.
- Eosinophilic esophagitis.
- Patients on aspirin for cardiac prophylaxis, or using nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids, who have a prior history of ulcer bleeding.
- Coadministration with pancreatic enzymes in chronic pancreatitis.
- Symptomatic GERD with failed attempts to reduce PPI dose.

Patterns of Misuse/Overuse

The most common being exceeding the duration of PPI use. Often, the prescription of a specialist doctor containing PPI is continued by family physicians or general practitioners. Availability of these medicines over-the-counter (OTC) makes it easy for patients to perpetuate their use.

Secondly, often they are used for incorrect indications. PPIs are used as a coprescription with antibiotics, NSAIDs, corticosteroids, and aspirin for cardioprophylaxis. They cannot be expected to reduce drug-induced nausea and vomiting, and using preemptively in all for ulcer prophylaxis has little justification, especially in young and low-risk patients.

Often, PPIs are used incorrectly for extraesophageal symptoms such as hoarseness of voice, globus sensation, asthma, etc., assumed to be due to reflux. Many of these patients do not have any esophageal symptoms and have normal pH-metry.

Reasons for Overuse

It is assumed that acid is responsible for all upper gastrointestinal symptoms. However, upper gastrointestinal symptoms can be due to excess acid, acid at the wrong place, disturbances of motility, and visceral hypersensitivity. Many patients having typical reflux symptoms have normal 24-hour pH-metry, the gold standard test for acid reflux.[6] They have "functional heartburn," due to visceral hypersensitivity, a disorder of the gut–brain axis. The term acidity is used so loosely that it can have umpteen meanings depending on patients' perspectives. Many patients who have migraine or even coronary artery disease describe their symptoms as "acidity." They take PPIs not only without any benefit, but also at risk of missing an important life-threatening disease.

Sometimes, PPIs are used when there is limited access or willingness to do investigations in cases of GERD or nonulcer dyspepsia (NUD). Patients often choose cheaper solutions over costly investigations. This is acceptable in a few situations, such as the first episode of symptoms, no warning symptoms, an obvious precipitating event, and a young patient. However, when the patient is not responding or has warning symptoms, investigations at the first go itself are the choice. Reluctance on the part of patients to modify behavior, for example, weight reduction or cessation of smoking to reduce reflux-like symptoms, is another hindrance. They prefer a simple pill of PPI over the difficult task of behavior modification. Physicians also need to consider alternative therapies such as H_2 receptor antagonists, sucralfate, or alginates for control of symptoms. In select patients, advising Nissen's fundoplication for those with a large hiatus hernia or bariatric surgery for morbid obesity and reflux is appropriate over long-term use of PPIs, especially when the patient is young. Patients, as well as physicians, have concerns about rebound symptoms after discontinuation of long-term PPI use. The rebound is due to hypergastrinemia, which occurs after long-term use of PPIs. Rebound symptoms are often transient and can be easily controlled.

Adverse Events of Long-term Proton Pump Inhibitor Use

The PPIs are safe when used appropriately. Long-term acid suppression adversely affects the physiological functions of gastric acid. Macrocytic or microcytic anemia, increased risk of bone fractures, small intestinal bacterial overgrowth, and increased risk of enteric infections are adverse events related to long-term acid suppression. Interstitial nephritis, drug interactions, especially reduced efficacy of clopidogrel, diarrhea, and vomiting are adverse events unrelated to acid suppression. Certain conditions, like dementia, increased risk of gastrinoma, and hypomagnesemia have very weak causal associations.[7]

Rational Use of Proton Pump Inhibitors

- The diagnosis for which PPI is being used should be clear, viz., reflux esophagitis, NUD, or duodenal ulcer. This can be a clinical judgment or based on investigations.
- There must be a definite plan about the duration of use and methods to stop PPI. Once decided, the plan must be conveyed to the patient clearly, and he must be informed about possible adverse events in long-term use.

Consultant Gastroenterologist, Satarkar Gastroenterology Center, Chhatrapati Sambhajinagar, Maharashtra, India;
*Corresponding Author

How to cite this article: Satarkar R. Use, Misuse, and Rational Use of Proton Pump Inhibitors. J Assoc Physicians India 2026;74(5):13–14.

- If the patient is not responding at the end of the prescribed course, an alternative diagnosis needs to be considered, and appropriate investigations should be carried out.
- Short-term use of PPI can be stopped abruptly. Patients on long-term PPI can be taken off the medicine by various strategies, like alternate-day PPI or half-dose PPI for some period and then stopping it, or changing over to on-demand therapy, or replacement with H2RA blockers, alginates, or sucralfate for some period to control rebound symptoms.
- For patients on long-term PPI use for an appropriate indication, one must be watchful for adverse events.

Any medicine, when used appropriately, is a friend; otherwise, it can become a foe. We must increase awareness among medical practitioners as well as patients about the rational use of PPIs. This will help all to "choose wisely."

References

1. Gotadki R. MRFR/med/17676-HCR; 2025.
2. Farrell B, Lass E, Moayyedi P, et al. Reduce unnecessary use of proton pump inhibitors. BMJ 2022;379:e069211.
3. Targownik LE, Fisher DA, Saini SD. AGA clinical practice update on de-prescribing of proton pump inhibitors: expert review. Gastroenterology 2022;162(4):1334–1342.
4. Scarpignato C, Gatta L, Zullo A, et al. Effective and safe proton pump inhibitor therapy in acid-related diseases—a position paper addressing benefits and potential harms of acid suppression. BMC Med 2016;14(1):179.
5. Dutta AK, Jain A, Jearth V, et al. Guidelines on optimizing the use of proton pump inhibitors: PPI stewardship. Indian J Gastroenterol 2023;42(5):601–628.
6. Naik RD, Vaezi MF. Extra-esophageal manifestations of GERD: who responds to GERD therapy? Curr Gastroenterol Rep 2013;15(4):318.
7. Salvo EM, Ferko NC, Cash SB, et al. Umbrella review of 42 systematic reviews with meta-analyses: the safety of proton pump inhibitors. Aliment Pharmacol Ther 2021;54(2):129–143.