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Current Diagnosis and Management of Gastric Acid Related Diseases: Questionnaire-based Clinical Insights from Indian Experts

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Abstract: ***The prevalence of gastric acid-related diseases in India is significant, with PPIs being the primary treatment option. We gathered questionnaire-based insights to explore the diagnosis and management of gastric acid-related diseases in India. The responses were received from 103 gastroenterologists from India, which revealed that while PPIs are widely prescribed, there are significant unmet needs such as nocturnal acid breakthrough, slow achievement of maximal effect and food dependent-dosing. With PPIs, patient compliance rates are hardly optimal, and about 20% of patients exhibit PPI resistance. Vonoprazan has shown superior efficacy in management of various diseases under the umbrella of gastric acid-related diseases such as H. pylori eradication and healing erosive esophagitis compared to PPIs. The majority of respondents were eager to adopt Vonoprazan and anticipated its positive impact on treatment outcomes. This shift towards PCABs represents a significant advancement in managing these disorders in India, promising better patient compliance and therapeutic success.***

Keywords: gastric acid-related diseases, proton pump inhibitors, Vonoprazan efficacy, patient compliance, treatment advancements

1. Introduction

The spectrum of gastric acid-related diseases consists of gastroesophageal reflux disease (GERD), gastric ulcers, duodenal ulcers, H. pylori infection and drug-induced ulcers. The prevalence of GERD in Indian patients is reported to range from 5 to 28.5% in a meta-analysis.[1]Proton pump inhibitors (PPI) are the cornerstone of the treatment of gastric acid-related diseases. Other available treatment options include H2 receptor antagonists (H2RA) and antacids.[2] PPIs are usually the first-line as they are associated with higher healing rates than H2RAs (12%/week vs 6%/week) and offer better heartburn relief in comparison to H2 receptor antagonists (H2RA).[3,4]

However, a large proportion of patients treated with PPIs such as pantoprazole do not respond adequately to it.[2](This population cohort of inadequate responders includes patients with extraesophageal symptoms, patients with concomitant use of non-steroidal anti-inflammatory drug(NSAIDs)use, and obese or overweight patients with severe symptoms.[2].Several guidelines recommend doubling the dose of PPI in such cases.[2] Another challenge posed by the use of PPIs is noncompliance to treatment, observed to be as high as 45 % in one month and of patients at one month of therapy in patients with GERD .[5]

The approach for patients with inadequate response to PPIs is to perform upper GI endoscopy. In patients with evidence of esophagitis, a double dose of PPI for eight weeks is prescribed, per the guidelines from the Indian Society of Gastroenterology and the Association of Physicians in India. Patients who do not respond to an 8-week course of double-dose PPI therapy are classified as having refractory GERD. In such patients, impedance-pH testing is required to evaluate the patient further and to determine the subsequent treatment course.[3]

Patients often self-treat with PPIs following irrational dosing regimens. Nocturnal acid-breakthrough (NAB) occurs in 40% to 70% of patients with GERD while on proton pump inhibitors (PPIs).[6]If PPIs are taken with food, their absorption is delayed, and variability of response is increased. As such, they are best administered under fasting conditions.[7]Genetic variations, particularly in the CYP2C19 gene, affect PPI metabolism and efficacy.[8] With PPIs, heartburn has been reported to be relieved in12.5% of patients on Day 1 of treatment .[9]

Vonoprazan is a novel potassium-competitive acid blocker (P-CAB)with a rapid and sustained acid inhibitory effect and has been shown to be more effective than conventional PPIs in gastric acid-related diseases Vonoprazanis generally safe and well tolerated. [10-13]

The objectives of this insight gathering were to understand the unmet need in the management of gastric acid-related diseases in India from gastroenterologists spread across different regions and to understand their management approach in the real-world setting for treating patients with various severity of gastric acid-related diseases related to gastroesophageal disorders.

