Introduction

The first proton pump inhibitor (PPI) came on the market thirty years ago. As of 2019, there are 6 commercially available generic PPIs approved by the United States Food and Drug Administration (FDA) [1] under several brand names (Table 1). PPIs work to reduce the amount of gastric acid in the stomach and prevent the movement of acid into the esophagus. Specifically, PPIs inhibit the action of the proton pump which is the last process of creating and excreting stomach acid [2]. They are effective in blocking acid secretion by up to 99 percent and offer up to 76% symptom relief [3].

Table 1: Proton Pump Inhibitors in the United States

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand Name(s)</th>
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</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td>Prilosec, Zegerid</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>Nexium</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>Prevacid</td>
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<tr>
<td>Dexlansoprazole</td>
<td>Dexilant, Kapidex</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>Protonix</td>
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<tr>
<td>Rabeprazole</td>
<td>AcipHex</td>
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</table>

Scope of the Problem

PPIs became one of the most widely prescribed, even overprescribed, as well as overused over the counter (OTC) treatments for gastroesophageal reflux (GERD), laryngopharyngeal reflux (LPR) and other gastrointestinal disorders due to their effectiveness to suppress gastric acid [2]. OTC PPIs are marketed at lower doses than prescription strength, and per directions for usage, are only intended for 14-day use up to 3 times per year. Although short-term use is considered to be somewhat safe, several safety concerns have arisen linking long-term use of PPIs to a variety of serious health problems. While randomized clinical trials are lacking, research findings including observational studies suggest long-term PPI use is associated with risk of vitamin B-12 deficiency, calcium, iron and magnesium malabsorption [4-7], myocardial infarction [8,9], osteoporosis and bone fractures of the hip, wrist and spine [5, 10-12], kidney disease [13-16], dementia [17-20], infections including Clostridium difficile, Salmonella and pneumonia [21-23] and neoplasm and gastric cancer [24-26], with some of these conditions reportedly impacting premature death [27,28]. Studies have shown increased risks not only with extended use but with increased dosage, which could prove detrimental in the case of LPR in which BID use of PPIs is recommended. Moreover, the FDA has released several consumer updates, press releases and other drug safety communications in 2010, 2011 and 2012 implicating long-term use with health risks, prompting label
revisions for prescription and OTC PPIs, reconsideration among physicians, and heightened consumer alarm.

Final Considerations

PPIs are known to cause serious health conditions and even death especially when taken long-term. Although the recommended treatment regimen for PPIs is 3-6 months or shorter for LPR, many end up continuing the drugs for years, prompting consideration for short-term or alternative treatment. Alternative medical management for treating LPR include H2-receptor antagonists (H2 blockers) or antacids; however, H2 blockers have also been linked to some of the same health risks as PPIs [8, 16, 17, 21, 22, 27]. Like PPIs, H2 blockers are prescribed and available OTC, and also work to suppress stomach acid production; hence, may cause similar conditions. Although investigations into PPIs and H2 blockers are ongoing, the FDA issued a recent statement in September 2019 alerting patients and health care professionals of N-nitroso dimethylamine, a probable human carcinogen, found in ranitidine products, including the brand name Zantac.

Antacids are a class of drugs available OTC that offer on demand system relief by neutralizing gastric acidity and inhibiting pepsin when taken within an hour after a meal [29]. There are differences between formulations and brands of commercially available antacids, but the most effective have high antacid neutralizing capacity (ANC), work rapidly, and have a long duration of neutralization. The FDA requires that antacids sold in the United States have a minimum ANC of 5 milliequivalents [of acid that is neutralized] per dose. While antacids are intended for PRN use and present few minor side effects, extensive use and heavy dosing of certain formulas has been reported to cause osteomalacia, milk-alkali syndrome, and hypophosphatemia [29]. As with any drug, there are warnings, precautions and drug interactions for select populations, depending on the type of antacid.

Reflux behavioral management is a beneficial adjunct to drug therapy and may be a successful nonpharmacological alternative as a solo treatment for mild to moderate LPR. Behavioral guidelines involve lifestyle strategies of dietary modifications, smoking cessation, weight management and elevating the head of the bed to avoid nocturnal reflux [30]. Dietary changes include avoidance of highly acidic or fatty foods, caffeine, alcohol, soda, binge eating, eating too close to exercising, and eating too close to bedtime.

Acknowledgement

None.

Conflict of Interest

No conflict of interest.

References

1. US Food and Drug Administration. Proton pump inhibitors.

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