GERIATRIC NURSING

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Risks versus Benefits of Long-Term Proton Pump Inhibitor Therapy in the Elderly

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Symptoms associated with chronic acid-related disorders such as gastroesophageal reflux disease and peptic ulcer disease can decrease quality of life. Approximately 1 in 10 individuals suffers from some form of dyspepsia. It is estimated that acid reflux is responsible for up to 50% of noncardiac chest pain.[1] Chronic or severe exposure of the esophagus to gastric acid can lead to complications such as erosive esophagitis, which in turn can lead to bleeding, ulceration, strictures, Barrett esophagus, and esophageal adenocarcinoma.[2,3] Therefore reduction of gastric acid is an important treatment modality for the prevention of morbidity and mortality.

Proton pump inhibitors (PPIs) have been shown to provide more potent acid suppression and greater clinical efficacy then histamine-2 receptor antagonists, leading to their popularity among prescribers for the treatment of acid-peptic disorders.[2] PPIs frequently are used for the prevention and treatment of gastroduodenal ulcers associated with nonsteroidal anti-inflammatory drugs and *Helicobacter pylori* infection.[4] A low incidence of side effects, quick efficacy, and dosing that requires once or sometimes twice daily administration makes them popular among patients. PPIs are among the most frequently prescribed drug classifications in the primary care setting. In 2006, esomeprazole alone exceeded $5 billion in sales, yet few studies have been conducted on safety in long-term PPI use, particularly in the elderly population.[5]

Currently there are 5 PPIs available on the U.S. market. Food and Drug Administration approval for PPIs is for short-term use and generally ranges anywhere from 4 to 8 weeks for the treatment of various gastroenterological symptoms; however, many patients require PPI therapy for extended periods of time to prevent relapse of symptoms or associated complications (Table 1).[6] It has only been in the last few years that potential adverse effects such as increased risk of respiratory infections, increased risk of *Clostridium difficile* infection, and, most recently, an increased risk of bone fractures has been identified with long term PPI use. The purpose of this article is to address the risks and benefits of long-term PPI use in the elderly patient.

Pharmacology of PPIs

PPIs are substituted benzimidazoles that are administered as an inactive prodrug. The enteric-coated tablets or capsules pass through the acidic environment of the stomach intact. The enteric coating dissolves when it enters the alkaline environment of the small intestine where the prodrug is absorbed. PPIs are lipophilic weak bases that readily cross the lipid membranes into the acid parietal cell canaliculus. Here the prodrug becomes protonated and undergoes a molecular conversion to produce an activated sulphenamide cation that binds with the H+/K+ ATPase enzyme. The result is irreversible inhibition of acid secretion by the proton pump.[6]

Standard doses of PPIs can reduce gastric acid secretion up to 98% by irreversibly deactivating the proton pump of the gastric parietal cell. PPIs should be administered on an empty stomach about 1 hour before meals to increase bioavailablility. The serum half-life of PPIs is approximately 1.5 hours, and the effect on acid secretion can last up to 24 hours. Full acid inhibiting potential can take up to 3–4 days.[6]

PPIs are generally well tolerated by most patients. This class of drugs undergoes a rapid first-pass effect and has minimal renal clearance, therefore, dose reduction is not required for patients with renal insufficiency.[6] The only contraindication listed for PPI use are for patients with a known hypersensitivity to any of the components of the formulation. For geriatric patients, dosage and administration does not

Table 1.
Food and Drug Administration–Approved Use of Proton Pump Inhibitors for the Management of Gastroesophageal Reflux Disease

Medication	Dosage	Recommended Duration of Therapy
esomeprazole (Nexium)	20 mg qd	4 weeks
lansoprazole (Prevacid)	15 mg qd	8 weeks
rabeprazole (Aciphex)	20 mg qd	4–8 weeks
omeprazole (Prilosec)	20 mg qd	4 weeks
pantoprazole (Protonix)	20 mg qd	Up to 8 weeks

qd = daily.

need to be altered.[7] Headache, abdominal pain, nausea, and diarrhea are the most common side effects. The incidence of diarrhea increases with age and dosage.[8] Additionally, diarrhea is the most commonly occurring side effect reported by patients receiving maintenance doses (3.8%). Uncommon side effects include rash, itch, and constipation. The overall incidence of side effects is less than 5%, making PPI use ideal for short-term therapy; however, there continues to be concerns about its long-term impact.

Risk of Respiratory Infection With PPI Use

Elderly people have numerous factors that increase their risk for infection. Comorbidities, together with the natural aging process, are responsible for a reduced innate immunity and an increased morbidity rate in the elderly.[9] Therefore the prevention of infection is a priority in the management of the elderly patient. The acidic environment of the stomach is considered a defense mechanism against ingested pathogens, and the use of a PPI will alter this barrier. Normal gastric pH that is not treated with acid suppressive medication will be below 4. The goal of PPI acid suppression therapy is to raise gastric pH levels to >4 (hypochloridic state).[10]

Of particular concern among the elderly population are respiratory infections and the high incidence of community-acquired pneumonia (CAP). For patients under age 50, mortality is rare, and treatment can usually be managed as outpatient. The older adult, however, has an increased mortality rate from such infections and frequently requires more aggressive treatment.[9] Biopsies of gastric mucosa in patients receiving acid suppression therapy have shown the presence of type B influenza virus during a time when the patient has no other signs of infection. Also discovered from the biopsies was the presence of bacteria that is normally found in the mouth and pharynx. Intestinal pathogens have been found in the oral cavity of mechanically vented patients receiving acid suppressive therapy, predisposing patients to lower respiratory tract infections.[10] Moreover, the greater the degree of acid suppression, the greater the amount of bacterial overgrowth, thus increasing the risk of respiratory infection. A study published in the *Journal of American Medical Association* in 2004 showed a correlation between CAP and acid suppression therapy. The study suggested that the resulting elevated pH or hypochloridic state failed to eliminate or may have even allowed an increased colonization of pathogens associated with CAP. Patients receiving acid suppressive therapy had a 4.5 times greater chance of developing community-acquired pneumonia.[10]

Risk of *Clostridium difficile* Infection With PPI Use

Another important pathogen that can thrive in the stomach as a result of a hypochloridic state is *C. difficile*. This gram-positive, spore-forming bacillus is part of the normal flora of the stomach in about 3% of the population and is not considered a health threat except to the very