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Review Article

A Review of Scientific Evidence Supporting Esomeprazole Use as the Preferred Proton Pump Inhibitor in Gastroesophageal Reflux Disease Management

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Abstract

Esomeprazole plays a crucial role in the effective management of gastroesophageal reflux disease (GERD) due to its superior acid-suppressing properties compared to other proton pump inhibitors (PPIs). By effectively reducing gastric acidity, esomeprazole helps alleviate common GERD symptoms such as heartburn and regurgitation while promoting the healing of esophageal damage. Its enhanced pharmacokinetic profile provides more consistent and long-lasting acid control, making it a preferred choice for patients with erosive GERD or those with symptoms refractory to other PPIs. Given its proven efficacy and safety, esomeprazole is a key therapeutic option for improving the quality of life and long-term GERD management. The current study aims to elaborate on esomeprazole's fast action in alleviating GERD symptoms, making it the preferred choice for patients who need quick and dependable relief.

Key words: Combination therapy, Domperidone, Esomeprazole, Gastroesophageal reflux disease

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a prevalent gastrointestinal disorder that affects an estimated 8–33% of the global population.[1] GERD is a complex, multifactorial condition primarily caused by excessive gastroesophageal reflux, impaired esophageal clearance, increased gastric acid production, or heightened sensitivity of the esophageal mucosa to refluxed content.[2] It is characterized by symptoms such as heartburn and regurgitation. It may also cause esophageal manifestations, including non-cardiac chest pain, cough, and asthma, all of which can severely impact the quality of life of patients.[1] Esomeprazole is the most recent proton pump inhibitor (PPI), developed as the S-isomer of omeprazole, as an improvement in its pharmacokinetic properties.[3] The current review article aims to evaluate the effectiveness, safety, and tolerability of esomeprazole in patients with erosive GERD compared to other PPIs.

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ESOMEPRAZOLE: A PREFERRED PPI FOR SUPERIOR GERD MANAGEMENT

Early clinical studies on esomeprazole have shown that both esomeprazole 40 mg and 20 mg achieve greater and more sustained acid control than omeprazole 20 mg, with a similar tolerability and safety profile.[4] Comparative studies by Srikanth *et al.* and others have demonstrated that esomeprazole provides superior symptomatic relief for GERD compared to other PPIs. Specifically, a daily dose of esomeprazole 40 mg was more effective than omeprazole 20 mg, lansoprazole 30 mg, and pantoprazole 40 mg in relieving heartburn symptoms, particularly within the 1st day and the initial 5 days of treatment. In addition, the rates of adverse events were comparable across all

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treatment groups, indicating that esomeprazole offers similar safety to other PPIs while providing enhanced symptom relief.[5]

In a prospective, randomized, observational study, esomeprazole 40 mg was shown to provide significantly greater healing than pantoprazole 40 mg after 4 weeks of treatment in patients with erosive esophagitis (56.36% vs. 49.09%). Further, by 8 weeks, the healing rates for patients treated with esomeprazole were greater than those treated with pantoprazole (94.54% vs. 70.90%). Furthermore, the study concluded that esomeprazole is more effective than pantoprazole in providing rapid relief from heartburn and acid reflux symptoms in patients with reflux esophagitis.[5] The study by Kalaitzakis and Björnsson found that esomeprazole 40 mg once daily (OD) outperformed omeprazole 20 mg, lansoprazole 30 mg, and pantoprazole 40 mg OD in effectively resolving symptoms associated with GERD.[3]

