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Original Article

Optimizing Proton-pump Inhibitor Therapy in Acid Peptic Diseases: Insights from Clinical Practice in India

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Abstract

Background: The global burden of acid peptic diseases (APDs) is rising, particularly in India, where gastro-oesophageal reflux disease (GERD) and peptic ulcer disease (PUD) are prevalent. Proton-pump inhibitors (PPIs) are the cornerstone in managing GERD, PUD and related conditions.

Aim: This study aimed to evaluate prescribing patterns and physician preferences regarding commonly used PPIs, such as Rabeprazole, Pantoprazole, Esomeprazole and Omeprazole, through a cross-sectional survey

Method: This cross-sectional survey collected data from 47 physicians (gastroenterologists and primary care doctors) on their PPI prescribing patterns for GERD. Participants evaluated the clinical effectiveness of Rabeprazole, Pantoprazole, Esomeprazole, and Omeprazole based on their real-world experience.

Results: The survey revealed varied PPI utilisation patterns–Pantoprazole and Rabeprazole are the most commonly used, while Omeprazole has the lowest usage among arriving patients. Physicians highlighted Rabeprazole as the most effective PPI for rapid symptom relief, particularly from day 1 of therapy, followed by Esomeprazole. Rabeprazole also provided superior sustained relief for daytime and nocturnal symptoms compared with other PPIs. Switching between PPIs was common, driven primarily by a lack of immediate symptom relief. Most physicians preferred Rabeprazole for switch therapy, citing its rapid activation, higher selectivity for proton-pump binding sites and minimal drug interactions. Additionally, Pantoprazole's consistent bioavailability and Rabeprazole's genotype-independent pharmacodynamics were notable advantages.

Conclusion: The findings emphasise the importance of selecting PPIs based on clinical efficacy, patient preference and cost-effectiveness. Rabeprazole's unique pharmacological properties make it a preferred choice for rapid and sustained symptom relief in GERD management. These insights can help optimise therapeutic strategies, addressing real-world challenges in APD treatment while improving patient outcomes.

Keywords: Acid peptic diseases, gastro-oesophageal reflux disease, peptic ulcer, proton-pump inhibitors, Rabeprazole, Pantoprazole, switch therapy, nocturnal symptoms, drug interactions.

Key words: Acid peptic diseases, Drug interactions, Gastro-esophageal reflux disease, Nocturnal symptoms, Pantoprazole, Peptic ulcer, Proton-pump inhibitors, Rabeprazole, Switch therapy

INTRODUCTION

The global burden of acid peptic diseases (APDs) is rising, driven by evolving lifestyles and dietary patterns. In India, the prevalence of gastroesophageal reflux disease (GERD) is notably high at 39.2%, followed by peptic ulcer disease (PUD) at 37.1% and non-ulcer dyspepsia at 25.2%.[1] The currently available drugs for APDs include proton-pump inhibitors (PPIs), histamine-2 receptor antagonists (H2RAs), antacids, sucralfate, and prostaglandin analogs.[1]

PPIs are the cornerstone therapy for managing conditions such as PUD, GERD, erosive esophagitis, Barrett's esophagus, Zollinger–Ellison syndrome, and upper gastrointestinal bleeding.[1] In India, the available PPIs include

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rabeprazole, pantoprazole, omeprazole, esomeprazole, lansoprazole, dexlansoprazole, dexrabeprazole, and ilaprazole.[1]

Compared to H2RAs, PPIs have demonstrated superior efficacy in achieving symptomatic relief and remission in both non-erosive and erosive reflux diseases.[1] Their mechanism of action involves profound and sustained acid suppression, which is critical for managing and preventing the complications associated with acid peptic disorders.[2]

The guidelines from the National Institute of Clinical Excellence emphasize that all PPIs are comparable in terms of clinical efficacy, with the primary differentiators being cost and approved indications.[3] For patients with severe esophagitis, it is recommended to offer a full-dose PPI for an initial treatment period of 8 weeks. The choice of PPI should consider the patient's preferences, clinical circumstances, underlying health conditions, and potential drug interactions. As long-term maintenance therapy, a full-dose PPI should be provided for individuals with severe esophagitis. This decision should also be a factor in the patient's preferences, the tolerability of the selected PPI, existing health conditions, potential drug interactions, and the cost of the medication.[3]