2. Methodology

a) Review of the literature

A systematic literature review was performed using the MEDLINE database to identify best practice evidence for diagnosing and managing gastric acid-related diseases based on randomized, double-blind trials and open-label comparative studies. The search period for English-language

literature ranged from January 2000 to July 2024. The search keywords included gastric acid-related diseases, PPIs, treatment, and diagnosis.

b) Data extraction and construction of questionnaire

The literature searches were performed under two categories: diagnosis and therapeutics. For the diagnostic search, randomized controlled trials related to history taking, investigations, and guidelines were included. For the therapeutic search, randomized controlled trials related to the treatment of raised liver enzymes were considered. The results of these searches were used to create a questionnaire. The questionnaire was validated during focus group discussions among 11 gastroenterologists across the country.

c) Validation and dissemination of the structured questionnaire

The structured questionnaire administered to gastroenterologists across India. The collected responses were analyzed without any modification.

3. Results

A total of 103 gastroenterologists responded to the questionnaire. About 87% of respondents opined that the prevalence of acid secretion disorders in their practice ranged from 50% to 70%. To arrive at a diagnosis, almost equivocal number of gastroenterologists preform symptom-based diagnosis (47%) and endoscopy-based diagnosis (52%).

Out of various indications for acid inhibition, the most common reason for acid inhibition therapy in patients was to prevent ulcers due to NSAID administration (**Table 1**).The respondents opined that the critical parameters of an ideal acid inhibition therapy would be administration without regard to meals(87%),consistent 24-hour acid inhibition (80%), proven high potency of the drug (77%), prevention of nocturnal acid breakthrough (75%),near-complete eradication rates for H pylori (69%), and low relapse rates for ulcers(64%).

Almost all of the respondents opined that PPIs were the most prescribed medications for acid inhibition in non-erosive esophagitis (94%) as well as for erosive esophagitis (71.8%) (**Figure 1** and **Figure 2**).

Table 1: Indications for acid inhibition therapy in the natural world setting

	10-30%	31-50%	51-70%	>70%
Acid inhibition to prevent ulcers from NSAID administration	39	23	23	29
Acid inhibition to prevent ulcers from Antibiotic administration	13	17	19	13
Duodenal ulcer	6	9	4	9
Erosive esophagitis (Reflux esophagitis)	16	16	20	21
Gastric ulcer	13	6	9	9
Non-erosive esophagitis	11	30	25	15
Post-surgical ulcer	5	2	3	7

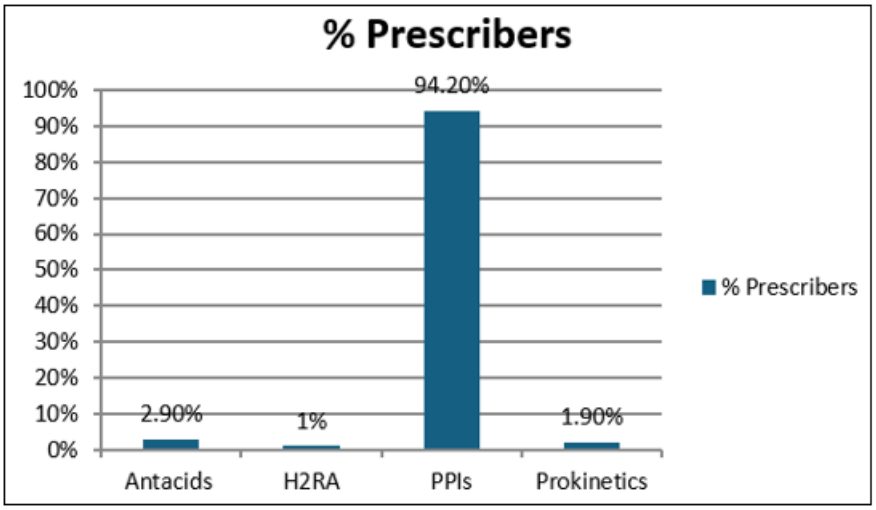


Figure 1: The most common medication prescribed for management of non-erosive reflux disease

