

Clinician's Perspectives on the Management of Gastroesophageal Reflux Disease and Prescription Practice of Proton Pump Inhibitors in Indian Settings

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Abstract: *Objective:* To assess the clinicians' perspectives on GERD management and the prescription practices of proton pump inhibitors (PPIs) in Indian settings. *Methods:* This cross-sectional study was conducted among clinicians specialized in GERD management. Participants completed a 24-question questionnaire distributed via email or online platforms. The survey explored prescription practices, clinical observations, and preferences regarding PPIs and GERD management. Data analysis involved descriptive statistics, with responses presented as frequencies and percentages. *Results:* Out of 123 survey participants, 57% identified diet as the most common predisposing factor for GERD. Nighttime heartburn and disturbed sleep were recognized as key alarm symptoms by 57% of participants. Epigastric tenderness was the most prevalent physical finding, reported by 68% of clinicians. PPIs were favored as the first-line treatment for GERD by 78.86% of respondents. Domperidone was preferred as an adjunctive treatment for functional dyspepsia and gastroparesis. An empirical PPI trial was widely supported for its simplicity and cost-effectiveness. Rabeprazole emerged as the preferred PPI for nighttime heartburn relief due to its rapid onset and sustained efficacy. *Conclusion:* This study highlighted a consensus among Indian clinicians on the use of PPIs as a primary treatment for GERD, with a preference for rabeprazole. Domperidone is favored as an adjunctive treatment for functional dyspepsia and gastroparesis. Rabeprazole emerged as the preferred option for nighttime heartburn relief, owing to its rapid onset and long-lasting effectiveness.

Keywords: GERD, PPIs, Diet, Alarm Symptoms, Domperidone, Empiric Trial, Rabeprazole, Endoscopy, Clinical Practices, Patient Outcomes.

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INTRODUCTION

Gastroesophageal reflux disease (GERD), marked by symptoms such as heartburn and regurgitation, is one of the most common gastrointestinal issues addressed at the physician and primary care level [1]. The global prevalence of GERD is estimated to be around 13.98%, with notable regional and national variations. In 2019, the global burden of GERD amounted to 783.95 million cases [2]. Between 1990 and 2019, the total number of prevalent cases, incident cases, and years lived with disability (YLDs) increased by 77.53%, 74.79%, and 77.19%, respectively [3]. The prevalence of GERD among the Indian population was 15.6%, with a 95% confidence interval ranging from 11.046% to 20.714%. Population studies generally show

GERD prevalence below 10%, while cohort studies report a range from 7.6% to 30% [4, 5].

Proton pump inhibitors (PPIs) are the most widely prescribed antisecretory agents globally due to their high efficacy and safety [6]. Rabeprazole, a PPI functions specifically by inhibiting the enzyme H⁺/K⁺-ATPase (proton pump). This mechanism reduces gastric acid secretion, aiding in the treatment and prevention of conditions exacerbated by excessive stomach acid, such as duodenal and gastric ulcers [7]. Domperidone, on the other hand, acts as a peripheral antagonist of dopamine-2 receptors, providing prokinetic and antiemetic benefits primarily targeting the upper gastrointestinal (GI) tract [8]. Rabeprazole and domperidone combination therapy not only alleviates symptoms but also enhances overall

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tolerability, potentially improving the quality of life for individuals with GERD [9].

Understanding the prescription practices of these drugs is paramount to optimizing their use, enhancing patient outcomes, and improving overall gastrointestinal health management in Indian settings. The survey aims to gather expert opinions on the clinical use of rabeprazole and its combination with domperidone as maintenance therapy for GERD in Indian healthcare settings.

METHODOLOGY

A cross sectional, questionnaire-based survey was carried out among gastroenterologists involved in treating GERD in the major Indian cities from June 2023 to December 2023.

An invitation was sent to leading gastroenterologists in treating GERD in the month of March 2023 for participation in this Indian survey. About 123 doctors from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. The participants were informed not to discuss the questions/ answers before and while answering the questions with anyone or online and are asked to answer them on their own. A written informed consent was obtained from each gastroenterologist before initiation of the study.

The questionnaire booklet named GRACE (Gastro Esophageal Reflux Disease: A Comprehensive Evaluation) study was sent to the gastroenterologists who were willing to participate in this study. The GRACE study questionnaire encompassed 24 questions focusing on current prescription practices, clinical observations, and preferences regarding the use of PPIs, as well as experiences with GERD in routine practice. The study was conducted after getting approval from Bangalore Ethics, an Independent Ethics Committee which is recognized by the Indian Regulatory Authority, Drug Controller General of India.

