Print ISSN: 2321-6379
Online ISSN: 2321-595X

Review Article

Esomeprazole for Effective Night-time Acid Suppression in Gastroesophageal Reflux Disease

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Abstract

Night-time gastroesophageal reflux disease (GERD) symptoms, such as heartburn, significantly impair sleep quality and overall quality of life. During sleep, physiological defences weaken, leading to prolonged acid exposure, mucosal injury, and complications such as erosive esophagitis and Barrett's esophagus. Nocturnal acid breakthrough is a common challenge that exacerbates these issues. Pharmacologic management with proton pump inhibitors (PPIs) is the mainstay, and among them, Esomeprazole has demonstrated superior efficacy in controlling nocturnal acid secretion, reducing acid breakthrough, and promoting mucosal healing. Clinical trials involving patients with symptomatic GERD reveal that Esomeprazole offers rapid symptom relief, better control of intragastric pH above 4.0, and sustained symptom resolution compared to other PPIs. Its flexible dosing options enable personalized treatment plans, with continuous therapy showing the most consistent symptom control. Moreover, Esomeprazole is well-tolerated with excellent safety profiles. Its efficacy extends to decreasing nocturnal reflux episodes, reducing mucosal injury, and improving sleep quality, ultimately enhancing patient quality of life. Despite its benefits, treatment success hinges upon adherence, which is often impacted by social, demographic, and behavioral factors. Overall, Esomeprazole stands out as a potent, safe, and effective option for managing nocturnal GERD symptoms, providing rapid relief and improving sleep-related and daily functioning, thereby reducing the risk of severe complications associated with chronic acid exposure during sleep.

Key words: Esomeprazole, Gastroesophageal reflux disease, Night-time heartburn, Night-time reflux, Nocturnal acid breakthrough, Sleep disturbances

INTRODUCTION

Patients with gastroesophageal reflux disease (GERD) commonly experience night-time heartburn, with approximately 80% reporting symptoms at night.[1,2] During sleep, key esophageal defence mechanisms, including primary and secondary peristalsis and salivary secretion, are diminished, increasing susceptibility to acid reflux damage. Although reflux episodes occur less frequently at night than during the day, nocturnal reflux episodes tend to last longer, leading to prolonged acid exposure and greater injury to the esophageal mucosa.[2]

Access this article online

www.ijss-sn.com

Month of Submission : 03-2026
Month of Peer Review : 04-2026
Month of Acceptance : 05-2026
Month of Publishing : 05-2026

Nocturnal acid reflux has been linked to complications such as reflux esophagitis, peptic strictures, Barrett's esophagus, and adenocarcinoma. In addition, night-time reflux is also associated with extra-esophageal manifestations, including asthma, dental erosion, and chronic cough.[2]

IMPLICATIONS OF NOCTURNAL ACID BREAKTHROUGH (NAB) ON SLEEP, NEXT-DAY FUNCTIONING, AND OVERALL QUALITY OF LIFE

Night-time heartburn has a substantial impact on individuals with GERD. Evidence indicates that approximately 50–75% of people with heartburn experience nocturnal reflux episodes that wake them from sleep, leading to sleep disturbance, impaired quality of life, and next-day fatigue.[3] Nocturnal gastroesophageal reflux symptoms – including heartburn and regurgitation – are known to impair sleep quality significantly and are often associated with more

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severe forms of reflux disease. In addition, these nocturnal symptoms have been linked to an increased risk of cardiovascular diseases, esophageal adenocarcinoma, and obstructive sleep apnea syndrome.[1,2] Overall, night-time reflux not only interferes with the ability to fall asleep but also causes frequent awakenings, contributing to a marked reduction in quality of life.[1]

Sleep disturbances related to reflux symptoms can result in daytime fatigue and marked impairments in daily functioning, work productivity, mood, and the overall health-related quality of life of patients.[3] The relationship between sleep disruption and heartburn is bidirectional, driven by normal physiologic changes in the upper gastrointestinal tract during sleep and by heartburn-induced sleep arousals [Figure 1].[4] Poor sleep quality appears to further aggravate reflux symptoms by prolonging esophageal acid contact time. Therefore, effective management of nocturnal acid reflux and its troublesome nocturnal symptoms is essential.[2]