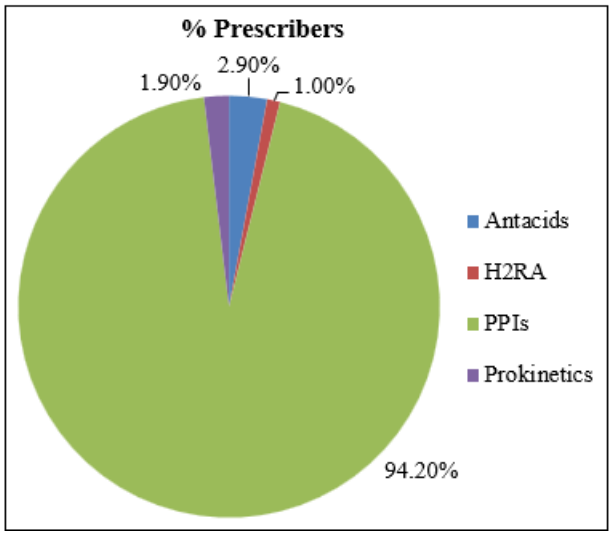
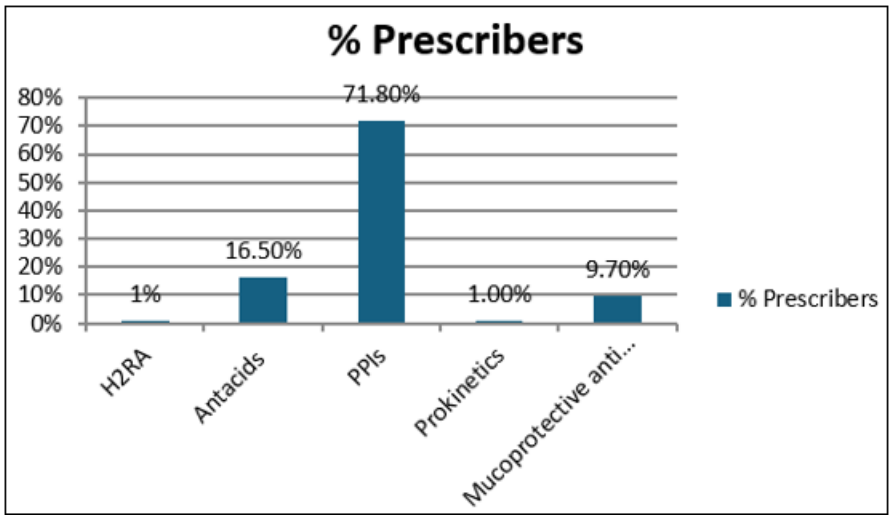
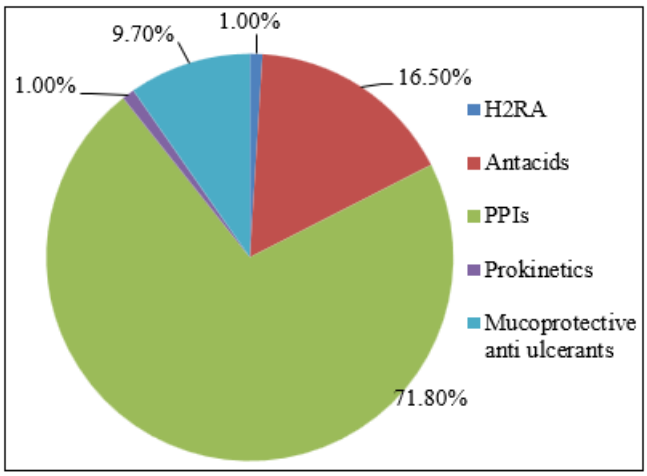


Figure 2: The most common medication prescribed for management of Erosive reflux disease





The approach to therapy was split between respondentswith48%preferring to initiate high dose PPI followed by down-titration; while46% preferred to start the treatment with a lower dose of PPI, then up-titrate.