Pharmacodynamically, lansoprazole and rabeprazole stand out due to their faster onset in achieving maximal acid suppression compared to other PPIs.[4] Both Pantoprazole and rabeprazole exhibit a predictable, linear relationship between dosage and plasma concentration, even with repeated administration.[1] Notably, Pantoprazole's absorption remains unaffected when taken alongside antacids, ensuring consistent bioavailability.[5]

Despite sharing a common mechanism of action, pantoprazole and rabeprazole demonstrate a higher selectivity for binding to cysteine 813/822 sites on the proton pump, enhancing their targeted effects.[1] In addition, rabeprazole rapidly converts into its active sulphenamide form and dissociates quickly from the H^+/K^+ ATPase enzyme, resulting in a faster onset +of action but a shorter duration of inhibition compared to other PPIs. This combination of rapid activation and selective binding makes rabeprazole and pantoprazole distinctive within the PPI class.[1]

METHODS

This study utilized a cross-sectional survey targeting practicing physicians to gather insights regarding the clinical use and comparative effectiveness of PPIs in managing GERD. The survey assessed prescribing patterns, therapeutic preferences, and clinical outcomes related to commonly used PPIs, including rabeprazole, pantoprazole, esomeprazole, and omeprazole. Physicians specializing in gastroenterology and primary care, who frequently manage patients with GERD, were invited to participate. Physicians provided their responses based on their clinical experience and observations.

RESULTS AND DISCUSSION

This survey provides insights into the prescribing patterns and clinical experiences of physicians managing patients with GERD using PPIs. The findings highlight trends in PPI utilization, symptom relief, and therapeutic preferences, offering perspectives on factors influencing clinical decision-making. The data indicate a varied distribution of patients already on specific PPI therapies upon arrival, with differences in perceived efficacy for symptom relief. In addition, physician preferences for switching PPIs suggest distinct patterns, which may reflect real-world treatment considerations and patient responses to different PPI molecules. These results are discussed in the context of optimizing PPI therapy to enhance clinical outcomes in GERD management.

A total of 47 respondents from various clinical settings completed the survey and their responses were analyzed for insights.

Figure 1 illustrates the percentage of patients who arrive already on certain PPIs. Pantoprazole has the highest percentage of patients already on it (35%), followed by rabeprazole (33%) and esomeprazole (23%) and omeprazole demonstrates the lowest proportion, at 11%. Figure 1 demonstrates that pantoprazole and rabeprazole are the most commonly used PPIs among arriving patients, while omeprazole is the least frequently used. Overall, the data offer insights into the distribution of PPI usage among patients at the time of treatment initiation.

PPIs are one of the most frequently prescribed classes of medications. Although they were considered safe earlier, recent studies have highlighted potential risks linked to their use, including an elevated risk of *Clostridium difficile* infection, pneumonia, and fractures.[6] The study by Palmowski *et al.* highlights that continuing unnecessary PPI therapy post-hospital discharge has a significant impact on morbidity and mortality.[7] The safety of PPIs used earlier – such as omeprazole and lansoprazole – has been well established for short-term use (<12 weeks). Newer agents, including rabeprazole and pantoprazole, show similar safety profiles in comparison to medications used earlier. PPIs should not be used in patients with a known hypersensitivity to them and must be administered with caution in those with

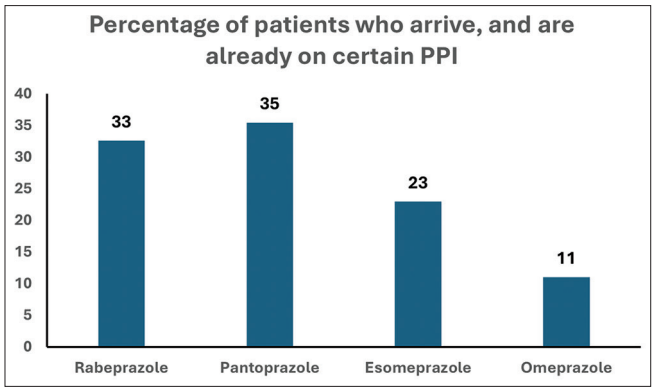

Figure 1: Percentage of patients arriving already on certain proton-pump inhibitors, including Rabeprazole, Pantoprazole, Esomeprazole and Omeprazole. Pantoprazole and Rabeprazole are the most commonly used, while Omeprazole has the lowest usage among arriving patients

