Reliving 25 years of Experience with Omeprazole in Acid-peptic Diseases

Praveen Sharma

Abstract

Background: Acid-peptic diseases (APDs) are commonly encountered in clinical practice. The identification of proton pump and the subsequent introduction of proton pump inhibitors (PPIs) can be heralded as a milestone in the treatment of APDs. They have been used for the past 25 years with a good track record of safety. Omeprazole is a well-established and most studied drug in the PPI class.

Objectives and methods: This review is an objective overview of the efficacy and safety of PPIs in APDs, with special focus on omeprazole.

Results: The efficacy of omeprazole in gastroesophageal reflux disease (GERD) and peptic ulcer disease (PUD), including those caused by non-steroidal anti-inflammatory drugs (NSAIDs) is well documented. In clinical studies, the newer, more potent PPIs, used at comparable doses, have not shown greater efficacy than omeprazole. The PPIs are in general well-tolerated. Most of the concerns regarding their long-term safety have been unfounded.

Conclusion: Twenty five years after the introduction of omeprazole, the first of the PPIs, omeprazole has still remained a valuable drug in the armamentarium of clinicians.

Introduction

Acid-peptic diseases (APDs) are a group of disorders with overlapping pathogenic mechanisms involving the effects of gastric acid on diminished mucosal defense. These include peptic ulcer disease (PUD) and gastroesophageal reflux disease (GERD). They impair the quality of life and productivity of the afflicted patients and are associated with morbidity and mortality.

This article presents an overview of our current understanding of APDs. An account of proton pump inhibitors (PPIs), which are the most commonly used pharmacotherapy in APDs, as well as an overview of omeprazole, the prototype of PPIs in the management of APDs, defining its role in APDs over 25-years after it was initially introduced for clinical use are presented.

Peptic Ulcer Disease

Peptic ulcer disease is a mucosal defect that extends to or beyond the muscularis mucosa, reaching the submucosa, mostly occurring in the stomach (gastric ulcers) and the proximal duodenum (duodenal ulcers) (Figure 1). The lifetime prevalence of PUD in the general population is reported to be 5–10%. In an epidemiologic study carried out in India, involving 30,216 patients, the prevalence of PUD was found to be 7.8%.

Etiopathogenesis

Infection with the bacteria, Helicobacter pylori (H. pylori) and the use of non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin are the main risk factors of both, gastric and duodenal ulcers. The pathophysiologic mechanisms associated with PUD are represented in Figure 2. The acid-peptic microenvironment has a vital role in the mucosal damage due to NSAIDs, as shown in many experimental and clinical studies.

Clinical Features and Diagnosis

A history of episodic epigastric pain, relief of pain after food intake, and nighttime awakening because of pain, with relief following food intake are suggestive of peptic ulcer and help in the diagnosis. Anemia, hematemesis, melena, or heme-positive stool suggests bleeding whereas vomiting suggests obstruction. Anorexia or weight loss indicates cancer; persisting upper abdominal pain radiating to the back indicates penetration; and severe, spreading upper abdominal pain suggests perforation. Endoscopy is considered as gold standard for the diagnosis of PUD. Detection of H. pylori using histology or rapid urease test serves as a guide to treatment.

Consultant Gastroenterologist, Institute of Liver, Gastroenterology & Pancreatico-Biliary Sciences, Sir Ganga Ram Hospital, New Delhi
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**H. pylori associated PUD**

<table>
<thead>
<tr>
<th>Inflammation associated with infection may lead to:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cytokine induced inhibition of parietal cells, pan-gastric and gastric ulcer</td>
</tr>
<tr>
<td>2. Increased gastric acid secretion consequent to hypergastrinaemia and reduced antral somatostatin content, causing duodenal ulcer</td>
</tr>
</tbody>
</table>

**NSAID-associated PUD**

<table>
<thead>
<tr>
<th>Damage to gastroduodenal mucosa occurs due to:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Systemic mechanisms due to constitutively expressed COX-1-derived PGs - Reduced PG levels are associated with low mucus and bicarbonate secretion, inhibition of cell proliferation, and decreased mucosal blood flow - thus compromising mucosal integrity</td>
</tr>
<tr>
<td>2. Local mechanisms - disruption of mucous phospholipids and cell membrane</td>
</tr>
</tbody>
</table>

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**Etiopathogenesis**

Usually, the anti-reflux barrier (the lower esophageal sphincter, the extrinsic crural diaphragm, and the supporting structures of the gastroesophageal flap valve) prevent the reflux of acid into the esophagus. When this barrier is compromised, an increasing numbers of reflux events as well as increasingly abnormal esophageal reflux exposure results. This, as well as the reduced ability of the esophagus to clear and buffer the refluxate are contributory to esophageal mucosal damage. Based on the presence or absence of esophageal mucosal damage seen on endoscopy, GERD can be classified as non-erosive reflux disease (NERD) or erosive reflux disease (ERD).

