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Expert Opinion on the Prescription Practice of Proton Pump Inhibitor for the Treatment of Gastroesophageal Reflux Disease

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Authors' contributions

This work was carried out in collaboration between both authors. Authors MS and KKM contributed equally in managing literature search, designing the study, performed the statistical analysis, wrote the protocol, and the first draft of the manuscript. Both of them read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Objective: To identify and evaluate the ideal therapeutic option for the management of gastroesophageal reflux disease (GERD) and associated nighttime heartburn in Indian settings with a special focus on rabeprazole prescription practice.
Methods: The cross-sectional, multiple-response questionnaire-based study was conducted among physicians specialized in the management of GERD. The questionnaire-based survey covered various aspects of GERD management, with a particular focus on the prescription preferences of rabeprazole.
Results: The survey collected responses from 192 experts, assessing their preference for proton pump inhibitors (PPIs) with 24-hour action. Approximately 91% of respondents favored rabeprazole over omeprazole and pantoprazole. Furthermore, approximately 53% of experts reported a higher

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incidence of GERD in subjects aged 40-55 years compared to other age groups. Obesity emerged as the predominant comorbid condition among patients experiencing nighttime heartburn associated with GERD. Rabeprazole was the preferred choice for managing nighttime heartburn with GERD symptoms, as indicated by 95% of experts. An overwhelming 97% and 90% of respondents preferred rabeprazole, acknowledging its rapid onset of action and suitability for long-term administration in the context of nighttime heartburn among GERD patients. Notably, 83% of the respondents preferred using domperidone as the prokinetic agent, particularly in conjunction with rabeprazole for the management of functional dyspepsia and gastroparesis.

Conclusion: Among other PPIs, rabeprazole was the preferred choice among experts for GERD management and nighttime heartburn relief, emphasizing its effectiveness in improving the quality of life for GERD patients. Also, it was also noted that domperidone was the preferred prokinetic agent for clinical use in combination with rabeprazole for the management of functional dyspepsia and gastroparesis.

Keywords: Gastroesophageal reflux disease; rabeprazole; domperidone; dyspepsia; heartburn.

1. INTRODUCTION

Gastroesophageal reflux disease (GERD) adversely affects patients' quality of life by causing frequent discomfort, disturbed sleep, and impairing daily activities [1]. Due to its association with elevated risk of esophageal cancer, Barrett's esophagus also imposes a considerable burden on affected subjects [2]. The prevalence of GERD in India ranges from 7.6% to 30% [3]. The development of histamine-2 receptor antagonists (H2RAs) represented a significant advancement in the treatment of peptic ulcer disease with a lower risk of adverse effects. Subsequent development of proton pump inhibitors (PPIs) has revolutionized the treatment of GERD, especially in cases where H2RAs have proven ineffective [3,4].

The emergence of generic PPIs in the market has led to an increased rate of PPI prescriptions for ongoing conditions, unapproved uses, and as therapeutic replacements [5]. Additionally, the over-the-counter availability of PPIs has further expanded their widespread use [6,7]. PPIs have been shown in certain studies to be both safer and more effective than H2RAs at repairing esophageal lesions, reducing heartburn symptoms, and preventing symptomatic and endoscopic relapse. Omeprazole and rabeprazole are both potent inhibitors of the H+/K+-ATPase, which regulates the last stage of stomach acid output [8]. The second-generation PPI, rabeprazole, has shown superiority over the first-generation PPI, omeprazole, with 2-10 times more effective anti-secretory action. This leads to a faster pharmacodynamic response and quicker symptom relief [9]. However, a meta-analysis by Caro et al. demonstrated that rabeprazole and omeprazole have comparable effectiveness in reducing heartburn, promoting healing rates, and preventing recurrence [10].

Omeprazole, 40 mg at dinnertime, has been found to be more effective in preventing nocturnal stomach acid breakthrough than the same dose administered in the morning [11]. Once daily dose of 20 mg of rabeprazole has been shown to be well tolerated and effective in preventing the relapse of erosive or ulcerative GERD. Rabeprazole was another PPI that has been shown to be as effective as omeprazole in reducing esophageal acid exposure when administered in the morning [12]. Additionally, rabeprazole and pantoprazole were discovered to be more effective at reducing acid regurgitation than lansoprazole (92.2% and 90.1% success rates; $P < 0.05$). Similarly, pantoprazole and rabeprazole beat lansoprazole (with a success rate of 82.6%; $P < 0.05$) in terms of reducing epigastric pain, with success rates of 95.2% and 100%, respectively [13]. The relationship between these variances and various therapeutic outcomes, such as healing rates and/or symptom reduction, is unclear, especially in the elderly.