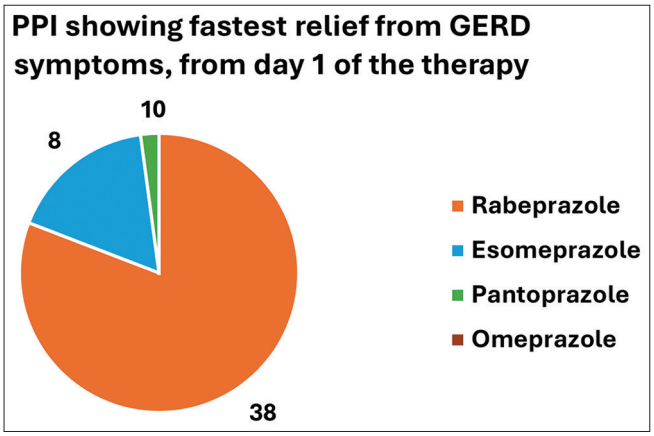

Figure 2: Percentage of patients on different PPIs upon arrival. This figure illustrates the perceived efficacy and strong association of Rabeprazole among all PPIs, showing faster relief from GERD symptoms from day 1 of the therapy as per the physicians' responses

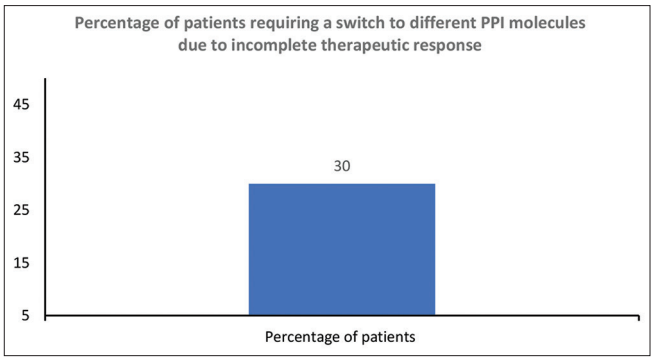

Figure 3: Percentage of patients requiring a switch to a different PPI due to an incomplete therapeutic response. The graph highlights that a notable proportion of patients did not achieve adequate symptom control with their initial PPI and required a change in medication

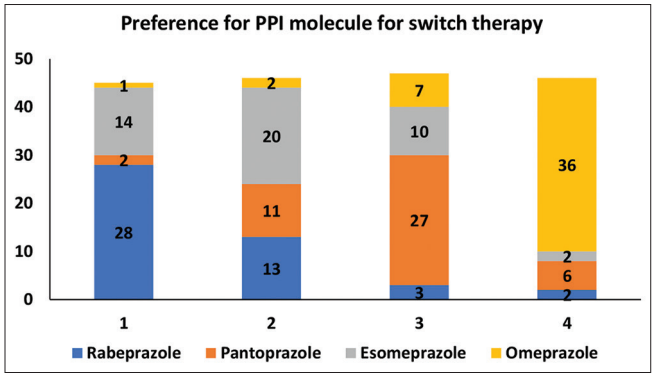

Figure 4: Preference for proton-pump inhibitor molecules (Rabeprazole, Pantoprazole, Esomeprazole and Omeprazole) in switch therapy across four Ranks. The y-axis represents the number of preference responses from the respondents, while the x-axis represents the Ranks (1–4). This figure illustrates the strong association between Rabeprazole being the most preferred PPI for switch therapy as suggested from the survey results

severe hepatic disease.[8] While omeprazole is categorized as a pregnancy category C drug, other PPIs are classified as category B. Furthermore, the use of PPIs is not advised for breastfeeding mothers.[8]

According to physicians' responses, rabeprazole provided faster relief from GERD symptoms from day 1 of therapy, followed by esomeprazole, whereas pantoprazole and omeprazole were reported less frequently for this purpose [Figure 2]. These findings suggest a variation in physician-reported experiences with different PPIs for initial symptom relief.