**Clinical features and diagnosis**

The clinical features of GERD are summarized in Table 1. A presumptive diagnosis of GERD is made if the patient presents with typical symptoms of heartburn and regurgitation as well as with a trial of treatment with PPIs. Objective testing with upper endoscopy and esophageal pH monitoring may be needed in patients who are not responsive to PPIs, with alarm features, at risk for Barrett’s esophagus.

**Treatment**

Empiric medical therapy with a PPI for 8-weeks is the first-line treatment in GERD to facilitate healing of esophagitis as well as for symptom relief. Maintenance therapy with PPI is recommended for GERD patients who continue to have symptoms after PPI is discontinued, and in patients with complications, including erosive esophagitis and Barrett’s esophagus. PPIs have been shown to be superior to H₂-blockers for symptom relief, healing of esophagitis, as well as preventing relapses in patients with erosive esophagitis and for symptom relief in NERD.

**Acid-peptic diseases in India**

In a cross-sectional study involving 1000 clinicians, which was carried out with the objective of understanding the epidemiology, clinical presentation, and associated overlapping co-morbidities in Indian patients with APDs, it was observed that:

1. The incidence of GERD was 39.2% and that of PUD was 37.1% (duodenal ulcer: 10.5%, gastric ulcer: 9.9% and peptic ulcer-non-specified: 16.7%).
2. Heartburn, the most common symptom in GERD, was reported in 60.5% patients while epigastric pain, which was the most common symptom of PUD, was noted in 73.2% patients.
3. Amongst patients with GERD, extra-esophageal symptoms were seen in 23% patients, with reflux cough being the most common feature noted in 53% patients.
4. Concomitant lower GI complaints like lower abdominal pain and constipation were reported in 28% GERD patients.
5. Alarm symptoms were seen in 49% GERD patients, with dysphagia being the most common feature associated with other symptoms.
(67%) while among patients with PUD, GI bleeding was the most common alarm symptom, seen in 47.6% patients.

6. The most common overlapping conditions associated with both, GERD and PUD included functional dyspepsia (25.9%), constipation (23.4%) and irritable bowel syndrome (23.4%).

Proton pump inhibitors in the management of acid peptic diseases

Proton pump inhibitors were introduced for clinical practice more than 25 years ago. The identification of hydrogen potassium adenosine triphosphatase (H+K+-ATPase) as the proton pump of the parietal cell by Forte and Lee and by Sachs et al may be regarded as a milestone in the management of APDs.

The PPIs have been widely used for the management of a variety of APDs and are recognized as the mainstay in the treatment of APDs. These drugs have been consistently demonstrated to be well tolerated, with excellent safety record, and generally superior acid-suppressing capability than prior agents. Proton pump inhibitors are recognized as the first-choice for treatment of esophagitis, NERD, PUD, prevention of NSAID-associated ulcers, Zollinger-Ellison syndrome (ZES), and functional dyspepsia and form an integral part of eradication therapy for H. pylori. Following the introduction of omeprazole in 1989, PPIs have steadily become the mainstay in treatment of acid-related disorders. As of 2015, six PPIs have been approved by the United States Food and Drug Administration (FDA) (Table 2).

Mechanism of action

Following absorption, PPIs are taken up by the activated gastric parietal cells, where they concentrate within the acidic secretory canaliculi to undergo acid-catalyzed cleavage of a sulfoxide bond to the active sulfenic acid and/or sulfenamide. These compounds then bind covalently to cysteine residues on the hydrogen/potassium ATPase (H+/K+ ATPase) or the proton pump. The proton pump, that is responsible for the secretion of hydrogen ions into the lumen of the gastric glands and stomach represents the last step in the secretion of gastric acid (Figure 4).

As PPIs require the expression of H+/K+ ATPases in the active canaliculi for binding, which occurs in response to a meal, PPIs as usually administered before a meal. They then inhibit acid secretion until replacement pumps can be synthesized (up to 36 hours).