In particular, rabeprazole binds covalently and inactivates the stomach parietal cell proton pump (H+/K+-ATPase), raising the pH of the stomach and preventing the production of gastric acid [14]. With a focus on oral rabeprazole as a treatment for GERD maintenance therapy in Indian settings, the current survey-based study aimed to seek clinicians' opinions regarding the use of PPIs in routine clinical practice.

2. METHODOLOGY

We carried out a cross sectional, multiple-response questionnaire-based study involving physicians with expertise in managing GERD patients in the major Indian cities from June 2022 to December 2022.

2.1 Questionnaire

The questionnaire booklet titled ERNE (Efficacy of Rabeprazole sodium and Domperidone in managing Nighttime heartburn in clinical practicE) study was sent to the physicians who were interested to participate. The ERNE study questionnaire involved various questions regarding the ideal therapeutic option for the management of GERD and associated nighttime heartburn with a special focus on the prescription practice of rabeprazole. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

2.2 Participants

Convenience sampling method was adopted where an invitation was sent to leading gastroenterologists in managing GERD in the month of March 2022 for participation in this Indian survey. 192 doctors from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. Participants were asked to complete the questionnaire without discussing with their peers. A written informed consent was obtained from each gastroenterologists prior initiation of the study.

2.3 Statistical Methods

The data were analyzed using descriptive statistics. Frequency and percentage distribution were used to represent the distribution of each variable. Bar charts were made using Excel 2013 (16.0.13901.20400).

3. RESULTS

The survey collected responses from 192 experts regarding the preference for PPIs with 24-hour action. Approximately 91% of the respondents indicated a preference for rabeprazole over omeprazole and pantoprazole (Table 1). About 53% of the experts reported an increased frequency of GERD in subjects aged between 40-55 years suffer compared to other age groups. Obesity was regarded as the common comorbid condition observed in patients with nighttime heartburn associated with GERD.

Table 1. Response on the preference of PPIs with 24-hour action

Preference of PPIs with 24-hour action	Response rate (n = 192)
Omeprazole	4 (2.08%)
Rabeprazole	175 (91.14%)
Pantoprazole	11 (5.73%)
Others	2 (1.04%)

Rabeprazole was also preferred for nighttime heartburn with GERD symptoms by 95% of experts. However, a lower percentage of participants preferred other PPIs such as omeprazole, pantoprazole, rabeprazole and domperidone combination, esomeprazole, and others (Fig. 1). About 97% and 90% of the respondents preferred rabeprazole, a PPI known for its rapid onset of action and long-term administration in nighttime heartburn among patients with GERD.

About 37% and 34% of respondents reported that they would prescribe a rabeprazole + domperidone combination for 4 weeks and 2 weeks for treating nighttime heartburn with GERD respectively (Table 2). For refractory GERD patients, 55% of the respondents preferred PPI + prokinetic agent for the treatment. The combination of H2 blockers with prokinetic agents, PPI alone, or the combination of two PPI drugs were the other preferred choices of treatment by a lower percentage of participants for refractory GERD (Fig. 2). Around 83% of the respondents preferred domperidone as the prokinetic agent along with rabeprazole for the management of functional dyspepsia and gastroparesis (Fig. 3).

4. DISCUSSION

The current study findings corroborated the effectiveness of rabeprazole in reducing GERD symptoms over omeprazole and pantoprazole. Consistent with previous clinical research, the current study participants also emphasized the negative effect of nighttime heartburn on the quality of life of GERD patients. According to a case-control study conducted in Sweden, individuals with nighttime reflux symptoms were significantly more likely to develop GERD-related complications, including esophageal cancer than healthy controls [15]. A cross-sectional study by