In a study by Lawate *et al.* 2023, a significant proportion of patients experienced rapid and complete symptomatic relief at the first visit (day 1–7) with rabeprazole compared to the baseline visit.[2] The study outcomes were assessed over 4 weeks (days 1–7 and 8–30 after the baseline visit) and between 4 and 8 weeks (days 31–60 and 61–90 after the baseline visit) of treatment. Improved symptom relief was observed with each subsequent visit, with the maximum number of patients exhibiting complete symptomatic relief for both daytime and nocturnal symptoms at 4th visit (day 61–90). Specifically, patients reported notable improvements in daytime heartburn and sleep disturbances. Rabeprazole provided faster relief at the first visit compared to pantoprazole for daytime heartburn, epigastric pain, and nocturnal water brash as well as for nocturnal nausea when compared to esomeprazole.[2] In addition, the proportion of patients showing a complete treatment response was higher with rabeprazole when compared with pantoprazole and esomeprazole.[2]

Figure 3 shows the percentage of patients who were required to switch to a different PPI due to an incomplete therapeutic response. Physician responses indicate that approximately 30% of patients changed their PPI medication because their initial treatment did not provide

sufficient relief. This suggests that while PPI therapy is generally effective, some patients may require adjustments in their treatment regimen.

Several clinical studies have reported that compared to omeprazole, lansoprazole, and pantoprazole, the pharmacodynamics of rabeprazole are the least influenced by the CYP2C19 genotype, which determines whether individuals are extensive or poor metabolizers of the PPI. Studies in healthy volunteers have shown no significant impact of the CYP2C19 genotype on Rabeprazole's effect on intragastric pH. For instance, in patients treated with Lansoprazole and Omeprazole, poor metabolizers exhibited significantly higher intragastric pH after 7–8 days of treatment, unlike those receiving rabeprazole, where no such effect was observed.[9] Studies suggest that genetic variations in CYP2C19 metabolism influence PPI response. When switching PPIs, opting for one with minimal reliance on CYP2C19, such as rabeprazole, may be preferable.[2]

Figure 4 illustrates the preference for different PPI molecules in switch therapy across four ranks, rank 1 being the most preferred to 4 being the least preferred PPI [Figure 4]. In rank 1, rabeprazole is the most preferred, followed by esomeprazole, pantoprazole, and omeprazole. Rank 2 shows a similar trend, with esomeprazole followed by rabeprazole and pantoprazole. In rank 3, pantoprazole is the most preferred molecule, followed by esomeprazole, omeprazole, and rabeprazole. Finally, in rank 4, omeprazole is the most preferred molecule, with a minimal preference for the other three PPIs. The chart highlights a shift in preference across the ranks, with rabeprazole gaining prominence in rank 1.

The American College of Gastroenterology (ACG) Clinical Guideline for the Diagnosis and Management of GERD, 2022, recommends evaluating the cytochrome (CYP2C19) metabolizer genotype and, based on the results, consider switching the PPI brand or transitioning to a CYP-independent PPI (such as esomeprazole or rabeprazole) if not already tried.[10] In a survey-based study, 44% of participants identified "lack of immediate symptom relief" as the most important factor impacting the switch from one PPI to another, whereas 59% agreed that this factor also influenced dose adjustments.[11]

Figure 5 presents data on the sustained relief provided by various PPIs for both daytime and nocturnal symptoms associated with GERD. Among the PPIs studied, Rabeprazole was reported to provide relief in approximately 35–40% of patients, followed by esomeprazole (10–15%), whereas omeprazole and pantoprazole had reported lower levels of sustained relief (<5%).

Nocturnal acid breakthrough is defined as an intragastric pH of <4 for >1 continuous hour during the night and has been recognized as a key factor contributing to nocturnal reflux. Nocturnal reflux is also commonly observed in patients with obstructive sleep apnoea.[12] Breakthrough nighttime symptoms in GERD patients on PPIs are well-established; proton pumps regenerate overnight, reducing the effectiveness of PPI blockade. To manage this, H2 blockers are sometimes prescribed as an adjunct therapy for nighttime GERD symptoms, even for patients already on PPIs, to help minimize nocturnal acid breakthrough.[13] Compared with placebo, PPIs are highly effective in treating nocturnal reflux symptoms. Due to their pharmacokinetics, PPIs exhibit optimal efficacy when administered on an empty stomach, approximately 30 min before breakfast or