Pharmacokinetics of proton pump inhibitors

The pharmacokinetic properties of the currently available PPIs are summarized in Table 3.

Clinical Uses of Proton Pump Inhibitors

The FDA approved indications for PPIs are listed below:

- Treatment of gastroesophageal reflux disease
- Healing of erosive esophagitis
- Maintenance treatment for healed erosive esophagitis
- Treatment of gastric and duodenal ulcers
- Treatment and prophylaxis for NSAID-induced ulcers
- Treatment of H. pylori infection in combination with antibiotics
- Management of pathologic hypersecretory conditions (including Zollinger-Ellison syndrome)

Table 2: Proton pump inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Oral formulations</th>
<th>Intravenous formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole</td>
<td>10, 20, 40 mg</td>
<td>Yes</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>20, 40 mg</td>
<td>Yes</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>15, 30 mg</td>
<td>Yes</td>
</tr>
<tr>
<td>Dexlansoprazole</td>
<td>30, 60 mg</td>
<td>No</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>20, 40 mg</td>
<td>Yes</td>
</tr>
<tr>
<td>Rabeprazole</td>
<td>20 mg</td>
<td>No</td>
</tr>
</tbody>
</table>

Table 3: Pharmacokinetic properties of proton pump inhibitors

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Omeprazole</th>
<th>Esomeprazole</th>
<th>Lansoprazole</th>
<th>Pantoprazole</th>
<th>Rabeprazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioavailability (%)</td>
<td>30–40</td>
<td>64–90</td>
<td>80–85</td>
<td>77</td>
<td>52</td>
</tr>
<tr>
<td>Time to peak plasma level (t&lt;sub&gt;max&lt;/sub&gt;) (hours)</td>
<td>0.5–3.5</td>
<td>1.5</td>
<td>1.7</td>
<td>2–3</td>
<td>2–5</td>
</tr>
<tr>
<td>Protein binding (%)</td>
<td>95</td>
<td>97</td>
<td>97</td>
<td>98</td>
<td>96.3</td>
</tr>
<tr>
<td>Liver metabolism</td>
<td>CYP2C19</td>
<td>CYP2C19</td>
<td>CYP2C19</td>
<td>CYP2C19</td>
<td>CYP3A4</td>
</tr>
<tr>
<td>Primary excretion</td>
<td>Hepatic</td>
<td>Hepatic</td>
<td>Hepatic</td>
<td>Hepatic</td>
<td>Hepatic</td>
</tr>
<tr>
<td>Half-life (hours)</td>
<td>0.5–1</td>
<td>1–1.5</td>
<td>1.6</td>
<td>1–1.9</td>
<td>1–2</td>
</tr>
</tbody>
</table>
Clinical advantages of PPIs

The PPIs represent the most potent inhibitors of gastric acid secretion as they directly block the final common pathway for acid secretion, the proton pump, unlike the anticholinergics and H₂-blockers. Their superior biochemical effect compared to H₂-blockers is due to their ability to reliably maintain intra-gastric pH >4 for between 15 and 21 hours daily, as compared to only 8 hours for H₂-blockers. The effectiveness of PPIs is also superior with respect to post-prandial and nocturnal intra-gastric pH control. Treatment with PPIs can also be maintained over the long-term without the need for dose escalation. This is in contrast to development of tachyphylaxis with H₂-blockers within 3 to 5 days of regular use, which may reduce their acid-suppressing effect by about one-half.¹¹

Omeprazole in acid peptic diseases - From bench to bedside - The journey of omeprazole

The discovery of omeprazole was the culmination of the efforts of scientists engaged in a research project initiated at the department of gastrointestinal pharmacology at Hässle in Mölndal, Sweden, in the late 1960s, with the objective of developing an antisecretory drug for use in acid hypersecretory disease states such as PUD. The finding that the substituted benzimidazoles inhibited acid secretion only when the immediate environment was acidic was an indication that these drugs need conversion to their protonated form to exert their action. The first PPI, picoprazole (compound H149/94) was highly effective; however, it was found to cause necrotizing vasculitis in toxicological studies. Omeprazole (compound H168/68) was synthesized in 1979, and was found to be the most powerful inhibitor of stimulated gastric secretion in experimental animals and in human tissue in vitro, without serious toxicity.¹²