ACID-SUPPRESSION THERAPY FOR THE RESOLUTION OF NAB

Nocturnal heartburn symptoms generally respond favorably to acid suppression therapy, which in turn enhances sleep quality. Although lifestyle and behavioral adjustments can help reduce nocturnal heartburn and improve sleep, they are often less consistent than pharmacologic interventions. Such measures include weight reduction, avoiding meals for at least 3–4 h before bedtime, avoiding foods that trigger heartburn, and adopting positional changes such as sleeping on an incline or in the left lateral position [Figure 2].[4]

Currently approved pharmacologic interventions for reflux include antacids, H2 receptor antagonists, and proton pump inhibitors (PPIs) [Figure 2].[2] PPI therapy has long been established as the fastest and most effective method for providing symptomatic relief in most patients.[5] It is considered effective therapy for GERD and for resolving both erosive esophagitis (EE) and reflux-related symptoms. When compared with placebo, PPIs demonstrate superior efficacy in controlling nocturnal reflux symptoms. Commonly used PPIs include Esomeprazole, Omeprazole, Pantoprazole, Rabeprazole, Lansoprazole, and Dexlansoprazole.[1,2]

EVIDENCE SUPPORTING ESOMEPRAZOLE FOR RESOLVING NAB

Data from multiple studies recommend the use of Esomeprazole 20 mg and 40 mg for the management of NAB in patients suffering from GERD.[2,4,6]

The study by Schuitenmaker *et al.* highlights that in a large clinical trial of 675 patients with symptomatic and/or endoscopic GERD who experienced night-time heartburn at least twice/week were enrolled. After 4 weeks of therapy, complete resolution of night-time heartburn occurred in 53.1% of those receiving Esomeprazole 40 mg, 50.5% with Esomeprazole 20 mg, and 12.7% with placebo.[2] Another study demonstrated that taking Esomeprazole once daily (OD) before breakfast significantly improved

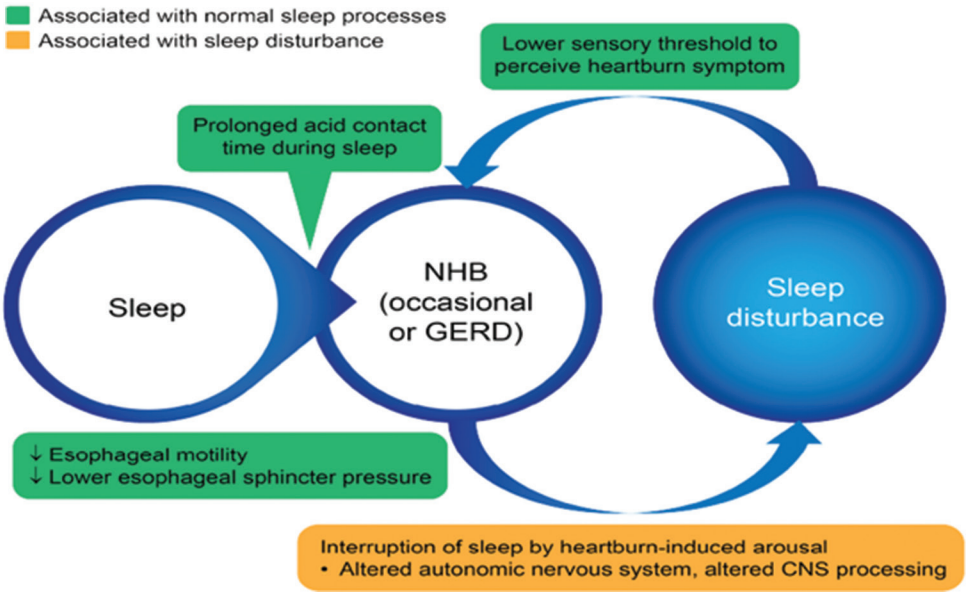

Figure 1: Bidirectional cycle of nocturnal heartburn and sleep disturbances.[4] CNS: Central nervous system, GERD: Gastroesophageal reflux disease

GERD-related sleep disturbances, which in turn enhanced work productivity compared to placebo.[4] A follow-up study involving 262 patients with symptomatic and/or endoscopic GERD found that Esomeprazole 20 mg provided relief from night-time heartburn in 34.3% of patients, compared to 10.4% with placebo. Both this and previous studies reported decreases in reflux-related sleep disturbances, alongside improvements in sleep quality and work productivity.[2]