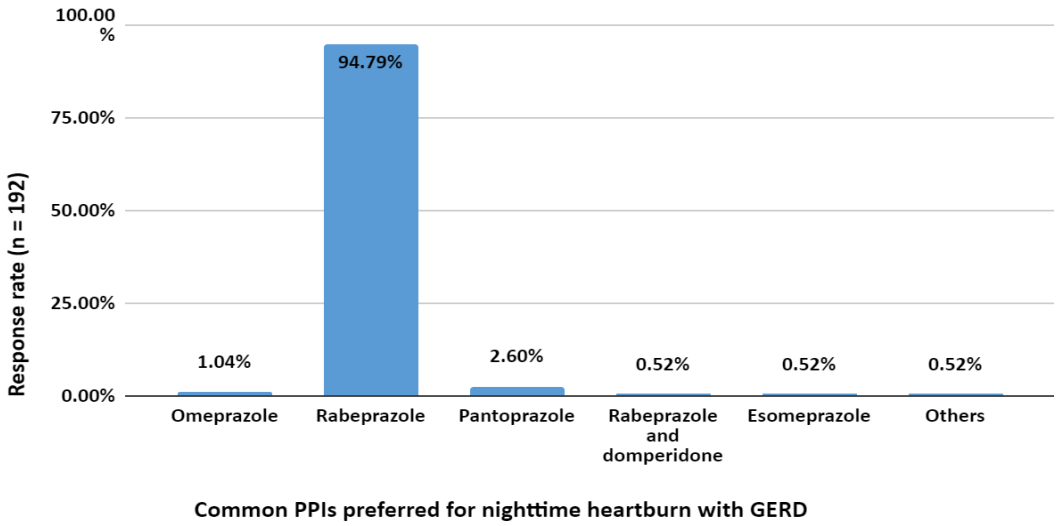

Fig. 1. Response on the commonly preferred PPIs for nighttime heartburn associated with GERD in clinical practice

Table 2. Response on the optimal duration of rabeprazole-domperidone combination therapy for managing nighttime heartburn with GERD

Response on the optimal duration of rabeprazole-domperidone combination therapy for managing nighttime heartburn with GERD	Response rate (n = 192)
1 week	13 (6.77%)
2 weeks	65 (33.85%)
4 weeks	71 (36.98%)
>4 weeks	42 (21.87%)
Others	1 (0.52%)