Esomeprazole Achieves a Higher 24-h Median Intragastric pH

Esomeprazole 40 mg twice daily (BD) has been shown to provide superior acid suppression compared to pantoprazole 40 mg BD (nocturnal acid breakthrough-E: 85.4% vs. *P*: 63.6%, $P = 0.0001$; E: 67.1% vs. *P*: 45%, $P < 0.001$) and lansoprazole 30 mg BD (E: 67.1% vs. L: 45%, $P < 0.001$) in maintaining an intragastric pH of 4.0 or lower, making it a more effective option for patients requiring enhanced acid control for GERD. Another double-blind, randomized, crossover study involving 25 healthy volunteers compared the 24-h intragastric pH profiles of esomeprazole 40 mg BD, 20 mg BD, and 40 mg OD. The results demonstrated that esomeprazole 40 mg BD maintained an intragastric pH of 4.0 for a mean duration of 19.2 h, or 80.1% of the 24-h, significantly outperforming esomeprazole 40 mg OD (14.2 h, 59.2%) and esomeprazole 20 mg BD (17.5 h, 73.0%).[3]

Esomeprazole also effectively maintained an intragastric pH >4.0 for 12 h/day. Similarly, study by Kalaitzakis *et al.* showed that esomeprazole 40 mg OD outperforms all other PPIs at standard doses, both in terms of achieving a higher 24-h median intragastric pH and the number of patients maintaining an intragastric pH above 4.0 for at least 12 h/day.[3]

Esomeprazole is Associated with a Low Incidence of Nocturnal Acid Breakthrough

Esomeprazole has been shown to effectively control nocturnal acid secretion, with a significantly lower incidence of nocturnal acid breakthrough than other PPIs. In a study by Kalaitzakis *et al.* assessing nocturnal pH levels, esomeprazole 40 mg maintained an intragastric pH ≥4.0 for a significantly higher proportion of time during the night, up to 85.4%, compared to 63.6% for pantoprazole 40 mg. Nocturnal acid breakthrough occurred in only 26.7% of patients treated with esomeprazole. In contrast, 73.3% of patients receiving pantoprazole experienced acid breakthroughs during the same period. These findings highlight the superior efficacy of esomeprazole in preventing nocturnal acid breakthrough and maintaining optimal acid control throughout the night.[3]

In addition, during the supine (sleep) phase of monitoring, esomeprazole 40 mg BD maintained a pH < 4.0 for 83.7% of the time (95% confidence interval [CI] 74.9–92.4%), compared to 79.2% (95% CI 70.5–87.9%) with 20 mg BD and 57.9% (95% CI 49.0–66.9%) with 40 mg OD. These findings highlight the superior efficacy of BD dosing, particularly during the night when GERD symptoms are most likely to occur. Overall, esomeprazole 40 mg BD provides significantly greater acid suppression than OD regimens and other PPIs, making it a valuable treatment option for patients who require enhanced control of gastric acid to manage GERD effectively.[3]

Esomeprazole Well Tolerated in the Maintenance (Long-Term Therapy) of a Healing Erosive Esophagitis

Long-term acid suppression is critical in maintaining the healing of erosive esophagitis, as over 80% of patients relapse within a year without maintenance therapy. Esomeprazole, the first optical isomer of PPI, has been reported to effectively maintain the healing of erosive esophagitis. After 6 months of treatment, healing was sustained in 93.6% of patients treated with esomeprazole 40 mg, 93.2% of those treated with esomeprazole 20 mg, and 57.1% of those treated with esomeprazole 10 mg.[6] Another study by Kalaitzakis and Björnsson involving 13,797 patients with erosive GERD has highlighted the superiority of esomeprazole 40 mg OD in healing rates for erosive esophagitis after 4 and 8 weeks of treatment compared to omeprazole 20 mg, lansoprazole 30 mg, or pantoprazole 40 mg OD. The enhanced efficacy of esomeprazole relative to omeprazole, lansoprazole, or pantoprazole remained consistent, even after adjusting for the baseline severity of esophagitis.[3]

