

Content available at: <https://www.ipinnovative.com/open-access-journals>

International Journal of Recent Innovations in Medicine and Clinical Research

Journal homepage: <https://www.ijrimcr.com/>

## Original Research Article

## Expert opinion on the prescription practice of a combination of rabeprazole and domperidone for managing nighttime heartburn in GERD among Indian patients

Manjula S<sup>1\*</sup>, Krishna Kumar M<sup>1</sup><sup>1</sup>Micro Labs Limited, Bangalore, Karnataka, India

## ARTICLE INFO

## Article history:

Received 20-08-2024

Accepted 18-09-2024

Available online 11-11-2024

## Keywords:

Gastroesophageal reflux disease

Proton pump inhibitors

Prokinetics

Rabeprazole

Domperidone

## ABSTRACT

**Background :** The synergistic effect of Rabeprazole and Domperidone suggested a more comprehensive treatment strategy, targeting both acid suppression and motility enhancement in GERD management in several clinical studies. However, studies regarding their prescription practices of this combination is scarce.

**Aims & Objective:** This study aimed to gather comprehensive insights into various aspects of gastroesophageal reflux disease (GERD) management in Indian settings.

**Materials and Methods :** This cross-sectional study was conducted from June 2023 to December 2023 using a 24-item structured questionnaire distributed via email and online platforms. Clinicians completed the survey independently, with the option to skip questions and provided written informed consent. The questionnaire covered GERD management aspects, including patient demographics, clinical challenges, treatment preferences, efficacy of treatment combinations, patient adherence, use of guidelines, comorbidities, risk factors and patient education methods.

**Results:** According to 39% of clinicians, 31-40 GERD patients per month report nighttime heart burn, while another 39% reported it as 21-30 cases monthly. Majority of the clinicians (95.65%) preferred rabeprazole for its longer action in managing nighttime heartburn in GERD. According to 96% and 89% of the clinicians, respectively, the combination of rabeprazole and domperidone was favored for managing nighttime heartburn and was more effective than other PPI combinations. Nearly 93% stated that this combination provides the fastest relief. The recommendation for taking the combination once a day was made by 67% of clinicians and 59% reported that their patients felt relieved within 1-2 weeks. Helirab D was preferred due to its advanced release profile 2 (ARP2) technology by 50% of clinicians.

**Conclusion:** There was a strong clinical preference for using a combination of rabeprazole and domperidone to manage nighttime heartburn in patients with GERD. This combination seems to have advantages in terms of effectiveness, quick onset of action and relief for patients. The once-daily dosing schedule and formulation technology (ARP2) may be contributing factors to its popularity among clinicians.

This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: [reprint@ipinnovative.com](mailto:reprint@ipinnovative.com)

## 1. Introduction

The global prevalence of gastroesophageal reflux disease (GERD) is estimated to be around 15%. According to the latest Global Burden of Disease Study (GBD), the total burden of GERD has surged by 77.53%, rising from

441.57 million cases in 1990 to 783.95 million in 2019.<sup>1</sup> While overall incidence in Asia was reported to be lower, regional variations exist with India showing a notably higher prevalence. Major population-based studies in India indicate a GERD prevalence of approximately 10%, a figure that was likely increasing due to changing lifestyles and rising obesity rates.<sup>2,3</sup> A meta-analysis by Rai et al. reported a pooled prevalence of 15.6% for GERD in the Indian

\* Corresponding author.

E-mail address: [drmanjulas@gmail.com](mailto:drmanjulas@gmail.com) (Manjula S).

population.<sup>3</sup>

Nocturnal heartburn affects up to 25% of the general population with GERD and was known to cause sleep disruption, further impacting quality of life and psychomotor performance.<sup>4</sup> Moreover, it may elevate the risk of developing conditions such as cardiovascular disease, esophageal adenocarcinoma and obstructive sleep apnea syndrome.<sup>5</sup> The introduction of proton pump inhibitors (PPIs) revolutionized GERD treatment. However, 30% of GERD patients receiving standard PPI doses continued to experience symptoms, highlighting a significant therapeutic gap.<sup>6</sup> Prokinetics, known for enhancing gastrointestinal motility, emerged as an alternative approach. Initially recommended as first-line treatment for functional dyspepsia patients with postprandial distress syndrome, prokinetics gained attention in GERD management.<sup>7</sup> Several studies demonstrated that combining prokinetics with PPIs provides additional benefits in global symptom improvement for GERD patients, compared to PPI monotherapy.<sup>8–11</sup>

