Original Research Article

Expert opinion on the prescription practice of rabeprazole and other common proton pump inhibitors for patients with gastroesophageal reflux disease

ABSTRACT

Objective: The current survey-based study aims to provide further insights on expert opinion regarding the commonly prescribed PPIs in clinical practice, with a specific focus on the use of oral rabeprazole 20 mg as a treatment for gastroesophageal reflux disease (GERD) maintenance therapy in Indian settings.

Methodology: The questionnaire-based survey involving 25 questions collected perspectives of experts across various regions of India regarding the prescription practice of rabeprazole 20 mg and other proton-pump inhibitors (PPIs) for treating GERD symptoms.

Results: Out of 512 study participants, 44% reported obesity as the common comorbid condition observed in GERD patients, while 28% noted co-morbid diabetes mellitus. According to 68% of the respondents, rabeprazole demonstrated superiority over other PPIs in terms of quicker onset of action, maintaining intragastric pH >4 over 24 hours' post-dose, and reduced nighttime heartburn. For GERD patients with functional dyspepsia and gastroparesis, 52% of responders favored the addition of domperidone as a prokinetic drug to the PPI treatment. Moreover, the majority of participants (61.91%) observed that rabeprazole 20 mg did not cause a delay in stomach emptying, nor did it raise somatostatin levels or alter baseline motilin levels in GERD patients. These findings underscore the effectiveness of rabeprazole 20 mg in comparison to omeprazole and lansoprazole.

Conclusion: Experts recommended rabeprazole 20 mg as the preferred treatment option over omeprazole and lansoprazole for GERD patients with coexisting obesity and diabetes mellitus conditions. Additionally, over half of the respondents reported using a combination of domperidone and other PPIs for GERD patients with functional dyspepsia and gastroparesis.

Keywords: Rabeprazole, Proton pump inhibitors, Gastroesophageal reflux disease, Heartburn, Omeprazole, Lansoprazole

1. INTRODUCTION

Gastroesophageal reflux disease (GERD) significantly lowers patients' quality of life leading to frequent discomfort, disrupted sleep, and difficulty in performing day-to-day activities [1].Additionally, Barrett's esophagus imposes a significant disease burden on affected individuals due to its association with the risk of esophageal adenocarcinoma [2].In India, the prevalence of GERD varies from 7.6% to 30%; it is typically 10% or more in cohort studies and higher in population studies [3].The advent of histamine-2 receptor antagonists (H2RAs) marked a significant breakthrough in the treatment of peptic ulcer disease with minimal side

effects. Subsequently, the introduction of proton pump inhibitors (PPIs) revolutionized the treatment of GERD, particularly in cases refractory to H2RAs [3,4].

Certain studies have reported PPIs to be safer and more efficient than H2RAs at healing esophageal lesions, alleviating heartburn symptoms, and preventing symptomatic and endoscopic relapse, according to prior clinical trials [5,6]. Both omeprazole and rabeprazole are effective H+/K+-ATPase inhibitors, which control the final stage of gastric acid secretion [7].Rabeprazole, which belongs to the second-generation PPIs, has been shown to outperform omeprazole, the standard PPI, with an antisecretory action that is 2 to 10 times more potent, leading to a rapid pharmacodynamic response and quicker alleviation of symptoms [8].However, in a meta-analysis conducted by Caro et al., rabeprazole and omeprazole showed similar effectiveness in terms of controlling heartburn, healing rates, and recurrence rates [9].Additionally, in comparison to lansoprazole, both rabeprazole, and pantoprazole were found to be more successful in reducing acid regurgitation (92.2% and 90.1% success rates; $P < 0.05$). Similarly, with regard to the reduction of epigastric pain, pantoprazole and rabeprazole (with success rates of 95.2% and 100%) outperformed lansoprazole (with a success rate of 82.6%; $P < 0.05$) [10]. However, it is uncertain if these variations, particularly in the elderly, are connected to various clinical outcomes, such as healing rates and/or symptom reduction.