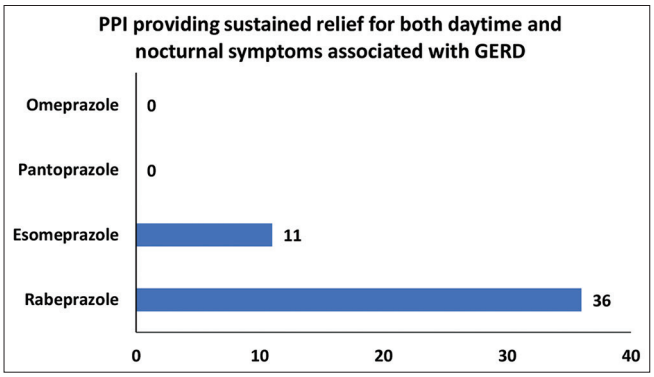

Figure 5: PPI providing sustained relief for both daytime and nocturnal symptoms associated with GERD. The x-axis of the bar graph represents the percentage of patients who experienced sustained relief from both daytime and nighttime GERD symptoms. The y-axis lists the different proton-pump inhibitors studied: Omeprazole, Pantoprazole, Esomeprazole and Rabeprazole. The length of each bar represents the percentage of patients who benefited from each PPI

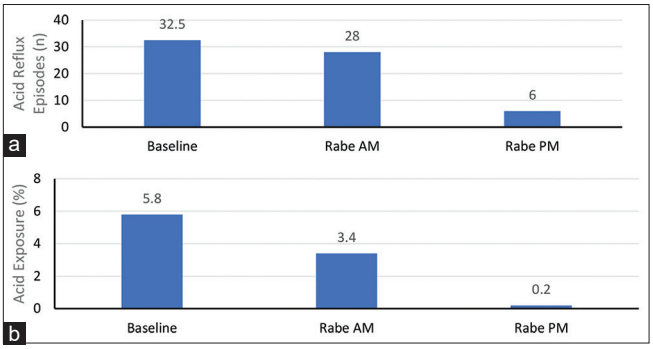

Figure 6: (a) Number of supine reflux episodes at baseline and for the two rabeprazole regimens. Note the significant difference in the number of reflux episodes between the evening dose of rabeprazole and baseline (no medication). Data are presented as median values. (b) Supine oesophageal exposure at baseline and for the two rabeprazole regimens. Note that the nocturnal acid exposure is significantly lower with the rabeprazole p.m. regimen in comparison with the rabeprazole a.m. regimen. Data are presented as median values. Adapted from Pahlivanov *et al.*, 2003.[20]

dinner. A small study assessing the impact of rabeprazole timing on nocturnal esophageal pH demonstrated that evening administration resulted in a significantly lower nocturnal esophageal pH (0.2%) compared with morning administration (3.4%). In addition, when comparing rabeprazole 20 mg to pantoprazole 40 mg taken in the morning, no significant difference in esophageal acid exposure time was observed.[12]

The data in Figure 6 compares two key aspects of supine conditions: Acid exposure and reflux episodes, across baseline measurements and two rabeprazole regimens (morning and evening dosing). The first part focuses on the number of supine reflux episodes. A significant reduction in reflux episodes is observed with the evening rabeprazole dose compared to the baseline condition without medication. The second part highlights the percentage of supine esophageal acid exposure. Nocturnal acid exposure is significantly reduced with the rabeprazole evening regimen compared to both the baseline and the morning regimen. This reduction is evident in the much lower acid exposure percentage (0.2%) with the evening dose compared to 5.8% at baseline and 3.4% with the morning dose. These findings reinforce the effectiveness of administering rabeprazole in the evening for managing nocturnal gastroesophageal reflux.

According to the survey, rabeprazole, which demonstrates the highest patient satisfaction, has been noted for its rapid onset of action and effective acid suppression [Figure 7]. Esomeprazole also ranks high in patient satisfaction, whereas pantoprazole and omeprazole rank lower. Some studies have found esomeprazole 40 mg to be superior to omeprazole 20 mg in treating GERD, with a relative risk of 1.18.[14] Patient satisfaction with PPI treatment for GERD was consistently high, surpassing other GERD medications in a study.[15] Thus positive correlation between patient satisfaction and symptom improvement highlights its utility as a valuable clinical endpoint in assessing treatment success.