A recent study by Ghosh *et al.* also reported that Esomeprazole demonstrated strong efficacy and safety in large clinical trials involving 15,000–29,000 patients. It was well tolerated in both short- and long-term use (6–12 months). Furthermore, a meta-analysis showed that standard-dose Esomeprazole offered superior healing of mucosal erosions and better relief of heartburn compared to other PPIs, confirming its effective and safe profile in patients with GERD.[6]

ENHANCED ACID SUPPRESSION AND CLINICAL BENEFIT OVER OTHER PPIS WITH ESOMEPRAZOLE

Esomeprazole is considered slightly more potent in suppressing gastric acid than other PPIs.[7,8] In cross-over studies conducted in both patients with GERD and healthy individuals, Esomeprazole has been compared with other PPIs and consistently shown superior acid suppression. Specially, Esomeprazole 40 mg OD was more effective in maintaining an intragastric pH above 4.0 compared with standard doses of other PPIs.[7,9,10]

A study by Rohss *et al.* compared Esomeprazole 40 mg OD with Lansoprazole 30 mg, Omeprazole 20 mg, Pantoprazole 40 mg and Rabeprazole 20 mg regarding intragastric pH control over 24 h.[11] On day 1, Esomeprazole maintained intragastric pH above 4 for a longer period compared to Lansoprazole (40.6% vs. 33.4%, $P = 0.0182$), Pantoprazole (50.3% vs. 29.1%, $P < 0.001$), and Rabeprazole (41.0% vs. 29.4%, $P = 0.002$). On day 5, Esomeprazole maintained pH >4 for 57.7% of the time versus 44.5% with Lansoprazole ($P < 0.0001$), 69.8% versus 43.7% with Omeprazole ($P < 0.0001$), 67.0% versus 44.8% with Pantoprazole ($P < 0.001$), and 59.4% versus 44.5% with Rabeprazole ($P < 0.0001$). In addition, Esomeprazole produced a higher 24-h median pH and a greater proportion of patients having pH >4 for at least 12 and 16 h compared to other PPIs. The study concluded that Esomeprazole 40 mg provides superior acid suppression and symptom relief in reflux symptoms in patients compared to Lansoprazole, Omeprazole, Pantoprazole, and Rabeprazole.[11]

In a randomised controlled study conducted by Zheng, 274 patients with endoscopically confirmed reflux esophagitis received daily morning doses of Omeprazole 20 mg, Lansoprazole 30 mg, Pantoprazole 40 mg, or Esomeprazole 40 mg over 8 weeks. Endoscopic healing at week 8 was similar among all four PPIs; however, Esomeprazole provided significantly faster heartburn relief during the 1st week of treatment. Patients treated with Esomeprazole experienced a more rapid reduction in mean heartburn scores, achieving complete symptom resolution by day 5 compared to other treatment groups. These findings suggest that Esomeprazole is particularly effective for patients seeking prompt relief from symptoms of reflux esophagitis.[12]

A meta-analysis of randomised trials in patients with EE showed that Esomeprazole has a modest overall advantage in healing EE compared to other PPIs. After 8 weeks, Esomeprazole showed an absolute risk reduction of 4%, corresponding to a number needed to treat (NNT) of 25. When stratified by Los Angeles (LA) grades of EE severity, the NNT decreased with increasing severity: for LA Grade C, the NNT was 14, and for LA Grade D, the NNT was 8. These findings indicate that Esomeprazole is more effective than other PPIs in patients with more severe EE. This clinical benefit aligns with physiological data showing superior 24-h intragastric pH control by Esomeprazole. Similarly, Esomeprazole provided a modest improvement in symptom relief for GERD compared to alternative PPIs at 4 weeks.[13]

In addition, results of a comparative study suggest that a daily dose of Esomeprazole 40 mg was more effective than Omeprazole 20 mg, Lansoprazole 30 mg, and Pantoprazole 40 mg in providing relief from heartburn symptoms during the 1st day and the first 5 days after the commencement of treatment.[14]

EFFECTS OF ESOMEPRAZOLE ON THE INCIDENCE OF NAB

As per the study by Das *et al.*, Esomeprazole 40 mg effectively controls nocturnal acid secretion, maintaining higher intragastric pH and causing fewer acid breakthroughs compared to Pantoprazole. It keeps pH above 4.0 for over 83% of the night and is more effective when dosed twice daily, especially during sleep. This makes it a superior option for managing night-time GERD symptoms and providing consistent acid suppression.[15]