Rabeprazole especially binds covalently to the stomach parietal cell proton pump (H+/K+-ATPase) and renders it inactive which elevates gastric pH and prevents the generation of gastric acid [11].The current survey-based study aims to gain further insights into the perceptions of clinicians regarding the commonly prescribed PPIs in clinical practice, with a specific focus on the use of oral rabeprazole 20 mg as a treatment for GERD maintenance therapy in Indian settings.

2. MATERIALS AND METHODS

We carried out a cross sectional, multiple-response questionnaire-based study involved clinical professionals skilled in treating GERD patients in the major Indian cities from June 2022 to December 2022.

2.1 Questionnaire

The questionnaire booklet titled GRACE (Gastro Esophageal Reflux Disease: A Comprehensive Evaluation) study was sent to the physicians who were interested to participate. The GRACE study questionnaire 25 questions that focused on the use of PPIs in GERD with a special focus on 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

An invitation was sent to leading gastroenterologists in treatingGERD in the month of March 2022 for participation in this Indian survey. About 512 clinicians from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. Gastroenterologists were asked to complete the questionnaire without discussing with their peers. A written informed consent was obtained from each gastroenterologists before initiation of the study.

2.3 Statistical Methods

The data were analyzed by using descriptive statistics. Percentages were used to represent categorical variables. Frequency and percentage distribution were used to represent the distribution of each variable. Pie and bar charts were made using Excel 2013 (16.0.13901.20400).

3. RESULTS

Out of 512 participants, a majority (44%) reported obesity as the common comorbid condition found in GERD patients, followed by diabetes mellitus (28%) and dyslipidemia (14%) (Fig. 1). Around 68% of the participants reported that rabeprazole is superior to other PPIs in terms of faster onset of action, maintaining intragastric pH >4 over 24 hours' post-dose, and reduced nighttime heartburns (Table 1).

Around 42% of the participants reported that nearly 3-5% of GERD patients present with atypical/extraesophageal reflux symptoms like hoarseness and cough at night. Approximately, 38% of the respondents indicated that 6-10% of GERD patients had atypical/extraesophageal reflux symptoms like hoarseness and cough at night. Around 66% reported that night-time heartburn had a negative impact on the patient's quality of life.

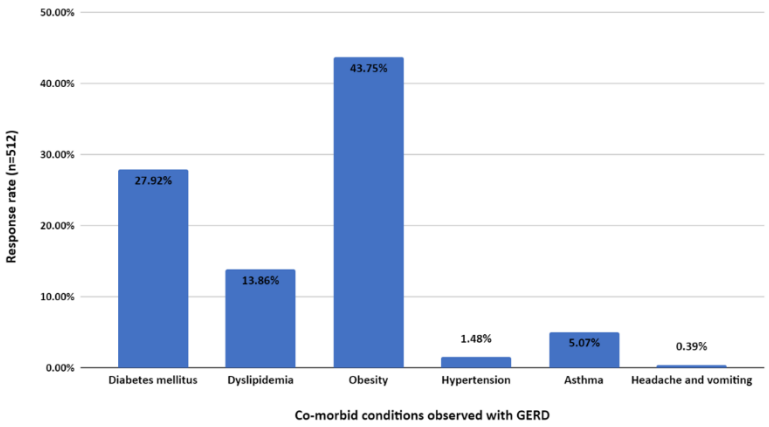

Fig. 1. Response on comorbid conditions observed with GERD

Table 1: Response on the superiority of rabeprazole over other PPIs

Superiority of rabeprazole over other PPIs	Response rate (n=512)
Faster onset of action	89 (17.38%)
Maintains intragastric pH >4 over 24 hours post-dose	62 (12.10%)
Decrease nighttime heartburns	35 (6.83%)
All the above	349 (68.16%)

About 46% of experts reported that 10-20% of GERD patients may have complications leading to sleep disturbance, while 33% observed gastroparesis complications in 20-30% of the subjects. Around 34% of the respondents reported sleep disturbance in 20-30% of GERD patients. Nearly half of the respondents (41.01% and 40.23%) have reported obese conditions in 10-20% and 20-30% of GERD patients. Approximately, 35% and 31% reported that 10-20% and 20-30% of GERD patients had refractory GERD respectively.