Rabeprazole, a second-generation PPI, covalently binds to and inactivates the gastric parietal cell proton pump (H<sup>+</sup>/K<sup>+</sup>-ATPase).<sup>12</sup> This mechanism effectively inhibits gastric acid secretion, making rabeprazole a potent treatment for gastrointestinal ulcers and GERD.<sup>13</sup> Compared to omeprazole, the prototypical PPI, rabeprazole demonstrates 2 to 10 fold greater anti-secretory activity in vitro, enhancing its efficacy in managing GERD symptoms and promoting ulcer healing.<sup>14</sup> Domperidone, a widely recognized antiemetic, serves as a prokinetic agent by blocking dopaminergic receptors, increasing lower esophageal sphincter pressure and stimulating gastric motility. By accelerating gastrointestinal peristalsis, domperidone effectively improves gastrointestinal function.<sup>11,15</sup>

This combination therapy approach addressed the limitations of PPIs alone, offering a potential solution for patients with refractory GERD symptoms. The synergistic effect of PPIs and prokinetics suggested a more comprehensive treatment strategy, targeting both acid suppression and motility enhancement in GERD management in clinical studies. So, this survey aimed to gather insights into GERD management in India, focusing on the prescription practices and effectiveness of combining rabeprazole with domperidone for nighttime heartburn. The survey findings help to understand the perceived efficacy and safety of this combination in managing nocturnal GERD symptoms.

## 2. Materials and Methods

We carried out a cross sectional study among clinicians specialized in GERD management in the major Indian cities from June 2023 to December 2023.

An invitation was sent to leading clinicians in managing GERD in the month of March 2023 for participation in this Indian survey. About 46 gastroenterologists from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. Clinicians had the flexibility to skip questions they chose not to answer. They were instructed to complete the survey independently, without consulting colleagues. All participants provided written informed consent prior to the initiation of the study. The questionnaire booklet titled RARE (Rabeprazole + Domperidone in night time heart burn in GERD) study was sent to the physicians who were interested to participate. The RARE study questionnaire comprised 24 questions focused on gathering various aspects of GERD management, including patient demographics and prevalence, clinical challenges, treatment preferences, efficacy of different treatment combinations, patient adherence, use of clinical guidelines, associated comorbidities, risk factors and patient education methods.

### 2.1. Statistical analysis

Descriptive statistics were used to analyze the data. Percentages were utilized to depict the distribution of categorical variables, displaying both the frequency and corresponding percentages for each variable. Microsoft Excel 2013 (version 16.0.13901.20400) was employed to create graphs and pie charts, visually representing the distribution of these variables.

## 3. Results

A total of 46 clinicians participated in the survey. According to 39% of clinicians, 31-40 cases of GERD patients per month report nighttime heartburn in their clinical practice, while another 39% of clinicians observe 21-30 such cases monthly. Most clinicians (54%) reported that the age group 45-60 years experiences the most complaints of nighttime heartburn in GERD patients. Majority of the clinicians (41.30%) reported that hypertension is the most common co-morbid condition observed in GERD patients who experience nighttime heartburn. Majority of clinicians (43.48%) indicated that an improper diet is the most significant factor increasing the risk of GERD in their clinical practice. Majority of the clinicians (41.30%) preferred individual one-to-one sessions for educating patients with GERD. Majority of clinicians (45.65%) reported that ensuring patient compliance with the regular consumption of medication is the most challenging aspect in managing GERD.

Around 48% of experts preferred using the American College of Gastroenterology (ACG) guideline for GERD care. Approximately 46% reported that a lack of patient education is the primary factor associated with patient non-adherence to medication for GERD. Most clinicians

(65.22%) preferred pellets or capsules as the dosage form for PPIs. According to 47.83% of clinicians, 21-30% of GERD patients require combination therapy for effective management. According to 33% and 30% of clinicians, fixed drug combinations in GERD are advantageous because they improve patient adherence and offer better tolerability. More than half of clinicians (52.17%) recommended medication for nighttime heartburn at night. A significant proportion of clinicians (63.04%) decided the PPI to be prescribed for nighttime heartburn based primarily on their clinical experience. Majority of the clinicians (67.39%) rated the technologically superior PPI with acid-resistant pellet technology (ARP2) as excellent for treating nighttime heartburn in GERD.

