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Letter to the Editor

Imprudent use of proton pump inhibitors in current practice

Sir,

"Hurry, worry and curry" can be commonly associated with acid peptic disease. Modern day hectic lifestyle along with the fact that Indian food is spicy, largely contribute to the increased occurrence of heartburn. This is a very common symptom faced by today's generation, which is often ignored and undiagnosed.

Repeated reflux of acid gastric contents into the lower third of esophagus causes esophagitis, erosions, ulcers, pain on swallowing, strictures and increases the risk of esophageal carcinoma. There may also be extraesophageal complications.[1]

It is appropriate to empirically treat patients with classic gastro esophageal reflux disease (GERD) symptoms first with lifestyle modifications only and if that fails patient-directed gastroprotective therapy should be started.[2] Lifestyle modification which can greatly help reduce reflux are:[3,4] to eliminate substances that reduce tone in the lower esophageal sphincter (caffeine, alcohol, tobacco, mint, chocolate, fatty or fried foods); to avoid large meals right before bedtime; to elevate the head of the bed; to avoid tight clothing that constricts the abdomen; do not recline within 2-3 hrs after a meal and to lose weight if overweight.

Gastroprotective agents (GPA) include, (i) acid lowering drugs namely H_2 blockers, proton pump inhibitors (PPIs), anti-cholinergics and prostaglandin analogs, (ii) acid neutralizers like antacids, (iii) ulcer protective, and (iv) anti-*Helicobacter pylori* drugs. The indications for this gastroprotective approach are peptic or duodenal ulcer, stress ulcer, gastritis, Zollinger–Ellison syndrome, GERD and non-steroidal anti-inflammatory drugs induced ulcers.

However in recent times, it is seen that almost all prescriptions include at least one antacid or acid lowering drug, commonly a PPI regardless of the need for these agents. Up to 7 of 10 hospitalized patients get acid suppressing drugs (40-70%); 2/3 do not have an indication; ½ of orders are new starts; ½ of these are continued when patient is discharged.[5] Administration of unnecessary medication could cause adverse effects and pharmacological interactions and lead to polypharmacy and increased cost of therapy.

Among the GPAs, PPIs are the most common. PPIs exert their effect by inhibiting the H+/K+ - adenosine triphosphatase, or proton pump, which is located in the highly acidic lumen of parietal cells.[6] This highly acidic environment enables the PPI to become protonated to its active metabolite, which then irreversibly inhibits the activity of the proton pump, resulting in an increase of gastric pH. As opposed to H2-receptor antagonists, another class of gastrointestinal (GI) agents, PPIs are longer-acting and produce a greater degree of gastric acid suppression, thus making them more effective.

Because PPIs decrease the acidity of the stomach, the main concern from the effect of profound acid suppression is hypergastrinemia. Patients receiving a PPI are also susceptible to the colonization of ingested pathogens, which can lead to bacterial gastroenteritis.[6,7] The US Food and Drug Administration just recently announced that overexposure or prolonged use of a PPI may be associated with a higher risk of infection by the deadly bacteria clostridium difficile.Evidence shows there is a distinct link between prolonged gastric acid suppression, hypergastrinemia and neuroendocrine cell hyperplasia, which may allow the production of carcinogenic substances.[7] Due to the fact that PPIs are commonly prescribed to regulate and prevent symptoms of a chronic implacable condition, it is probable that the duration of therapy may exceed more than 4 years. This prolonged treatment is believed to hinder calcium absorption in the small intestine.[8] The ability of the small intestine to absorb calcium salts is highly pH dependent, and since PPIs cause an increase in gastric pH, calcium salts are rendered insoluble and cannot be absorbed. This inhibition of calcium absorption has a direct correlation to osteoporotic fractures in those individuals taking a PPI. A study conducted in Canada determined that after 7 years of continuous exposure to a PPI, there was a statistically significant increase in osteoporosis-related fractures and an increased risk of hip fracture after 5 years.[8] Increase of serum potassium levels and low magnesium levels have been reported in patients taking long-term PPIs.[9] Last but not least overuse of PPI unnecessarily burdens national health care budgets.

In a developing country like India, where over 500 branded formulations of PPI are available, probability of misuse and abuse increases exponentially. Although a safe and very effective class of pharmaceutical agent, PPIs should be used only when there is documented evidence of a GI disorder that cannot be treated with an H2-receptor antagonist, and where a PPI use is clinically justified. Increased clinician awareness on appropriate PPI prescription will lead to better patient outcome at lower cost.

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