According to the study by Johnson *et al.*, Esomeprazole significantly improves well-being in individuals suffering from night-time heartburn and related sleep disturbances, even in those with severe baseline sleep issues.[3] Data

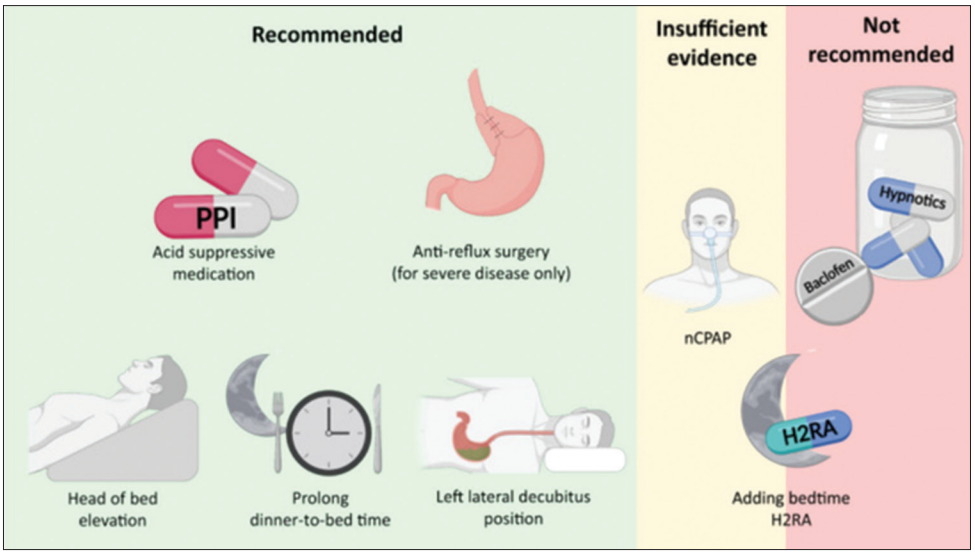

Figure 2: Interventions for effective treatment of nocturnal acid reflux.[2] H2RA: H2 receptor antagonists; nCPAP: Nasal continuous positive airway pressure, PPI: Proton pump inhibitor

pooled from two similar randomised, double-blind studies involving subjects with frequent heartburn and sleep disturbances showed that Esomeprazole 20 mg significantly predicted complete resolution of sleep disturbances after 14 days. Subjects in both treatment groups (Esomeprazole 20 mg OD and placebo) who experienced no daytime or night-time heartburn episodes during the 14-day treatment had higher rates of complete sleep disturbance resolution compared to those with one or more heartburn episodes during treatment [Figure 3]. The absence of daytime or night-time heartburn during treatment was a strong predictor of sleep improvement, whereas frequent baseline sleep disturbances reduced the likelihood of resolution. Notably, Esomeprazole's therapeutic benefit increased with higher baseline symptom frequency, highlighting its effectiveness, especially in patients with severe symptoms.[3]

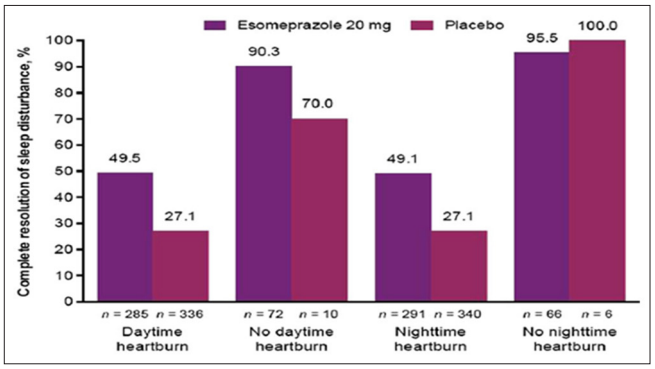

Figure 3: Effect of the presence/absence of daytime and night-time heartburn on complete resolution of sleep disturbance due to heartburn or other reflux symptoms by 14 days (presence of daytime and night-time heartburn defined as C1 episode during 14-day treatment period)

RECOMMENDED DOSING REGIMENS OF ESOMEPRAZOLE IN NAB

Data from clinical trials and meta-analyses show that Esomeprazole 40 mg OD for up to 8 weeks results in higher healing rates of erosive GERD and a greater proportion of patients with sustained resolution of heartburn compared to Omeprazole 20 mg, Lansoprazole 30 mg or Pantoprazole 40 mg OD.[7]