The use of domperidone has been preferred by 52% of responders as a prokinetic agent along with PPIs in GERD patients with functional dyspepsia and gastroparesis. Approximately, 43% of the responders preferred the use of PPIs in combination with rabeprazole and domperidone in such patients (Fig. 2).

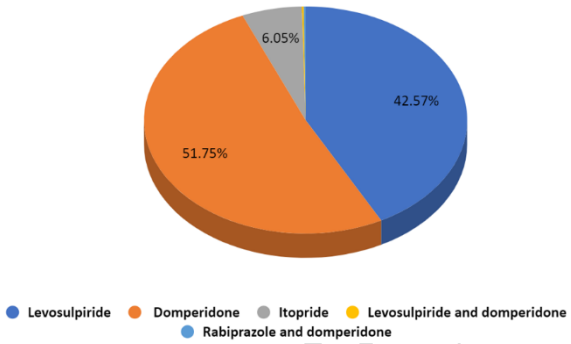

Fig. 2. Response on the preference of prokinetic agent along with PPIs in GERD patients with functional dyspepsia and gastroparesis

A significant proportion of participants (61.91%) reported that rabeprazole 20 mg does not increase somatostatin level, maintains baseline motilin level, and does not cause delayed gastric emptying in GERD patients. However, smaller percentages of respondents (16.40% and 13.67%) indicated that the use of rabeprazole 20 mg helps in maintaining baseline motilin levels and it does not cause gastric emptying. These findings highlight the superiority of rabeprazole 20 mg over omeprazole and lansoprazole (Table 2).

Table 2: Response on the superiority of rabeprazole 20 mg to omeprazole and lansoprazole

Reasons for the superiority of rabeprazole 20 mg to omeprazole and lansoprazole	Response rate (n=512)
Does not increase somatostatin level	42 (8.20%)
Maintains baseline motilin level	84 (16.40%)
Does not cause delayed gastric emptying	70 (13.67%)
All the above	317 (61.91%)

About 38% of individuals suggested that the use of PPIs along with nonsteroidal anti-inflammatory drugs (NSAIDs) would increase the adverse gastrointestinal effects. However, 29% and 21% of the respondents indicated that tricyclic antidepressants and celecoxib

medications may increase the adverse gastrointestinal effects when used with NSAIDs respectively (Fig. 3).

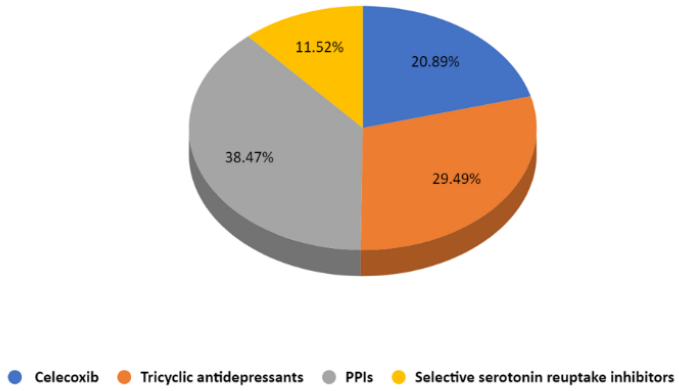

Fig. 3. Response on drugs that increases adverse gastrointestinal effects when used with NSAIDs

4. DISCUSSION

According to the current study findings, rabeprazole is highly effective in relieving GERD symptoms. A significant proportion of participants reported that rabeprazole is superior to other PPIs in terms of quicker onset of action, maintaining intragastric pH >4 over 24 hours' post-dose, and reducing nighttime heartburn. The night-time heartburn was reported to have a negative impact on the GERD patient's quality of life. A case-control study in Sweden showed that patients experiencing reflux symptoms at night have a greatly increased risk of acquiring GERD complications, such as esophageal adenocarcinoma when compared to healthy controls [12]. According to the findings of a double-blinded cross-over study, administering a PPI before dinner maximizes acid control and should be the ideal dose schedule for GERD patients, especially those who experience nocturnal symptoms [13].