Esomeprazole Action on Acid Suppression and Effect on Gastric Acidity

Esomeprazole 40 mg BD offers significantly improved acid control over OD regimens and may be a preferable treatment option for patients with GERD who require more intensive acid suppression.[3] Several crossover studies have compared acid control with esomeprazole to that with other PPIs in both patients with GERD and healthy individuals. All studies demonstrated that esomeprazole 40 mg OD was more effective in maintaining an intragastric pH of 4.0 or lower compared to omeprazole 20 mg OD,

lansoprazole 30 mg OD, rabeprazole 20 mg OD, and pantoprazole 40 mg OD. These studies also showed that esomeprazole 40 mg OD outperformed other PPIs in achieving a higher 24-h median intragastric pH and in the number of patients maintaining an intragastric pH of ≥4.0 for at least 12 h/day.[3]

Impact of Esomeprazole on Esophageal Acidity Control

In a double-blind, crossover study of 35 patients with GERD symptoms, patients were randomized to esomeprazole 40 mg OD and pantoprazole 40 mg OD to compare the effect on intraesophageal pH. At baseline, the median percentage of total time during which the intraesophageal pH was below 4.0 was 20.1% in the esomeprazole group and 21.3% in the pantoprazole group, indicating a similar degree of acid exposure in both groups at the start of the study. Following 7 days of treatment, the percentage of time with a pH <4.0 significantly decreased in both groups, with the esomeprazole group showing a reduction to 0.9% and the Pantoprazole group to 2.6%. These results suggest that both treatments effectively reduced acid reflux, with esomeprazole achieving a more pronounced reduction in intraesophageal acidity than pantoprazole.[3]

Esomeprazole in Healing Erosive Esophagitis

Approximately 30–50% of individuals with chronic GERD develop erosive esophagitis. Even after initial healing, about 80% of patients experience symptomatic relapse within the following 12 months.[7] Esomeprazole OD for 6 months has proven to be an effective therapy for maintaining the healing of erosive esophagitis and GERD symptoms.[6] The EXPO study's maintenance phase results demonstrate that esomeprazole 20 mg is more effective than pantoprazole 20 mg in maintaining endoscopic and symptomatic remission in patients with healed erosive esophagitis over a 6-month treatment period. In addition, esomeprazole 20 mg was associated with a higher proportion of patients free from moderate-to-severe GERD symptoms and fewer discontinuations due to symptoms compared to pantoprazole 20 mg (92.2% vs. 88.5%, $P < 0.001$).[7]

ESOMEPRAZOLE IN THE TREATMENT OF *HELICOBACTER PYLORI* INFECTION

H. pylori infection is a key factor in gastroduodenal ulcers and poses a major risk for ulcer bleeding.[8] Globally, the recommended approach for eradicating the infection involves a triple-therapy regimen, which includes an anti-secretory agent and two antibiotics (such as amoxicillin or metronidazole and clarithromycin), typically administered for 1 week. Esomeprazole-based triple therapy for 1 week is highly effective in eradicating *H. pylori* infection in duodenal ulcer disease and offers comparable efficacy to omeprazole-based therapy and good tolerability. The findings of the study by Veldhuyzen Van Zanten *et al.* indicated that in patients with *H. pylori* infection, esomeprazole-based combination therapy demonstrated high cure rates, coupled with good tolerability and high patient compliance, which are well above the eradication rate of 80%.[4]

In a meta-analysis by McNicholl *et al.*, esomeprazole offered better overall eradication rates (78.7%) compared to first-generation PPIs, with more pronounced clinical benefit with 40 mg BD regimens. In addition, it was highlighted that CYP2C19 extensive metabolizers, new-generation PPIs, are more effective than first-generation PPIs for *H. pylori* eradication.[9]

ESOMEPRAZOLE AND PROKINETICS IN GERD SYMPTOM ALLEVIATION

Acid suppression, particularly with PPIs, is widely considered the cornerstone of medical management for GERD. However, approximately 30% of patients with GERD remain refractory to PPI treatment. PPIs are the first-line treatment for GERD; however, they primarily target acid production and do not address other contributing mechanisms. As a result, prokinetic agents have been increasingly incorporated into GERD therapy. These agents work by enhancing the lower esophageal sphincter pressure, improving esophageal peristalsis, and accelerating gastric emptying. The main classes of prokinetics include dopamine receptor antagonists, 5-hydroxytryptamine receptor agonists, gamma-aminobutyric acid type B receptor agonists, acetylcholinesterase inhibitors, and motilin agonists.[1]