Pharmacological studies demonstrated that omeprazole exhibited a specific binding to the target site and resulted in long-lasting inhibition of acid secretion. It was at the World Congress of Gastroenterology, Stockholm, 1982 that the first clinical results obtained from the use of omeprazole were presented at a satellite symposium titled “Substituted benzimidazole - a new approach to control of gastric secretion”. Following early clinical studies in PUD and ZES, omeprazole was subsequently evaluated in GERD and as a part of H. pylori eradication regimen.¹³ Omeprazole was introduced for clinical practice in 1989.¹³

Omeprazole for prevention of peptic ulcer relapse

Following initial healing of peptic ulcers, maintenance therapy should be considered for patients at high-risk for recurrence, e.g., those with PUD-related complications, recurrences, or H. pylori-negative ulcers.¹¹

A double-blind, randomized, parallel-group clinical trial compared the efficacy of omeprazole 10 mg and 20 mg given in the morning with ranitidine 150 mg at bet-time in 928 patients with endoscopically proven healed duodenal ulcers, over a 12-month period. More duodenal ulcer patients were maintained in remission with omeprazole 20 mg daily than with omeprazole 10 mg daily or with ranitidine 150 mg at bedtime (Figure 6).¹⁷

Omeprazole for prevention and treatment of NSAID-induced ulcers

In view of the gastrointestinal toxicity associated with NSAIDs, the American College of Gastroenterology guideline recommends prophylaxis for patients perceived to be at risk for NSAID-induced GI toxicity. The various options for reducing the risk of NSAID-associated GI toxicity include addition of misoprostol or acid antisecretory therapy, the use of a COX-2 selective NSAID, or any combination.
of these strategies. Omeprazole has been shown to be effective both, for prevention and treatment of NSAID-associated ulcers and was superior to ranitidine and misoprostol for prevention of peptic ulcer relapse and superior to ranitidine for healing peptic ulcer associated with NSAIDs (Table 4). Omeprazole for H. pylori infection

Omeprazole has been shown to inhibit H. pylori via a urease-independent mechanism, with inhibition of growth seen at a low pH, both in the absence of urea and in a urease-deficient strain of H. pylori. A meta-analysis reported that triple therapies with omeprazole were more effective than comparable regimens containing ranitidine, lansoprazole, or bismuth. Omeprazole also appeared to be successful in triple therapy regimens used in children with H. pylori infection.

Omeprazole for GERD with and without esophagitis

In patients with acute GERD with esophagitis, omeprazole was found to be as effective as lansoprazole or pantoprazole in promoting healing and was found to be superior to ranitidine, cimetidine or cisapride in healing of esophagitis and symptom relief. In patients with symptomatic GERD without esophagitis, more patients reported symptom relief after short-term treatment with omeprazole than with ranitidine, cisapride or placebo, and symptoms were more readily prevented by omeprazole than by cimetidine or placebo. Omeprazole was also effective in healing and relieving symptoms of reflux esophagitis in children with esophagitis refractory to histamine H₂-receptor antagonists.

Omeprazole for maintenance of healing in erosive esophagitis

In a prospective trial by Vignieri et al., involving 175 patients with endoscopically confirmed erosive esophagitis, it was found that after 12 months of maintenance, omeprazole alone (or in combination with cisapride) was significantly superior in maintaining endoscopic remission to ranitidine alone (p<0.001), cisapride alone (p = 0.003), or both ranitidine and cisapride (p = 0.03). The proportion of patients in remission remaining in the five treatment groups at 12 months are shown in Figure 7.

Omeprazole for Zollinger-Ellison syndrome

A prospective study was carried out by Maton PN et al., to demonstrate long-term efficacy and safety of omeprazole in patients with Zollinger-Ellison syndrome. It was observed that long-term treatment of up to 4 years with omeprazole was safe, with no evidence of hematologic, biochemical, or gastric toxicity. Furthermore, omeprazole remained effective, with only 23% of patients requiring an increase in dose, and continued to control symptoms in patients who had not been entirely symptom-free despite high doses of H₂-receptor antagonists.

Omeprazole for functional dyspepsia

Omeprazole (20 mg daily) provided complete symptom relief in patients with dyspeptic symptoms and negative endoscopy when compared with placebo (38% versus 28%, p = 0.002). Among those with ulcer-like and reflux-like dyspepsia, complete symptom relief was seen in 40% and 54% on omeprazole 20 mg, and 35% and 45% on omeprazole 10 mg, respectively, compared with 27% and 23% on placebo (p <0.05).