It is important to consider the co-morbid conditions in GERD patients to tailor the treatment approach accordingly. GERD patients were reported with atypical/extraesophageal reflux symptoms like hoarseness and cough at night in this current survey as reported by survey participants. These patients were found to be identified with coexisting comorbid conditions such obese and diabetes mellitus. Besides, sleep disturbance, gastroparesis complications, obesity, and refractory GERD were the other comorbid conditions in GERD patients. Moraes-Filho et al. reported a total of 1,664 comorbidities in 586 patients (87.5%), with arterial hypertension (21%) and hypercholesterolemia (9%) being the most prevalent, followed by obesity (9%), type II diabetes mellitus (5%), and depression (4%). These findings highlight the significance of considering and managing comorbidities in GERD patients for comprehensive and effective treatment [14].

In GERD patients with functional dyspepsia and gastroparesis, nearly half of the survey participants favored using domperidone as a prokinetic drug in addition to PPIs. Prokinetics have been used with varying degrees of efficacy in individuals with functional dyspepsia, but because they do not speed up the healing of esophagitis, they are ineffective in treating GERD [15]. To comprehend safety and efficacy profiles, prokinetic and PPI therapeutic regimens have been compared to PPI monotherapy. In a double-blinded, randomized clinical trial conducted by Ndraha et al., the researchers evaluated 60 dyspeptic patients

experiencing heartburn and regurgitation. The trial demonstrated a statistically significant improvement in GERD patients with the high-frequency scale of symptoms for GERD (frequency scale for the symptoms of gastroesophageal reflux disease) scores when treated with a combination of omeprazole and domperidone, compared to those receiving omeprazole monotherapy [16].

Majority of the participants in the current study observed that rabeprazole 20 mg does not affect stomach emptying in GERD patients, nor does it elevate somatostatin levels or alter baseline motilin levels. These findings indicate that rabeprazole 20 mg outperforms omeprazole and lansoprazole. In four randomized cross-over studies, esomeprazole 40 mg demonstrated superior intragastric acid management compared to lansoprazole 30 mg, omeprazole 20 mg, pantoprazole 40 mg, and rabeprazole 20 mg in patients with GERD symptoms [17]. Another randomized clinical trial concluded that rabeprazole 20 mg is non-inferior to esomeprazole 20 mg in treating heartburn and regurgitation symptoms in GERD symptoms [18]. However, a randomized single-blinded study reported that rabeprazole 40 mg has better efficacy when compared to esomeprazole 40 mg in mild-to-moderate GERD patients [19]. These findings underscore a favourable aspect of rabeprazole 20 mg as a treatment option for GERD, as it appears to provide symptom relief without causing additional disruptions in stomach function or hormone levels.

The survey findings shed light on the optimal treatment strategies for managing GERD and its associated comorbidities, emphasizing the importance of individualized therapeutic approaches for better patient outcomes. A larger sample size of 512 experts and the inclusion of specialized opinions from skilled GERD practitioners, and a comprehensive assessment of rabeprazole effectiveness are the major strengths of the study. The study also recognizes the significance of adjusting therapy choices to specific patient features to achieve optimal treatment outcomes. However, the reliance on self-reported data may introduce recall bias, and potential response bias might impact the representativeness of the sample. The non-randomized design limits causality establishments. However, the survey contributes valuable insights into rabeprazole effectiveness but should be considered alongside its limitations for a more comprehensive understanding.

4. CONCLUSION

In conclusion, experts recommend rabeprazole 20 mg as a superior treatment option for GERD patients with coexisting obesity and diabetes mellitus compared to omeprazole and lansoprazole. Additionally, over half of the respondents suggested using domperidone in combination with other PPIs for GERD patients with functional dyspepsia and gastroparesis. However, it is essential to be cautious regarding potential adverse gastrointestinal effects when combining PPIs with NSAIDs in these patients.

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