Most of the respondents (95.65%) preferred rabeprazole for its longer action in managing nighttime heartburn in GERD (Table 1). A significant number of clinicians (95.65%) preferred prescribing the combination of rabeprazole and domperidone for managing nighttime heartburn in GERD (Table 2). Majority of the clinicians (89.13%) stated rabeprazole + domperidone is more effective in treating nighttime heartburn with GERD compared to other PPI combinations (Figure 1). Majority of the experts (93.48%) preferred that the combination of rabeprazole and domperidone provides the fastest relief for nighttime heartburn in GERD (Figure 2). Approximately 54% reported that <5% of their patients had switched from rabeprazole + domperidone to another PPI due to lack of efficacy or adverse effects.

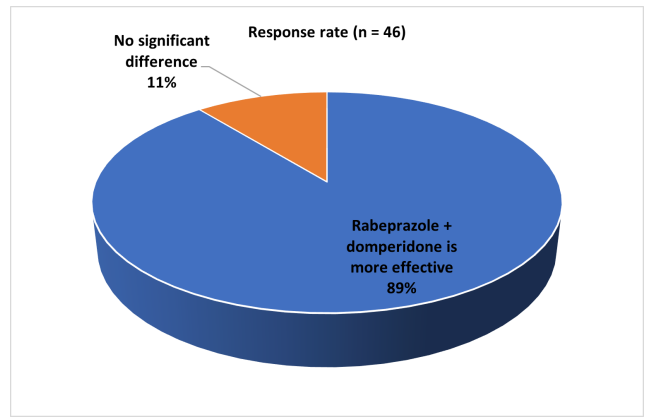
**Table 1:** Distribution of response to preferred proton pump inhibitor for longer action in nighttime heartburn in GERD

Proton pump inhibitor	Response rate (n = 46)
Rabeprazole	44 (95.65%)
Pantoprazole	1 (2.17%)
Esomeprazole	1 (2.17%)
Omeprazole	0 (0%)

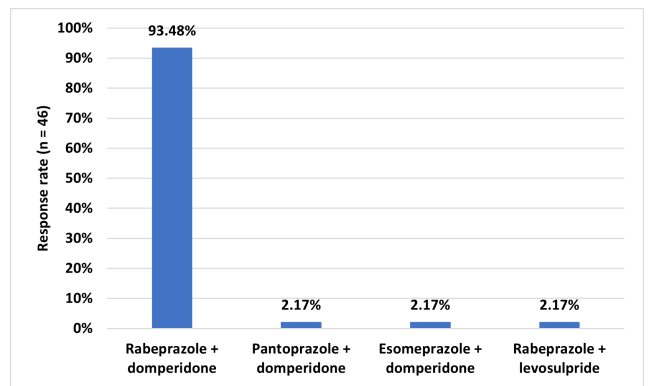
**Table 2:** Distribution of response to typical prescription for nighttime heartburn with GERD

Drug combination	Response rate (n = 46)
Rabeprazole + domperidone	44 (95.65%)
Pantoprazole + domperidone	1 (2.17%)
Esomeprazole + domperidone	1 (2.17%)
Omeprazole + domperidone	0 (0%)

The majority of the clinicians (41.30%) reported that 40-60% of their patient’s experience relief from nighttime heartburn in GERD after using the rabeprazole plus domperidone combination. Additionally, another 41% of clinicians observed that 60-80% of patients experienced relief with this treatment (Table 3). Most clinicians (67.39%) recommended that patients with nighttime heartburn in GERD receive rabeprazole plus domperidone



**Figure 1:** Distribution of response to efficacy comparison of rabeprazole + domperidone with other PPI combinations in treating nighttime heartburn in GERD