Comparative studies with other PPIs

Several head-to-head trials have
compared the newer PPIs with omeprazole. In general, the results of these trials have shown that the efficacy of the newer PPIs, both, in respect of healing and symptoms relief of PUD and GERD as well as maintaining remission was comparable to omeprazole, when the drugs were used at comparable doses. Though some head-to-head trials comparing esomeprazole (40 mg/day) with omeprazole (20 mg/day) have reported that esomeprazole is superior to omeprazole, the doses are not comparable as per the US Food and Drug Administration’s clinical review, which indicates that esomeprazole 40 mg is pharmacodynamically three-times as effective as omeprazole 20 mg.23

Symptom relief and healing in patients with erosive esophagitis

No differences in symptom relief or healing of esophagitis was seen in a review of 16 head-to-head trials using comparable doses of PPIs. There was no difference between omeprazole, lansoprazole, pantoprazole, and rabeprazole for healing of esophagitis, both, at 4 and 8 weeks.23

In a multicenter study involving 202 patients with erosive or ulcerative GERD, it was found that the healing rates for rabeprazole 20 mg and omeprazole 20 mg were equivalent: 81% after 4 weeks of treatment and >90% after 8 weeks of treatment. Both the PPIs also provided similar relief of heartburn, as measured by frequency and severity of symptoms.23

In a double-blind, randomized, multicenter study involving 286 patients with reflux esophagitis, pantoprazole (40 mg daily) was compared with omeprazole (20 mg daily). The length of time required for symptom relief was similar for the two drugs. The healing rates were comparable at 4- and 8-weeks (Figure 8).27

Prevention of relapse in patients with erosive esophagitis

For maintenance of healed esophagitis, no difference was reported between omeprazole, lansoprazole, and rabeprazole.23

Symptom relief in patients with non-erosive gastroesophageal reflux disease

An analysis of three head-to-head trials involving patients with GERD but without erosive esophagitis on endoscopy revealed no difference between esomeprazole 20 mg and omeprazole 20 mg, pantoprazole 20 mg, or rabeprazole 10 mg.23

Peptic ulcer disease

An analysis of 10 head-to-head trials comparing PPIs in patients with duodenal ulcer showed no evidence of difference among the different PPIs, both, for healing and symptom relief.23 Healing rates were comparable in patients receiving rabeprazole (20 mg/day) or omeprazole (20 mg/day) in a randomized double-blind study involving 205 patients with duodenal ulcer (Figure 9).20

Limited comparative data in patients with gastric ulcer revealed no significant difference in healing rates between omeprazole and rabeprazole (Figure 10).25,26 Symptom relief was reported to be better with rabeprazole 20 mg, but not with rabeprazole 10 mg, compared to omeprazole 20 mg daily.25

In healing of NSAID-associated peptic ulcers, no differences were noted between omeprazole, esomeprazole, and lansoprazole. In arthritis patients receiving NSAIDs, a direct comparison of pantoprazole 20 mg, 40 mg, and omeprazole 20 mg daily did not demonstrate statistically significant differences in rates of therapeutic failure (defined as peptic ulcer, >10 erosions, reflux esophagitis, and discontinuations of study drug due to an adverse event or severe gastrointestinal symptoms) or endoscopic failure at 6 months. For eradication of H. pylori infection, pooled analysis revealed no statistically significant differences in eradication rate among the PPIs.25

Safety aspects of proton pump inhibitors

The PPIs are remarkably well-tolerated, with adverse events reported in 1–3 % patients, with no differences between the PPIs. The commonly reported adverse events include headaches, nausea, abdominal pain, constipation, flatulence, diarrhea, rash, and dizziness. In long-term studies, the tolerability profile of PPIs is similar to that found in short-term trials.28

With the widespread use of PPIs, there is a growing concern amongst the clinicians about their long-term safety, based on the emergence of reports during the last decade.29 Several reviews on the long-term safety of PPIs have, however, shown that most associations of PPIs with severe adverse events are not based on sufficient evidence, probably due to confounding factors and a lack of plausible mechanisms (Table 5).29–32 Thus, a causal relationship between PPI use and most of these adverse effects remains to be proven.29 Thus, the harms associated with PPI therapy do not outweigh the benefits associated with their use.30