Statistical Analysis

Descriptive statistics were employed for data analysis with categorical variables presented as percentages. The frequency of each variable and corresponding percentage was calculated to illustrate its distribution. Graphs and pie charts were created using Microsoft Excel 2013 (version 16.0.13901.20400) to visually depict the distribution of categorical variables.

RESULTS

Out of 123 survey participants, approximately 57% of the clinicians indicated that diet is the most common predisposing factor in patients with GERD (Figure 1). Similarly, about 57% of the participants noted that nighttime heartburn and disturbed sleep are the most recognized alarm symptoms of GERD associated with serious complications (Figure 2).

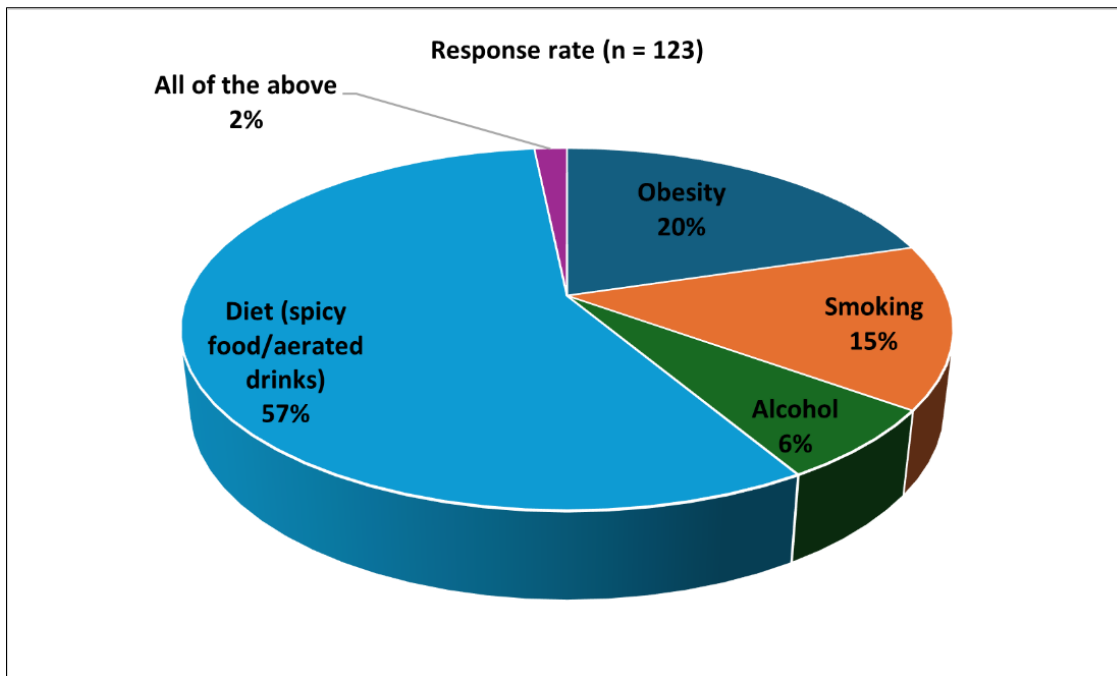


Figure 1: Distribution of response to most common predisposing factor in patients with GERD