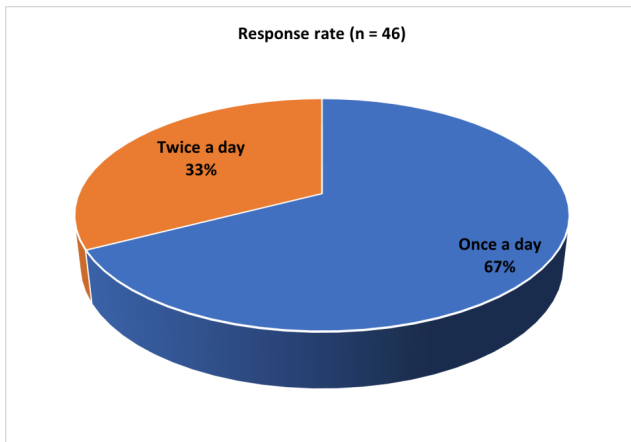


**Figure 2:** Distribution of response to drug combinations providing the fastest relief for nighttime heartburn in GERD

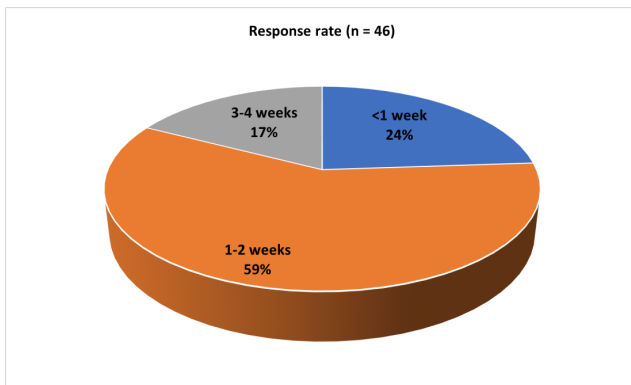
once a day (Figure 3). Around 59% of the experts reported that their patients felt relieved from nighttime heartburn in GERD within 1-2 weeks after starting the rabeprazole plus domperidone regimen (Figure 4). Approximately half of the respondents (50%) indicated that they were most likely to prescribe Helirab D to their patients due to the advantages of ARP2 Technology (Table 4). Most clinicians (60.87%) reported that the typical prescribed duration of treatment with rabeprazole plus domperidone for patients with nighttime heartburn in GERD is 4 weeks.

**Table 3:** Distribution of response to proportion of patients who experienced relief from nighttime heartburn in GERD with rabeprazole + domperidone

Proportion of patients	Response rate (n = 46)
20-40%	2 (4.35%)
40-60%	19 (41.3%)
60-80%	19 (41.3%)
80-100%	6 (13.04%)



**Figure 3:** Distribution of response to recommended frequency of rabeprazole + domperidone for nighttime heartburn with GERD



**Figure 4:** Distribution of response to time to relief from nighttime heartburn in GERD with rabeprazole + domperidone

**Table 4:** Distribution of response to the likelihood of prescribing Helirab D with ARP2 technology

Likelihood (1 = least likely, 5 = most likely)	(n = 46)
1	2 (4.35%)
2	0 (0%)
3	5 (10.87%)
4	16 (34.78%)
5	23 (50%)

#### 4. Discussion

The current study provides a framework for understanding the clinician’s perspectives on GERD management, particularly focusing on night-time heartburn and may offer valuable insights for improving patient care and treatment strategies. The survey results indicate a strong preference among clinicians for rabeprazole, particularly in combination with domperidone, for managing nighttime heartburn in GERD. This preference is likely due to rabeprazole’s longer duration of action and the synergistic

effect when combined with domperidone. A systematic review and meta-analysis by Jung et al., which included 16 randomized controlled trials (RCTs) with a total of 1,446 participants, reported that the combination of prokinetics with PPI treatment was more effective than PPI alone in patients with GERD.<sup>16</sup> The synergistic action of rabeprazole and domperidone addresses both acid secretion and gastrointestinal motility, making this combination particularly effective for patients with GERD, especially those experiencing nighttime heartburn.

Majority of the current survey clinicians preferred rabeprazole in managing nighttime heartburn in GERD, which aligns with previous studies demonstrating similar effects. The POWER GERD Study by Lawate et al. demonstrated that rabeprazole effectively provided rapid and sustained relief for both daytime and nighttime GERD symptoms in patients with moderate to severe GERD.<sup>17</sup> Several other clinical trial studies also reported the effectiveness of rabeprazole in the reduction of nighttime heartburn in GERD patients.<sup>18–20</sup> The combination of rabeprazole with domperidone, a prokinetic agent, appears to enhance the therapeutic effect, as supported by most of the clinicians reporting greater efficacy compared to other PPI combinations. A systematic review and meta-analysis of RCTs by Zamani et al., evaluated 11 studies with a total of 841 participants, reported that the combination of domperidone with a PPI was generally safe and more effective in treating GERD compared to PPI alone.<sup>11</sup>

With a significant number of clinicians noting the fastest relief from the rabeprazole-domperidone combination, this represents a notable clinical advantage. This quick response may contribute to improved patient compliance and satisfaction. The majority of clinicians observed relief in 40-80% of patients within 1-2 weeks of treatment initiation, suggesting a high rate of clinical success. The once-daily dosing regimen recommended by most clinicians aligns with convenience, potentially enhancing adherence. Additionally, the preference for Helirab D (a combination of rabeprazole and domperidone) by 50% of clinicians due to its ARP2 technology suggests that formulation advancements play a role in prescription decisions. This technology may offer benefits in terms of drug delivery or absorption, though further research is needed to confirm its clinical significance.