High-dose PPI therapy (80 mg bolus followed by 8 mg/h Omeprazole infusion) is a well-recognized approach for managing ulcer bleeding with endoscopic stigmata, supported by evidence from a large multinational randomized placebo-controlled trial.[16] However, a meta-analysis of seven randomized controlled trials (1,157 patients) found no significant differences in rebleeding, surgical intervention, or mortality rates between high-dose and non-high-dose PPIs. Subgroup analyses confirmed that outcomes were unaffected by hemorrhage severity, PPI administration route, or dosage.[17] Figure 8 depicts the distribution of high-dose PPI use across various gastrointestinal conditions based on the responses from surveyed physicians. GERD was the most commonly reported condition for prescribing high-dose PPI therapy, cited by nearly 50% of physicians. This was followed by duodenal ulcers, which were reported by approximately 30% of respondents, and oesophagitis by about 20%. In addition, Figure 7 shows the preferred duration of high-dose PPI treatment, with 4–8 weeks being the most frequently recommended duration (by nearly 40% of physicians), followed by durations of 4 weeks and 6–8 weeks. A very small percentage of physicians recommended other treatment durations. This suggests that high-dose PPI therapy is most frequently used for GERD management, with a typical treatment duration of 4–8 weeks according to physician practices.

The ACG Clinical Guideline for the diagnosis and management of GERD, 2022, recommends that if initial

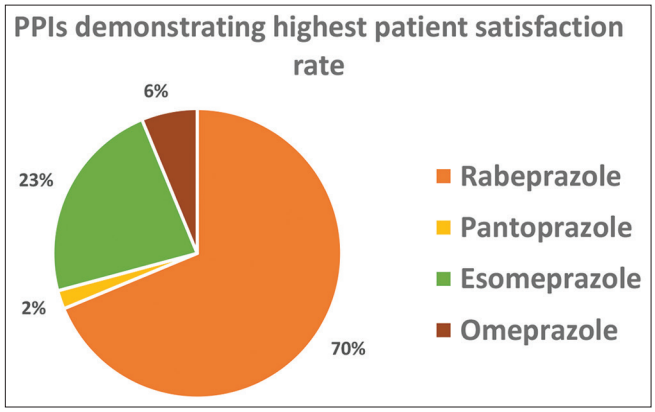

Figure 7: Ranking of proton-pump inhibitors based on highest patient satisfaction as reported by surveyed physicians. Rabeprazole demonstrated the highest patient satisfaction rate, followed by Esomeprazole, Omeprazole and Pantoprazole

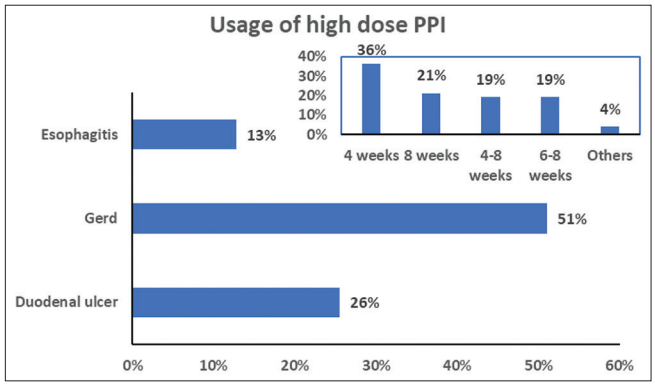

Figure 8: Usage of high-dose proton-pump inhibitors in different gastrointestinal conditions as reported by surveyed physicians. Gastro-oesophageal reflux disease was the most commonly treated condition, followed by duodenal ulcers and oesophagitis. The inset graph highlights the preferred duration of treatment, with 4–8 weeks being the most frequently recommended period

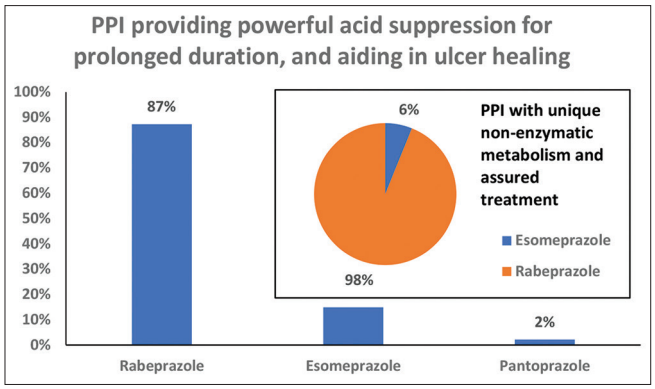

Figure 9: Preferred molecule in managing comorbid conditions alongside GERD or APD, as reported by surveyed physicians. The inset pie chart highlights the reason for selecting the PPI with less drug interaction being the most preferred