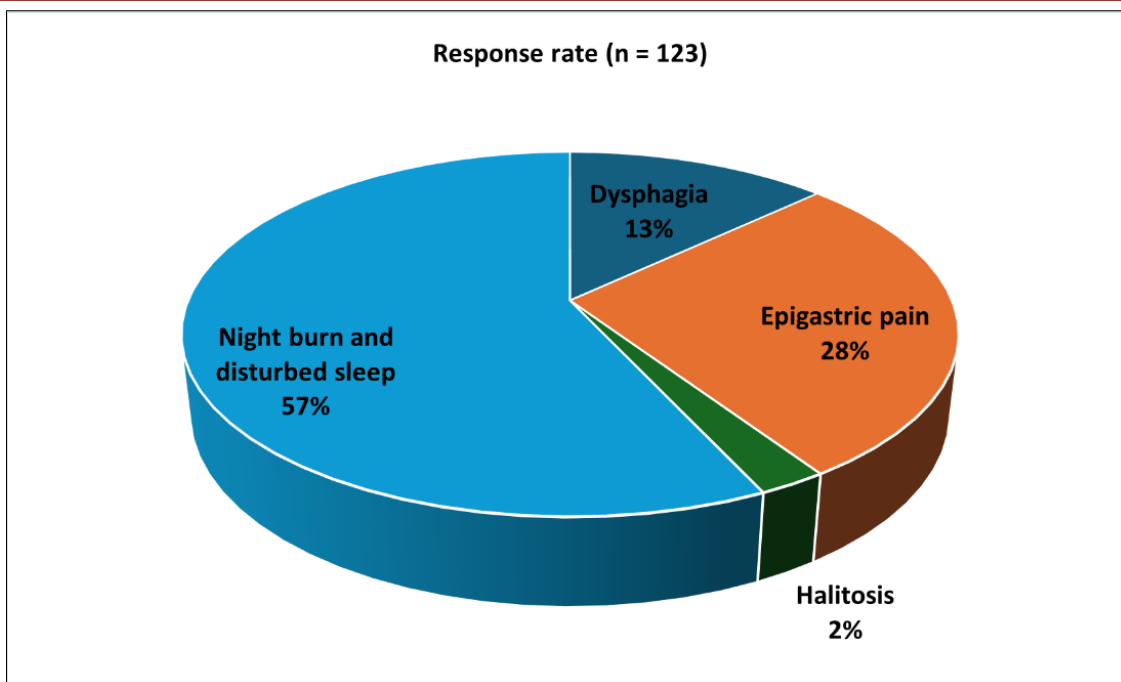


Figure 2: Distribution of response to most recognized alarm symptoms of GERD associated with serious complications

Approximately 68% of the clinicians reported that epigastric tenderness is the most prevalent physical finding observed in GERD patients in clinical practice.

The majority (78.86%) of the participants preferred PPIs as the first-line treatment for GERD in clinical practice (Table 1).

Table 1: Distribution of response to first-line treatment for GERD in clinical practice

First-line drug	Response rate (n = 123)
PPIs	78.86%
Antacids	4.07%
Prokinetic agents	11.38%
Histamine-2 receptor antagonists (H2RAs)	5.69%

About 74% of the experts stated that administering PPIs 30 to 60 minutes before the first meal of the day is ideal for achieving optimal efficacy. Nearly half (43.09%) of the participants indicated that 21-30% of diabetic patients are at risk of developing gastroparesis. Around 41% noted that abdominal or

esophageal surgery are risk factors for developing gastroparesis in addition to diabetes. Half (49.59%) of the respondents indicated that domperidone is the preferred prokinetic agent to use with PPIs in functional dyspepsia (FD) and gastroparesis (Table 2).

Table 2: Distribution of response to preferred prokinetic agent with PPI in FD and gastroparesis

Choice	Response rate (n = 123)
Levosulpiride	45.53%
Domperidone	49.59%
Itopride	4.88%

Approximately 52% of the participants stated that drinking water is a factor contributing to lower esophageal sphincter (LES) malfunction. About 43% noted that adjustable gastric banding is the recommended surgical approach for obese patients with GERD. Around 58% observed that patients using PPIs respond to GERD, and diet and habits play a significant role in managing

non-acid reflux. Additionally, the respondents noted that non-acid reflux does not trigger functional esophageal disorders. Most respondents (63.41%) agreed that all the listed characteristics of an empiric PPI trial such as its simplicity, cost-effectiveness, role in initial diagnosis, and ability to indicate the need for further investigation are true (Table 3).

Table 3: Distribution of response to characteristics of empiric PPI trial for GERD treatment

Characteristics	Response rate (n = 123)
It is simple and cost-effective.	16.26%
It is the core approach to initial GERD diagnosis.	15.45%
It is informative of whether further investigation is required.	4.88%
All the above	63.41%

Around 63% of participants reported that concurrent use of NSAIDs with tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRIs) increases gastrointestinal adverse effects. More than half (60.98%) of the participants indicated that nighttime heartburn has a significant impact on the quality of life

of patients with GERD symptoms. Approximately 42% of clinicians reported that 21-30% of patients with GERD experience complications related to disturbed sleep. Nearly half (47.97%) of the participants preferred endoscopy as a diagnostic investigation for GERD in clinical practice (Table 4).