An open, prospective study conducted among Indian subjects by Shahani et al. assessed the efficacy and tolerability of rabeprazole and domperidone combination in treating GERD among 50 patients. Daily administration of the combination for up to 4 weeks resulted in significant symptom improvement, with noticeable effects within 2 weeks and additional gains over the full period. The treatment was well tolerated, with 94% of patients receiving excellent or good relief and 86% rating it as good or excellent. The study concluded that rabeprazole and

domperidone combination not only effectively alleviated GERD symptoms but also improved patients' quality of life.<sup>21</sup> Another open-label, multicenter study that enrolled 2,579 patients showed that an 8-week treatment with 20 mg of rabeprazole once daily significantly and rapidly reduced the severity of both daytime and nighttime heartburn while also improving symptoms of regurgitation and belching.<sup>18</sup>

This survey provides valuable insights into clinicians' preferences and experiences with rabeprazole and domperidone combination therapy for nighttime heartburn in GERD. It highlights the perceived efficacy and convenience of this treatment. The high rate of clinical preference and reported patient relief suggests that this combination may offer a promising treatment option for managing nighttime GERD symptoms. A major strength of the survey is the use of a meticulously designed and validated questionnaire for collecting expert data. However, the reliance on clinician-reported data rather than direct patient outcomes or randomized controlled trials limits the robustness of these findings. The smaller sample size of 60 clinicians may not represent the broader medical community and regional variations in practice patterns may exist. The lack of a specified sample size, potential selection bias and absence of comparative data with other treatments further constrain the generalizability of the results. Additionally, the survey does not address long-term efficacy, safety profiles, or patient-reported outcomes, which are crucial for a comprehensive evaluation of any treatment regimen. While these findings provide a useful starting point for understanding real-world clinical preferences, they should be interpreted cautiously and validated through more rigorous, patient-centered research methodologies.

## 5. Conclusion

The survey results demonstrated a strong clinical preference for the combination of rabeprazole and domperidone in managing nighttime heartburn in GERD. This combination appears to offer advantages in terms of efficacy, speed of onset and patient relief. The once-daily dosing regimen and formulation technology (ARP2) may contribute to its favored status among clinicians.

## 6. Ethical Approval

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

## 7. Source of Funding

None.

## 8. Conflict of Interest

None.

## 9. Acknowledgement

We would like to thank all the gastroenterologists who were participated in this study.