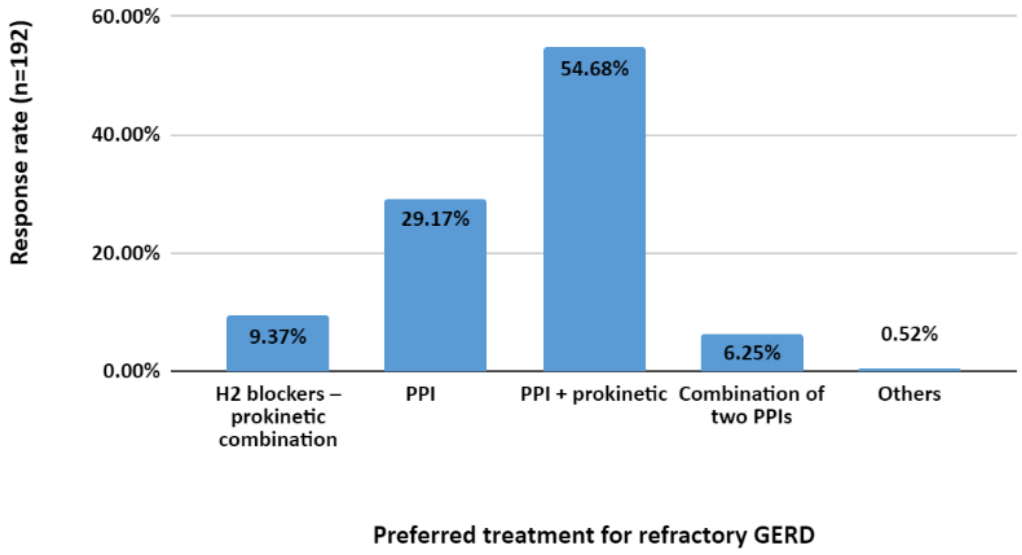

Fig. 2. Response to the preferred treatment for refractory GERD

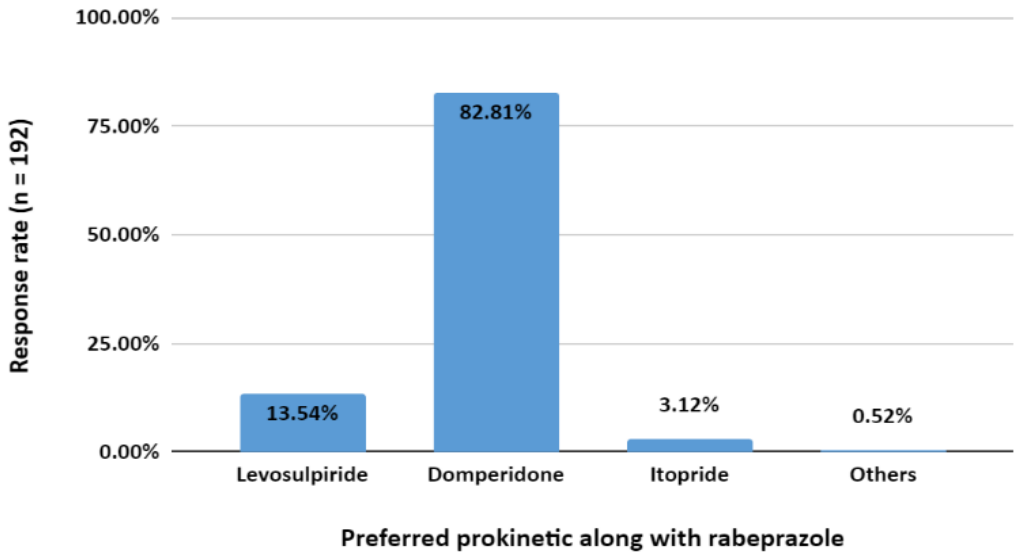

Fig. 3. Response on the preference of prokinetic along with rabeprazole in patients with functional dyspepsia and gastroparesis

Muacevic and Adler also concluded that increasing age and a high body mass index have a detrimental impact on the quality of life in individuals with GERD [16].

The current study has also noted obesity as the common comorbid condition associated with GERD. It was important to consider the co-morbid conditions in GERD patients to tailor the treatment approach accordingly. A review by Thalheimer and Bueter reported that GERD occurrence was closely linked to excess body weight, thereby emphasizing the physiological significance of the abdominothoracic pressure gradient. The researchers also underscored the advantages of weight reduction in managing GERD in obese individuals [17].

Almost 97% and 90% of participants preferred rabeprazole, pointing out its rapid onset of action and suitability for long-term administration in terms of nighttime heartburn among GERD patients. Based on the findings of a double-blinded cross-over research study, it was advisable to administer a PPI before dinner as an appropriate dosing schedule for individuals with GERD, especially those experiencing nocturnal symptoms [18]. Similarly, an open-label, multicenter study enrolled 2579 patients who received an 8-week treatment of 20 mg rabeprazole once daily demonstrated that rabeprazole had a significant and rapid impact on reducing the severity of daytime and nighttime heartburn, as well as improving symptoms of regurgitation and belching [19].

In the present study, a sizeable proportion of participants reported that they would prescribe a rabeprazole-domperidone combination for 4 weeks and 2 weeks for treating nighttime heartburn with GERD. Majority of the respondents preferred domperidone prokinetic agent along with rabeprazole for the management of functional dyspepsia and gastroparesis. A prospective, non-comparative study conducted among Indian subjects by Shahani et al. concluded that rabeprazole and domperidone combination yielded substantial symptomatic improvement in individuals with GERD. The improvement became apparent as early as the first follow-up visit, which occurred within two weeks of starting treatment. Furthermore, extending the treatment for an additional four weeks resulted in more significant clinical benefits [20].

A larger sample size involving 192 experts specialized in GERD management served as a comprehensive dataset for evaluation. The survey's focus on rabeprazole allowed for an in-depth exploration of its prescription patterns, potentially assisting in making well-informed decisions to achieve optimal treatment outcomes. However, it was important to acknowledge that the current study has certain limitations. Considering that the study findings

rely on expert opinions, it was essential to recognize that inherent biases or personal perspectives may influence the study's interpretations. It was crucial to consider these factors when interpreting and implementing the survey's outcomes within clinical practice.

5. CONCLUSION

It was found that majority of experts preferred rabeprazole among the PPIs for managing GERD and alleviating nighttime heartburn which emphasized its remarkable effectiveness in enhancing the quality of life in GERD patients. Furthermore, the survey revealed that domperidone was the preferred prokinetic agent for clinical use, particularly when used in combination with rabeprazole, for the management of functional dyspepsia and gastroparesis.

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CONSENT

A written informed consent was obtained from each gastroenterologists prior initiation of the study.

ETHICAL APPROVAL

The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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