Table 4: Distribution of response to preferred diagnostic investigation for GERD in clinical practice

Preference	Response rate (n = 123)
24 hr intraluminal PH monitoring	41.46%
Manometry	4.88%
Barium swallow	5.69%
Endoscopy	47.97%

About 41% of participants stated that 11-20% of patients with GERD report symptoms of irritable bowel syndrome. About 47% of clinicians indicated that lack of patient education is a factor associated with

patient non-adherence to medication. According to 90% of the participants, rabeprazole is the preferred PPI for long-lasting nighttime heartburn relief in GERD (Figure 3).

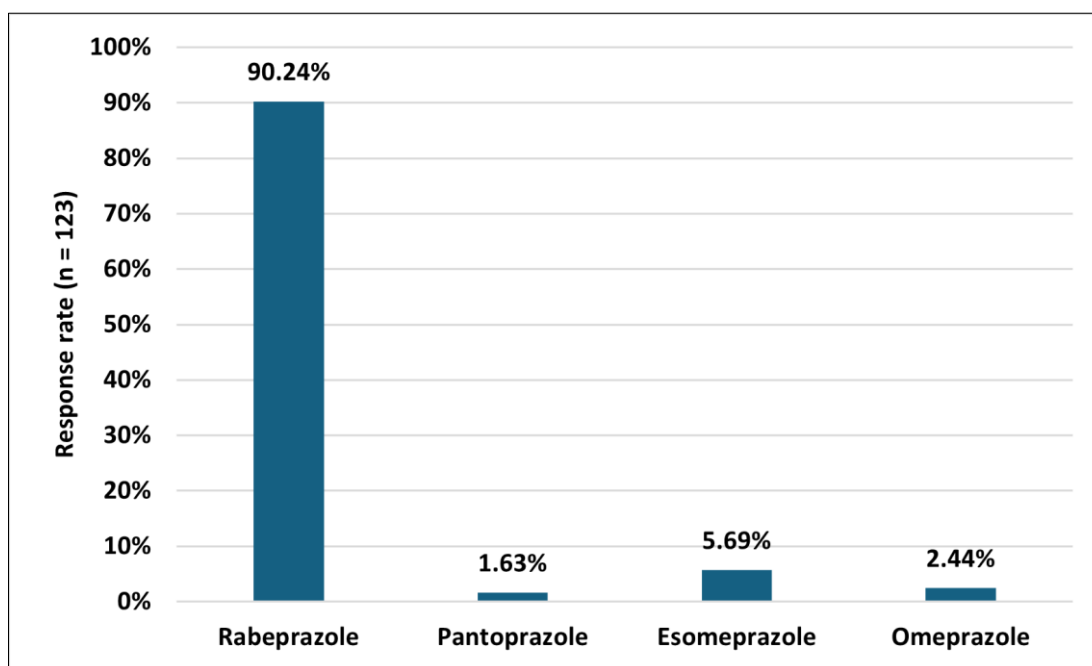


Figure 3: Distribution of response to preferred PPIs for long-lasting nighttime heartburn relief in GERD

Most (88.62%) of the participants indicated that pellets/capsules are the preferred dosage forms for PPIs. According to 76% of the participants, the difference between rabeprazole 20 mg and omeprazole or lansoprazole is that rabeprazole does not increase somatostatin levels, maintains baseline motilin levels, and does not cause a delay in gastric emptying. Majority (79.67%) of the participants reported that rabeprazole exhibits a quicker onset of action, maintains intragastric

pH >4 for 24 hours post-dose, and reduces nighttime heartburn, demonstrating its superiority over other PPIs (Figure 4).

Approximately 54% stated that 11-20% is the estimated proportion of non-erosive reflux disease (NERD) in the GERD population. Around 37% reported that 8 weeks is the typical duration of rabeprazole treatment for patients with GERD.