## References

- Zhang D, Liu S, Li Z, Wang R. Global, regional and national burden of gastroesophageal reflux disease, 1990-2019: update from the GBD 2019 study. *Ann Med.* 2022;54(1):1372–84.
- Eusebi LH, Ratnakumaran R, Yuan Y, Dodaran MS, Bazzoli F, Ford AC. Global prevalence of and risk factors for gastro-oesophageal reflux symptoms: A meta-analysis. *Gut.* 2018;67:430–40.
- Rai S, Kulkarni A, Ghoshal UC. Prevalence and risk factors for gastroesophageal reflux disease in the Indian population: A meta-analysis and meta-regression study. *Indian J Gastroenterol.* 2021;40(2):209–19.
- Johnson DA, Parikh-Das AM, Atillasoy E, Davtyan H, Shur L, Blevins-Primeau A, et al. Sleep disruption due to nocturnal heartburn: a review of the evidence and clinical implications. *Explor Med.* 2023;4:1014–25.
- Choi Y, Shin CM. Nighttime Acid Reflux in Gastroesophageal Reflux Disease - Is It a Problem That Can Be Solved? *J Neurogastroenterol Motil.* 2023;29(1):1–2.
- Fass R, Shapiro M, Dekel R, Sewell J. Systematic review: proton-pump inhibitor failure in gastro-oesophageal reflux disease—where next? *Aliment Pharmacol Ther.* 2005;22(2):79–94.
- Stanghellini V, Chan FKL, Hasler WL, Malagelada JR, Suzuki H, Tack J, et al. Gastrointestinal Disorders. *Gastroenterology.* 2016;150(6):1380–92.
- Miwa H, Inoue K, Ashida K, Kogawa T, Nagahara A, Yoshida S, et al. Randomised clinical trial: efficacy of the addition of a prokinetic, mosapride citrate, to omeprazole in the treatment of patients with non-erosive reflux disease - a double-blind, placebo-controlled study. *Aliment Pharmacol Ther.* 2011;33(3):323–32.
- Miyamoto M, Manabe N, Haruma K. Efficacy of the addition of prokinetics for proton pump inhibitor (PPI) resistant non-erosive reflux disease (NERD) patients: significance of frequency scale for the symptom of GERD (FSSG) on decision of treatment strategy. *Intern Med.* 2010;49(15):1469–76.
- Liu Q, Feng CC, Wang EM, Yan XJ, Chen SL. Efficacy of mosapride plus proton pump inhibitors for treatment of gastroesophageal reflux disease: a systematic review. *World J Gastroenterol.* 2013;19(47):9111–8.
- Zamani NF, Sjahid AS, Kamauzaman THT, Lee Y, Islam MA. Efficacy and Safety of Domperidone in Combination with Proton Pump Inhibitors in Gastroesophageal Reflux Disease: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. *J Clin Med.* 2022;11(18):5268.
- Pace F, Pallotta S, Casalini S, Porro GB. A review of rabeprazole in the treatment of acid-related diseases. *Ther Clin Risk Manag.* 2007;3(3):363–79.
- Hasanzad M, Sarhangi N, Meybodi HRA, Nikfar S. Pharmacogenetics and toxicology. In: *Encyclopedia of Toxicology.* vol. 7. United states: Elsevier; 2024. p. 467–91.
- Xia XM, Wang H. Gastroesophageal Reflux Disease Relief in Patients Treated with Rabeprazole 20mg versus Omeprazole 20 mg: A Meta-Analysis. *Gastroenterol Res Pract.* 2013;2013:327571.
- Marakhouski KY, Karaseva GA, Ulasivich DN, Marakhouski YK. Omeprazole-Domperidone Fixed Dose Combination vs Omeprazole Monotherapy: A Phase 4, Open-Label, Comparative, Parallel Randomized Controlled Study in Mild to Moderate Gastroesophageal Reflux Disease. *Clin Med Insights Gastroenterol.* 2017;10:1179552217709456.

16. Jung DH, Huh CW, Lee SK, Park JC, Shin SK, Lee YC. A Systematic Review and Meta-analysis of Randomized Control Trials: Combination Treatment With Proton Pump Inhibitor Plus Prokinetic for Gastroesophageal Reflux Disease. *J Neurogastroenterol Motil.* 2021;27(2):165–75.
17. Lawate P, Jilawar N, Vyas K, Pebbili KK, Desai S, Rathod R, et al. Effectiveness of Rabeprazole and Other Proton Pump Inhibitors in Managing GERD with Varying Severity: A Retrospective, Real-world EMR-based Study (POWER GERD Study). *J Assoc Physicians India.* 2023;71(10):37–44.
18. Robinson M, Fitzgerald S, Hegedus R, Murthy A, Jokubaitis L, FAST Trial Investigators. Onset of symptom relief with rabeprazole: a community-based, open-label assessment of patients with erosive oesophagitis. *Aliment Pharmacol Ther.* 2002;16(3):445–54.
19. Jr PM, Orr W, Filippone J, Jokubaitis L, Sloan S. Rabeprazole in nonerosive gastroesophageal reflux disease: a randomized placebo-controlled trial. *Am J Gastroenterol.* 2002;97(6):1332–9.
20. Holtmann G, Bytzer P, Metz M, Loeffler V, Blum AL. A randomized, double-blind, comparative study of standard-dose rabeprazole and high-dose omeprazole in gastro-oesophageal reflux disease. *Aliment Pharmacol Ther.* 2002;16(3):479–85.
21. Shahani S, Sawant P, Dabholkar P. Rabeprazole plus domperidone: the answer for gastro-oesophageal reflux disease. *J Indian Med Assoc.* 2008;106(4):266–8.

### Author's biography

**Manjula S**, Senior Vice President  <https://orcid.org/0000-0001-9402-7244>

**Krishna Kumar M**, Senior General Manager  <https://orcid.org/0000-0002-8004-5297>

**Cite this article:** Manjula S, Kumar M K. Expert opinion on the prescription practice of a combination of rabeprazole and domperidone for managing nighttime heartburn in GERD among Indian patients. *Int J Recent Innov Med Clin Res* 2024;6(4):116-121.