A growing concern with PPIs use is the interaction between omeprazole and clopidogrel which was first observed during in vitro studies, which demonstrated that synchronous administration of omeprazole diminished the effect of clopidogrel on platelet inhibition. In 2009, the FDA recommended avoiding the use of both drugs simultaneously. Despite this initial concern, there have been
Table 5: Long-term safety of PPIs – Concerns and evidence

<table>
<thead>
<tr>
<th>Theoretical concern</th>
<th>Possible mechanism</th>
<th>Clinical evidence</th>
<th>Clinical implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal malignancies</td>
<td>PPI-induced structural and functional changes in the gastric mucosa due to potent acid suppression, which are exaggerated during Helicobacter pylori infection</td>
<td>No clinical data supporting increased risk of gastric or colorectal cancer</td>
<td>PPIs alone are unlikely to be related to gastric and gastrointestinal malignancies.</td>
</tr>
<tr>
<td>Risk of bacterial enteric infections with Clostridium difficile, Salmonella and Campylobacter</td>
<td>Long-term PPI-induced hypochlorhydria</td>
<td>C. difficile infection: OR 2.10 (95% CI: 1.20-3.50) SIBO: OR 2.28 (95% CI: 1.23-4.21)</td>
<td>Risk is low-to-modest; impact of both, dose and duration of PPI treatment on this association is not clear.</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Long-term PPI-induced hypochlorhydria</td>
<td>Conflicting data; risk reported in studies possibly due to confounders</td>
<td>Insufficient evidence for causality</td>
</tr>
<tr>
<td>Intestinal nephritis</td>
<td>Idiosyncratic, rare effect</td>
<td>Increased risk has been shown; causal relationship established.</td>
<td>In such cases, it is advised to withdraw the PPI and avoid re-exposure. After PPI withdrawal and corticosteroid therapy, almost all patients recovered a normal renal function.</td>
</tr>
<tr>
<td>Nutrient absorption</td>
<td>Long-term PPI-induced hypochlorhydria</td>
<td>No consistent effects on calcium or iron absorption have been reported. There is evidence to support interference with vitamin B12 absorption.</td>
<td>Low evidence of causality</td>
</tr>
<tr>
<td>Bone fractures</td>
<td>Reduction in BMD and osteoporosis</td>
<td>PPI use has not been shown to be associated with accelerated bone mineral density loss or osteoporosis; bone fractures not consistently seen in clinical studies</td>
<td>Prevalence of bone fractures in older adults is low; in patients with risk factors for osteoporotic changes, calcium and vitamin D supplementation is required*</td>
</tr>
<tr>
<td>Hypomagnesemia</td>
<td>By inhibiting intestinal transport of magnesium</td>
<td>May occur in patients with CKD on diuretic therapy</td>
<td>Monitoring for magnesium levels needs to be considered in at risk patients and in those suspected to have symptoms potentially due to hypomagnesemia, such as cramps, paresthesias and cardiac arrhythmias.</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>Not known</td>
<td>No association found in RCTs</td>
<td>More data needed</td>
</tr>
</tbody>
</table>

*Pre-existing osteoporosis, steroid therapy or malabsorption.* In 2010, the US FDA issued warning about possible risk for fracture of the hip, wrist, and spine with PPIs at high dose (more than once daily) or for a long duration (greater than 1 year). PPI: Proton pump inhibitor; FDA: Food and drug administration; OR: Odds ratio; CI: Confidence interval; RCTs: Randomized controlled trials; SIBO: Small intestinal bacterial overgrowth; BMD: Bone mineral density.

no in vivo data which has conclusively connected the use of omeprazole and clopidogrel with adverse clinical outcomes.11

Conclusion

Proton pump inhibitors have revolutionized the treatment of acid-peptic diseases. They have been used for the past 25 years with a good track record of safety. Omeprazole is a well-established and most studied drug in the PPI class. Its effectiveness in the treatment of all acid-related diseases is well documented. Newer PPIs administered at comparable doses are similar in efficacy to omeprazole in GERD, PUD and NSAID-related peptic ulcers. In patients with ulcers associated with long-term non-steroidal, anti-inflammatory drug use, omeprazole has demonstrated superior efficacy than ranitidine and misoprostol for healing and maintaining remission in PUD. Thus, after 25 years of its introduction for clinical use, omeprazole still remains a valuable therapy for acid-peptic diseases.

References