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Focus: Proton Pump Inhibitor (PPI) Use and Infection Risk

Proton pump inhibitors (PPIs) are a frequently utilized class of medications with multiple indications, and with availability to patients through both prescription and over-the-counter purchase. PPIs are used as acid-suppressive therapy in common disease states including gastroesophageal reflux disease (GERD) and gastrointestinal ulceration or bleeding. Often perceived to be a relatively benign class of medications, recent data shows PPI use is not without risks. Prolonged use of PPIs can lead to malabsorption of vitamins and minerals, loss of bone density, and increased incidence of fracture. A growing body of evidence additionally shows PPIs are associated with an increased risk for both *Clostridium difficile* infection (CDI) and pneumonia. Here we will review the evidence-based indications for PPI use and the data supporting a link between the drug class and infection risk.

Proton Pump Inhibitor Use and *C. difficile* Infection

Clostridium difficile is a common and costly healthcare-associated infection with a rising prevalence. Several risk factors are associated with CDI including antibiotic use, prolonged hospitalization, and immunocompromising conditions. Recent evidence has also demonstrated an association between PPI use and the incidence of CDI. Several meta-analyses have shown a significantly increased risk of CDI following PPI exposure, with odds ratios for developing CDI with PPI use ranging from 1.65 to 1.81.[1-3] The underlying mechanism for this increased risk is thought to be decreased host defense against *C. difficile* spore germination and alteration of the normal GI flora due to acid suppression by PPI therapy.

Proton Pump Inhibitor Use and Pneumonia

Use of PPIs has also been linked with an increased risk of both community- and hospital-acquired pneumonia. The underlying process is attributed to an increase in gastric pH leading to easier colonization by pathogens in the upper GI tract. Meta-analyses have demonstrated significant positive associations between the use of PPIs and the incidence of CAP, with odds ratios ranging from 1.27 to 1.89.[4-5] The increase in risk appears to be greatest within one month of PPI initiation, possibly due to the development of tolerance to acid suppressive therapy. A 30% increased risk of HAP has additionally been reported with the use of PPIs.

Indications for Proton Pump Inhibitor Use*

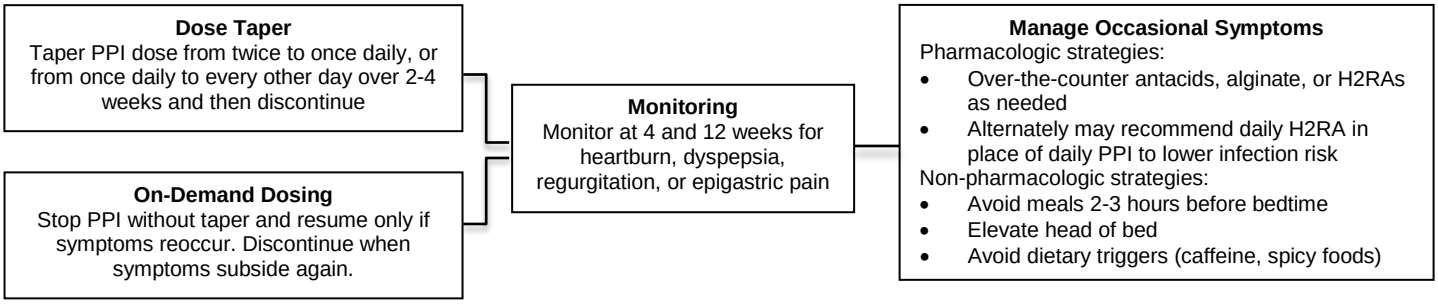
Gastroesophageal Reflux Disease (GERD)	• Initial 8-week course of PPI therapy • Maintenance therapy should continue in patients with persistent symptoms or with complications including erosive esophagitis, Barrett's esophagus, intestinal metaplasia, ulcer, or stricture
Acute GI Bleed	• PPIs should be used during the initial evaluation and management of acute GI bleed • Need for maintenance therapy is determined once the source of bleeding has been identified and treated
Gastric and Duodenal Ulcers	• PPIs should be utilized for treatment of active ulcers • Maintenance therapy extending beyond 4-8 weeks should continue only in patients with idiopathic ulcers or who have high risk features at presentation (life threatening hemorrhage, shock, etc.)
Stress Ulcer Prophylaxis (SUP)	• PPIs should be utilized for SUP only in patients admitted to the ICU at high risk for GI ulceration • Risk factors: mechanical ventilation >48 hours, coagulopathy, history of GI bleeding within 1 year, traumatic brain injury, trauma, spinal cord injury, burn, renal or liver transplant, sepsis, high dose corticosteroids, ICU stay ≥1 week, occult bleeding ≥6 days • PPIs can be discontinued in most patients upon transfer from the ICU (note: transplant patients will often continue on PPI therapy beyond ICU stay)
Prevention of NSAID-related ulcers	• PPIs should be used in patients requiring NSAID therapy who are at moderate to high risk of GI ulceration • Risk factors: history of GI ulceration, age ≥65, concurrent use of ASA, anticoagulants, or corticosteroids
H. pylori infection	• 7-14 day course of PPI therapy and antibiotics is recommended as first-line treatment
Pancreatic Insufficiency	• Patients requiring pancreatic enzyme supplementation require PPI therapy with certain drug formulations to reduce enzymatic inactivation by gastric acid
Zollinger-Ellison Syndrome	• Lifelong PPI therapy is recommended to reduce gastric acid secretion

*Indications reviewed in conjunction with the gastroenterology physicians at UW Medicine/Northwest Hospital & Medical Center

Reducing Infection Risk through "Deprescribing" PPIs

Judicious prescribing of PPIs during a patient's hospital stay can help reduce short-term risks of CDI and pneumonia associated with their use. This can be accomplished by ensuring only patients with one of the above clinical indications receive a PPI during admission. Appropriate discontinuation of PPIs can also reduce unnecessary long-term risks and costs associated with the drug class. This includes patients who have been on long-term outpatient therapy without a clear indication. Two strategies used to aid discontinuation of a long-term PPI include a dose taper to reduce rebound symptoms, or the use of on-demand dosing. In patients with GERD, the use of non-pharmacologic strategies, antacids, or H_2-receptor antagonists (H2RAs) can also be employed for symptomatic management. Although there are infection risks associated with the use of H2RAs, these risks appear to be lower when compared to the use of PPIs.

Discontinuing PPIs in GERD



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