Domperidone, a dopamine receptor antagonist, is a prokinetic known for its ability to accelerate gastrointestinal peristalsis and improve GERD symptoms. As a result, combination therapies involving PPIs and prokinetic agents are commonly prescribed to enhance treatment efficacy.[1] Clinical trials have shown that the addition of prokinetics to PPIs can significantly improve symptoms compared to monotherapy and the quality of life of patients with GERD.[1] In a prospective study by Qurtulain *et al.*, the combination of sustained-release domperidone 30 mg and fixed-dose esomeprazole 20 mg was found to be an effective and well-tolerated option for managing dyspepsia associated with GERD in adults.[10] Another prospective study confirmed that a fixed-dose combination of esomeprazole 20 mg and sustained-release domperidone 30 mg is an effective and well-tolerated therapeutic choice for symptomatic relief of GERD-related dyspepsia in Indian adults.[11] No statistically

significant difference between combination therapy and monotherapy was noticed.[12]

CONCLUSION

When compared to other PPIs, esomeprazole is a superior therapeutic option in the management of GERD, offering enhanced acid suppression, better control of esophageal acidity, and improved healing rates for erosive esophagitis. Its ability to maintain an intragastric pH of 4.0 for extended periods, coupled with its lower incidence of nocturnal acid breakthrough, makes it an effective treatment for patients with refractory GERD. Moreover, when combined with prokinetic agents such as domperidone, esomeprazole further optimizes symptom relief and enhances quality of life. The efficacy of esomeprazole, coupled with its safety and tolerability profile, highlights its critical role in both acute and long-term management of GERD, providing significant clinical benefits to patients worldwide.

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EXPERT OPINION

Consensus from Orthopedics

In the context of orthopedic practice, among PPIs, esomeprazole is often preferred due to its ability to maintain a higher intragastric pH for more than 12 h, offering superior acid suppression compared to other PPIs such as pantoprazole. The pharmacokinetic properties of esomeprazole, including its faster peak plasma levels and higher bioavailability, contribute to its more consistent acid control and reduced frequency of nocturnal acid breakthrough. Furthermore, esomeprazole has shown better *H. pylori* eradication rates than first-generation PPIs and is particularly effective in CYP2C19 extensive metabolizers. In patients with erosive esophagitis, esomeprazole offers faster and more consistent healing, with significant improvements seen in 4 weeks of treatment. Combining PPIs with prokinetic agents has been shown to significantly improve symptom response and provide greater symptomatic relief for patients with GERD when PPI monotherapy is found to be ineffective. This combination therapy helps alleviate discomfort and enhances patients' overall quality of life.

Consensus from Consulting Physicians

Consulting physicians believe that esomeprazole use is associated with better *H. pylori* eradication rates and is less dependent on CYP2C19 pathways than first-generation PPIs. It promotes faster healing in patients with erosive esophagitis, with significant improvements seen within 4–8 weeks. It also facilitates faster healing in patients with erosive esophagitis, with significant improvement often seen within 4 weeks of treatment. The combination of PPIs and prokinetics is also endorsed in clinical practice to enhance symptom response, provide better symptomatic relief, and improve patients' overall quality of life.

Consensus from Surgeons

Surgeons prefer esomeprazole over other PPIs because it offers better consistency and less frequent nocturnal acid breakthrough compared to pantoprazole, making it a more effective option for maintaining pH control, especially in patients recovering from surgery or those with chronic gastrointestinal issues. Esomeprazole has also shown better overall *H. pylori* eradication rates compared to first-generation PPIs, which is relevant for surgical patients with peptic ulcers or gastric issues. Esomeprazole's superior treatment profile, including its ability to maintain a higher 24-h median intragastric pH and a low incidence of nocturnal acid breakthrough, ensures that it is well-tolerated and effective for maintaining healing in erosive esophagitis, which is important for long-term post-operative care.