Both Esomeprazole 40 mg and Lansoprazole 30 mg OD significantly reduced esophageal acid exposure in patients with reflux-related esophageal complications, including ulcerative reflux esophagitis and Barrett's esophagus. Notably, Esomeprazole was considerably more effective than Lansoprazole in lowering total and supine nocturnal acid reflux time.[16]

In a randomised crossover study, nocturnal pH was compared between Esomeprazole 40 mg and Pantoprazole 40 mg administered twice daily. During the night, the time with intragastric pH above 4.0 was 85.4% with Esomeprazole compared to 63.6% with Pantoprazole ($P = 0.0001$). NAB, defined as intragastric pH below 4.0 for at least 1 consecutive h between 10 pm and 6 am, occurred in 26.7% of subjects on Esomeprazole and 73.3% on Pantoprazole ($P = 0.009$).[7]

FACTORS AFFECTING TREATMENT ADHERENCE AND ONCE-DAILY DOSING OF ESOMEPRAZOLE

Several factors can influence a patient's response to PPIs, including individual differences in how the drug is metabolized, as well as factors such as non-acid reflux,

visceral hypersensitivity, or delayed gastric emptying. Therefore, interpreting a lack of therapeutic response to acid suppression can be complex. In addition, an important consideration is whether the patient is fully adherent to the prescribed treatment regimen. Studies indicate that approximately 40% of patients fully adhere to prescribed medications, and non-adherence is a significant factor in treatment failure. Adherence is usually seen to be influenced by social, demographic, financial, educational, cultural factors, medication side effects, disease awareness, and the patient-provider relationship.[17]

A recent study by Das *et al.* highlighted that Esomeprazole provides superior symptomatic relief in patients with GERD compared to other PPIs. When taken as a daily dose, Esomeprazole 40 mg is more effective than Omeprazole 20 mg, Lansoprazole 30 mg, and Pantoprazole 40 mg in relieving heartburn symptoms, especially within the 1st day and during the initial 5 days of treatment.[15]

Esomeprazole's once and twice daily dosing strategies can be adapted to the severity of the condition and individual patient needs. Continuous dosing tends to offer the most reliable symptom control and significantly enhances quality of life for patients with GERD. This approach ensures more consistent and effective relief compared to other dosing regimens, making it the preferred option when sustained symptom management is necessary.[18] Studies show that Esomeprazole led to rapid improvement in sleep disturbances and sleep quality, significantly outperforming placebo, with noticeable benefits starting from the very first night of treatment.[3] A study evaluating the effect of PPI therapy in patients with GERD found that Esomeprazole provided more effective heartburn relief than other PPIs. It was also well-tolerated, demonstrated a favorable safety profile, and showed high patient compliance in this population.[14,19,20]

CONCLUSION

Night-time reflux significantly disrupts sleep quality, leading to daytime fatigue, impaired functioning, and reduced quality of life. Acid suppression therapy is the cornerstone of managing nocturnal acid reflux. Lifestyle modifications – such as avoiding late meals, weight reduction, and positional changes – can be helpful but are often insufficient without pharmacologic treatment. PPIs remain the most effective drugs for controlling nocturnal reflux symptoms and promoting mucosal healing. Among available PPIs, Esomeprazole has demonstrated superior efficacy in maintaining intragastric pH above 4.0, reducing NAB, and providing faster relief and better symptom control compared to other PPIs such as Omeprazole, Lansoprazole, and Pantoprazole.

Clinical trials involving thousands of patients have consistently shown that Esomeprazole is well tolerated and results in significant improvements in sleep disturbance, heartburn resolution, and overall patient quality of life. Flexible dosing regimens, OD or twice daily, allow for personalized treatment, with continuous therapy offering the most consistent symptom relief. Thus, it can be concluded that Esomeprazole stands out as a highly effective and safe option for nocturnal GERD management. Its potent acid suppression, quick symptom relief and positive impact on sleep quality make it a valuable therapy to improve patient outcomes and reduce complications associated with nocturnal acid reflux.

ACKNOWLEDGMENT

We would like to acknowledge Scientimed Solutions Pvt. Ltd. for assistance in developing the manuscript.

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How to cite this article: Ajinkya CM, Rao BV, Tudu PK. Esomeprazole for Effective Night-time Acid Suppression in Gastroesophageal Reflux Diseas. Int J Sci Stud 2026;14(2):4-9.

Source of Support: Nil, **Conflicts of Interest:** None declared.