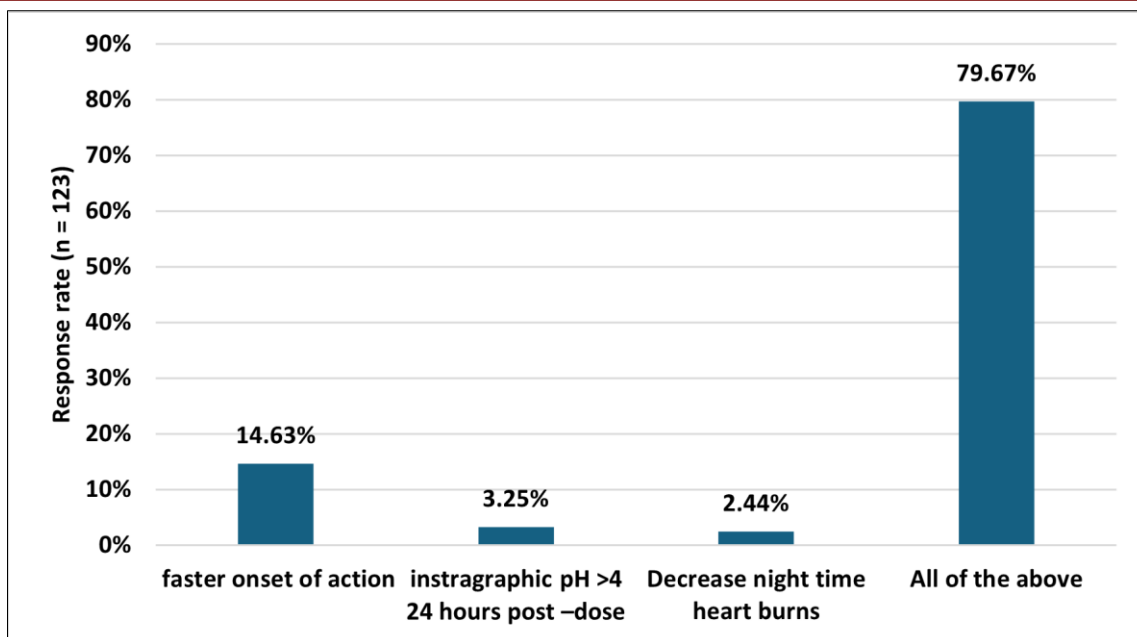


Figure 4: Distribution of response on superiority of rabeprazole compared to other PPIs

DISCUSSION

The survey findings emphasize the critical role of PPIs, particularly rabeprazole, in managing GERD and highlight the importance of dietary management and patient education in improving treatment adherence and outcomes. The majority of respondents highlighted that diet is the predominant predisposing factor in GERD patients. Yeoh *et al.*, suggested that while spicy foods do not induce physiological changes, they can directly irritate the esophageal mucosa, mimicking classic heartburn symptoms, which may prompt individuals sensitive to spice to consider avoiding it. Gomes *et al.*, noted that acidic beverages are commonly reported to worsen GERD, as they can lower the pH of refluxed stomach contents and prolong esophageal clearance time. Phel *et al.*, observed that high-fat diets, particularly those rich in fried or greasy foods, are suspected to aggravate GERD symptoms [10-12].

The majority of the survey respondents indicated that nighttime burning sensations and disrupted sleep are widely recognized as ‘alarm symptoms’ suggesting potential serious complications associated with GERD. Peter Kahrilas highlighted that heartburn is the predominant symptom of GERD, with both heartburn and acid regurgitation frequently reported. Vela *et al.*, reported that GERD increases the likelihood of poor sleep quality. Fujiwara *et al.*, underscored that nighttime reflux during sleep significantly affects various conditions associated with GERD. Clinical evidence strongly supports a link between GERD and sleep disturbances, encompassing shortened sleep duration, difficulty falling asleep, sleep interruptions, diminished sleep quality, and early morning awakenings [13-15].

Most of the respondents reported that PPIs are considered as the first line of treatment for GERD. Theo

Scholten stated that PPIs are widely recognized as the most effective therapy for both initial treatment and long-term management of GERD. Helgadottir and Bjornsson reported that PPIs are recommended as a first-line treatment for GERD and other acid related disorders [16]. Otake *et al.*, stated that PPIs are widely prescribed as first-line therapy for the treatment of acid-related diseases, such as peptic ulcers and GERD, and for the eradication of *Helicobacter pylori* [17].

Half of the respondents indicated that domperidone is the preferred prokinetic agent in combination with PPIs for treating FD and gastroparesis. Zamani *et al.*, stated that the combination of domperidone and a PPI is generally safe and effective in treating GERD compared to PPI alone. Yang *et al.*, stated that metoclopramide, trimebutine, mosapride, and domperidone demonstrate superior efficacy in treating FD compared to itopride or acotiamide [18, 19].