Consensus from ENT Specialists

Among all the available PPIs, esomeprazole promotes faster healing in patients with erosive esophagitis, which is important for managing patients with reflux-related damage to the esophagus and throat, offering better symptomatic relief and preventing further complications. Compared to pantoprazole, esomeprazole has superior pharmacokinetic properties, such as a faster time to peak plasma concentration and higher bioavailability. This may provide more consistent acid suppression, potentially reducing symptoms such as hoarseness/throat irritation associated with acid reflux and improving patients' quality of life. It is specifically favored due to its ability to maintain a higher intragastric pH for over 14 h, which may be beneficial in preventing acid reflux, a common issue in ENT patients with laryngopharyngeal reflux or chronic cough related to reflux.

Consensus from Gynecologists

Gynecologists in the survey noted that esomeprazole's pharmacokinetic properties are more effective than other PPIs, providing better systemic control in managing GERD. This is particularly important for treating chronic reflux symptoms in women, especially during pregnancy, when medication safety and efficacy are critical. In addition, esomeprazole has shown higher *H. pylori* eradication rates compared to first-generation PPIs, making it a valuable treatment for women with gastric issues or peptic ulcers, especially those with *H. pylori* infections, which can

complicate both pregnancy and gastrointestinal health. Furthermore, esomeprazole's superior treatment profile includes maintaining a higher 24-h intragastric pH, sustaining a pH >4 for at least 12 h, minimizing nocturnal acid breakthrough, and being well-tolerated for healing erosive esophagitis.

Consensus from Psychiatrists

Esomeprazole is preferred by many health-care providers due to its ability to maintain a higher intragastric pH for over 14 h, potentially reducing the psychological distress associated with chronic reflux symptoms. Compared to pantoprazole, esomeprazole offers more consistent results and fewer episodes of nocturnal acid breakthrough due to its superior pharmacokinetics (fast peak plasma levels and higher bioavailability). For patients with *H. pylori* infections, esomeprazole has demonstrated higher eradication rates than first-generation PPIs, which could also reduce stress related to persistent gastrointestinal issues. The ability of esomeprazole to promote faster healing of erosive esophagitis in 4 weeks, with continued improvement in 8 weeks, not only benefits physical health but could also alleviate anxiety or depression caused by chronic gastrointestinal discomfort.

Consensus from Pulmonologists

The opinion of pulmonologists on the use of esomeprazole among other PPIs aligns with other specialists. They also support the use of esomeprazole over other PPIs due to its ability to maintain a higher intragastric pH for over 12 h, helping reduce acid reflux symptoms that can contribute to worsening respiratory issues such as chronic cough or asthma. Compared to pantoprazole, esomeprazole offers more consistent control with fewer nocturnal acid breakthroughs due to its superior pharmacokinetic properties. It also shows higher *H. pylori* eradication rates, which helps patients with reflux-related respiratory symptoms. Esomeprazole promotes faster healing in erosive esophagitis and is well-tolerated, making it a valuable treatment for pulmonologists managing reflux issues in comorbid patients.

Consensus from Gastroenterologists

From a gastroenterologist's perspective, esomeprazole is highly considered due to its superior pharmacokinetic properties, making it a preferred choice over other PPIs. It effectively maintains a higher intragastric pH for over 12 h, which helps control acid reflux and promotes healing in patients with conditions such as erosive esophagitis. Compared to pantoprazole, esomeprazole offers more consistent acid control with fewer episodes of nocturnal acid breakthrough. Esomeprazole also demonstrates better *H. pylori* eradication rates and is particularly effective in patients with GERD, offering better outcomes than first-generation PPIs. In addition, it provides significant healing within 4 weeks for erosive esophagitis and maintains effective healing for the majority of patients within 8 weeks, making it a well-tolerated and reliable option in GERD management. Finally, it effectively maintains a pH above 4 for at least 12 h/day, which reduces acid reflux and promotes healing. Finally, it is associated with a low incidence of nocturnal acid breakthrough and is well-tolerated, making it an ideal option for maintaining healing in patients with erosive esophagitis.