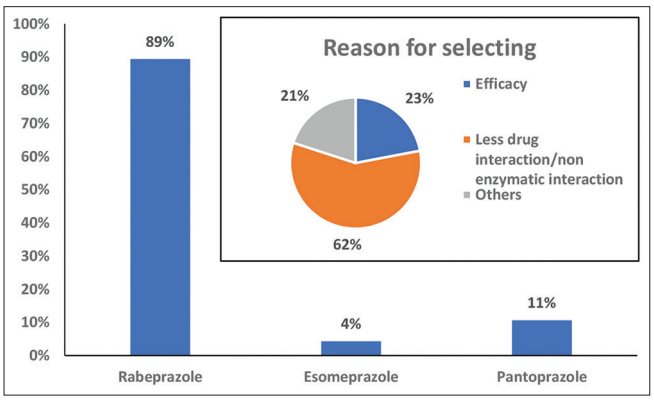

Figure 10: Preferred molecule in providing powerful acid suppression over a prolonged duration and aiding in ulcer healing as reported by surveyed physicians. The inset pie chart highlights the PPI with unique non-enzymatic metabolism, ensuring treatment satisfaction

treatment with a PPI fails to heal severe esophagitis, consider escalating to a high-dose regimen of the same PPI, switching to another full-dose PPI, or opting for a different high-dose PPI. The choice should be guided by patient preference, clinical factors (e.g., tolerability and comorbidities), and potential drug interactions.[10]

The preferred molecule in managing comorbid conditions alongside GERD was rabeprazole (selected by 89% of physicians) followed by pantoprazole (11%) and esomeprazole (4%) [Figure 9]. Most surveyed physicians cited rabeprazole's minimal enzymatic interaction (62%), making it particularly advantageous for patients on polypharmacy, followed by efficacy (23%) as the primary reason for selecting rabeprazole.[9] Rabeprazole's pharmacological profile, including its weak interaction with the CYP P450 enzyme system, has been widely documented, making it a suitable option for patients concurrently using medications such as Clopidogrel.[18] In addition, real-world studies have shown that rabeprazole provides faster acid suppression and symptom relief in GERD and PUD compared with other PPIs.[2,9]

Although esomeprazole and pantoprazole were less frequently selected, they remain essential in certain clinical contexts, particularly in the management of GERD and erosive esophagitis.[19] However, their preference is relatively lower due to enzyme-mediated interactions and variable patient response rates.[18,19] Overall, physician selection of PPIs appears to be driven primarily by clinical efficacy and safety concerns, with rabeprazole emerging as the favored choice in this sample.

Figure 10 presents data on the preferences of surveyed physicians regarding PPIs for providing effective acid suppression and aiding in ulcer healing, indicating that rabeprazole (87%) was most commonly preferred among the surveyed physicians for prolonged acid suppression, compared to esomeprazole (15%) and pantoprazole (2%). Rabeprazole's unique non-enzymatic metabolism is highlighted as a key factor contributing to its consistent efficacy profile and treatment satisfaction, which is crucial for patients requiring long-term management of acid-related disorders.[9,10] Esomeprazole was also selected, but less frequently than rabeprazole. The inset pie chart in Figure 9 further emphasizes the preference for rabeprazole (98%), reinforcing its position as a leading PPI in clinical practice. The current survey also suggests that rabeprazole is the preferred choice of physicians for its superior acid suppression capabilities and its unique metabolic profile, which enhance patient satisfaction and treatment outcomes.

CONCLUSION

The survey results suggest that rabeprazole is the most preferred PPI for managing GERD, demonstrating superior effectiveness in providing rapid symptom relief, sustained efficacy, and high patient satisfaction. Physicians favored rabeprazole due to its unique non-enzymatic metabolism, which ensures more consistent therapeutic outcomes, especially in patients with comorbid conditions requiring polypharmacy. Pantoprazole and esomeprazole were also considered viable options; physicians' responses indicated varying preferences based on the clinical context. In addition, rabeprazole's minimal enzymatic interaction with the CYP P450 system makes it the preferred option for patients on multiple medications. Despite its lower preference in certain contexts, pantoprazole and esomeprazole still have essential roles in managing long-term GERD and erosive oesophagitis. Overall, the survey underscores the importance of clinical efficacy, safety, and patient satisfaction in selecting the most appropriate PPI therapy. The results highlight the

importance of individualized treatment approaches in GERD management.

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