Many respondents noted that the characteristics of an empiric PPI trial in GERD treatment include its simplicity and cost-effectiveness, making it the primary approach for initial GERD diagnosis and providing information on whether further investigation is necessary. The use of an empiric PPI trial is widely accepted among clinicians for its ease of implementation and economic benefits. According to Fass, a short course of high-dose PPI is an effective alternative as an empirical trial. This method acts as a straightforward diagnostic test that is both accurate and cost-effective, especially for patients experiencing symptoms indicative of GERD or noncardiac chest pain [20]. Vardar *et al.*, highlighted that compared to other diagnostic approaches, an empiric trial of PPIs for GERD treatment is non-invasive, straightforward to administer, and cost-effective for diagnosing GERD [21].

Nearly half of the participants indicated that endoscopy is the preferred diagnostic approach for GERD in clinical practice. According to Badillo *et al.*, upper endoscopy is the primary method used to assess the esophageal mucosa in GERD patients, allowing for biopsies of suspicious lesions [22]. Katz *et al.*, also noted that upper endoscopy is the most commonly utilized objective test for evaluating the esophageal mucosa. For GERD patients presenting with alarming symptoms like dysphagia, weight loss, bleeding, vomiting, or anemia, endoscopy should be promptly conducted, as recommended [23]. Similarly, Shaheen *et al.*, corroborated that upper endoscopy is frequently employed for diagnosing and managing GERD [24].

The majority of the respondents stated that rabeprazole is the preferred PPI for long-lasting nighttime heartburn relief in GERD. Lawate *et al.*, highlighted that rabeprazole is effective in providing rapid and sustained relief for both daytime and nocturnal symptoms of GERD in patients with moderate to severe conditions. The study also found rabeprazole is more effective than pantoprazole and esomeprazole in alleviating the severity of various GERD symptoms [25]. Wang *et al.*, reported that oral rabeprazole on day 1 exhibited superior inhibition of acid output for a longer duration compared to pantoprazole. Additionally, rabeprazole maintained a significantly higher intragastric pH than pantoprazole during the initial 8.3 hours [26].

According to the survey findings, rabeprazole exhibits a quicker onset of action, maintains intragastric pH >4 for 24 hours post-dose, and reduces nighttime heartburn, demonstrating its superiority over other PPIs. Vardanyan *et al.*, noted that rabeprazole demonstrates a slightly quicker onset of acid inhibition compared to other PPIs [27]. Williams *et al.*, reported that rabeprazole 20 mg administered once daily exhibits a notably quicker onset of antisecretory activity compared to omeprazole 20 mg once daily. They found that after 8 days, the differences in intragastric pH >3 and >4 holding times persisted between the two medications, although there was no significant distinction in 24-hour acidity levels [28]. Miner *et al.*, observed that both doses (10 mg and 20 mg) of rabeprazole provided rapid and effective relief from heartburn, showing significant improvements as early as day 1 of treatment. They also noted improvements in other GERD-related symptoms such as regurgitation, belching, bloating, early satiety, and nausea. Both doses were well tolerated with no significant difference between them, but they demonstrated significant superiority over placebo in terms of time to achieve the first 24-hour heartburn-free interval (2.5 and 4.5 days for 10 mg and 20 mg of rabeprazole, respectively, compared to 21.5 days for placebo), as well as achieving day-time or night-time heartburn-free intervals (1.5–3 days for rabeprazole groups vs 12.5–15 days for placebo), and the percentage of time free from heartburn and antacid use [29].

The major strengths of the survey are its extensive sample size, input from experienced GERD specialists, and comprehensive evaluation of the effectiveness of rabeprazole alone and in combination with domperidone. The results may be biased due to the reliance on expert opinion, and diverse perspectives among clinicians could influence the outcomes. Additionally, the survey may not fully account for emerging evidence or evolving trends in GERD management. It is important to recognize these limitations when interpreting the results, highlighting the necessity for additional research to validate the survey outcomes. Further studies could explore the long-term impacts of PPI therapy, strategies for enhancing patient education, and the effectiveness of different prokinetic agents in combination with PPIs.

CONCLUSION

Based on the survey, PPIs are pivotal for both initial treatment and ongoing management of GERD. Diet is a significant predisposing factor, with nighttime symptoms identified as crucial indicators of potential complications. PPIs are unanimously considered first-line therapy, with domperidone preferred for adjunctive use in FD and gastroparesis. Rabeprazole emerged as the preferred choice for nighttime heartburn relief due to its rapid onset and sustained efficacy.

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DECLARATIONS

- **Funding:** No funding sources
- **Conflict of Interest:** None declared
- **Ethical Approval:** This study was approved by the Independent Ethics Committee.

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