Consensus from Nephrologists

The survey found that nephrologists preferred the use of esomeprazole among all other PPIs due to its superior pharmacokinetic properties, which provide consistent control of gastric acid secretion. Esomeprazole maintains a higher intragastric pH for over 12 h, effectively reducing the risk of acid reflux, which is particularly important in patients with chronic kidney conditions who may be at increased risk of complications from prolonged acid exposure. Compared to pantoprazole, esomeprazole offers more reliable acid suppression with fewer instances of nocturnal acid breakthrough, owing to its faster time to peak plasma concentration and higher bioavailability. In addition, esomeprazole demonstrates better *H. pylori* eradication rates, which can be significant for kidney patients with concurrent gastric issues. Its ability to promote healing of erosive esophagitis in a short time frame – within 4 weeks for many patients – along with its low incidence of adverse effects, makes it an effective and well-tolerated option in managing reflux-related complications in kidney patients.

Consensus from Diabetologists

For diabetologists, the use of esomeprazole presents a compelling option, particularly in managing GERD and related gastrointestinal issues in patients with diabetes. Given the increased prevalence of reflux symptoms in this population, esomeprazole's ability to maintain a higher intragastric pH for over 12 h proves crucial in mitigating acid reflux. This is especially beneficial for patients with diabetes, who may be more susceptible to complications from prolonged gastric acid exposure. Esomeprazole's superior pharmacokinetic profile, including quicker time to peak plasma concentration and higher bioavailability compared to pantoprazole, ensures more consistent acid control, with fewer instances of nocturnal acid breakthrough. Furthermore, its higher eradication rates of *H. pylori* and superior healing effects in patients with erosive esophagitis within 4–8 weeks offer important therapeutic benefits. These features, combined with its ability to maintain a pH above 4 for extended periods and its low incidence of adverse effects, make esomeprazole an optimal choice for managing GERD in patients with diabetes.

Consensus from Cardiologists

Esomeprazole is increasingly recognized by cardiologists as an effective option for managing GERD-related symptoms, particularly in patients with comorbid cardiovascular conditions. Its ability to maintain a higher intragastric pH for over 12 h is essential in controlling acid reflux. When compared to pantoprazole, esomeprazole offers more consistent control with fewer nocturnal acid breakthrough episodes, owing to its superior pharmacokinetic properties, including quicker peak plasma levels and higher bioavailability. In addition, esomeprazole demonstrates improved *H. pylori* eradication rates compared to first-generation PPIs, making it a preferred treatment in patients with gastric issues or peptic ulcers, conditions that can complicate cardiovascular care. In patients with erosive esophagitis, esomeprazole promotes faster healing, often within 4 weeks, and is effective for most patients within 8 weeks. Its ability to achieve a higher 24-h median intragastric pH, maintain a pH >4 for at least 12 h/day and reduce nocturnal acid breakthrough makes it a well-tolerated treatment, especially for those with reflux-related cardiovascular concerns.

Consensus from Clinical Oncologists

Clinical oncologists favor esomeprazole due to its superior pharmacokinetics, which provide extended intragastric pH control for over 12 h. This is particularly beneficial for cancer patients experiencing reflux and gastrointestinal side effects. Esomeprazole offers more consistent acid suppression and fewer nocturnal breakthroughs compared to pantoprazole. It also has a higher *H. pylori* eradication rate and promotes faster healing of erosive esophagitis, typically within 4–8 weeks. Its ability to maintain a pH >4 for at least 12 h a day makes it a well-tolerated and effective choice for managing acid reflux in patients with cancer.

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