In terms of preferring one PPI over other, 38% of respondents did not have any specific PPI preference. Some preferred specific PPIs with esomeprazole being preferred most (37%), followed by rabeprazole (16%) and pantoprazole (9%). Upto 20% of the patients were termed PPI–resistant by 50%of respondents; while 21% of respondents pegged PPI resistance at about 10% rate. For patients who did not respond to PPI therapy, diverse approaches are adopted. 23% stated that they increased the dose and frequency of the existing PPI, 21% added a prokinetic, 19% added H2RA, 18% co-prescribed mucoprotective anti-ulcerants, and another 18% co-prescribed neutralizing antacids. (Table 2)

Table 2: Frequencies of approach to patients who fail PPI therapy

Treatment options	% respondents
Increase the dose of existing PPI.	**23.2%**
Prescribe Prokinetics	21.4%
H2 receptor antagonists prescribed	19.4%
Prescribe Neutralizing antacids	18.5%
Prescribe neuroprotective anti ulcers	17.5%

Majority (78%) of the respondents agreed on low (<70%) compliance rates observed with PPIs with about one third of respondents observing compliance rates were as low as 50%, and majority of them – about half of the respondents – pegged the compliance rates to PPIs as ranging from 51% to 70%.

Almost all (99%) respondents were aware of the new class of drugs—Potassium Competitive Acid Blockers (PCABs).

31% of respondents felt it was appropriate to replace PPIs in the majority of their patients with Vonoprazan; while majority (65%) of respondents opined that they would start to replace PPIs with Vonoprazan in a select patients. 80.6% of respondents stated that they were eager to adopt Vonoprazan given the clinical evidence.

4. Discussion

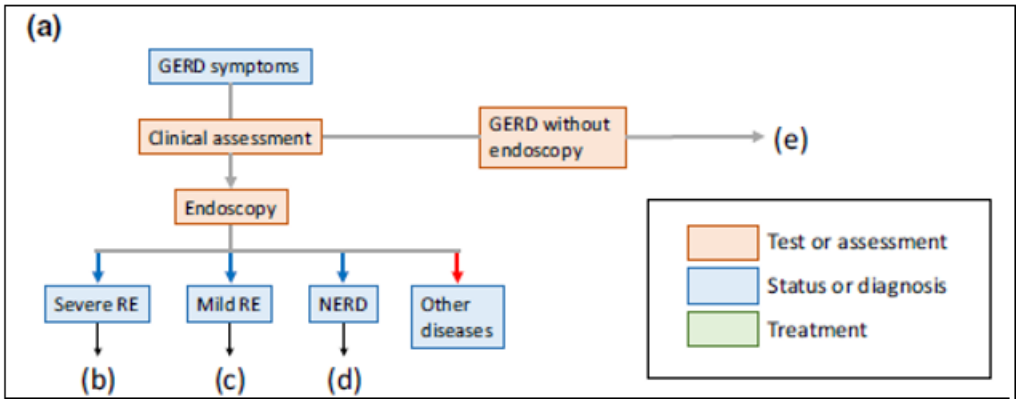
It was clear from the gathered insights that PPIs were the cornerstone of the management of gastric acid-related diseases despite a substantial proportion of patients having inadequate responses. The API has given a treatment algorithm for the management of GERD.[3] The NICE guidelines from the UK recommend8 weeks of the standard dose of PPI for the healing reflux esophagitis. In patients with inadequate response, alternative strategies suggested are escalating the dose of the initial PPI to double the initial amount or switching the patients to another PPI at a total therapeutic dose. The responses in the study were in line with these recommendations. The American College of Gastroenterology Clinical guidelines for diagnosing and managing GERD also suggest that in patients with both extra-esophageal and typical symptoms of GERD, a trial of twice-daily dose of PPI should be given for 8–12 weeks. It also recommends the use of PPI over H2RA for healing as well as maintenance of healed EE.[13]

Several causes for failure of PPI therapy put forth include noncompliance, incorrect dose timing, rapid PPI metabolism, a hypersecretory state in patients, hiatus hernia, visceral hypersensitivity and non-reflux esophageal causes like dysmotility, eosinophilic esophagitis, pill-induced esophagitis, and infectious esophagitis.[14]

The current real-world expert opinion survey has corroborated the global place of PPIs for the management of gastric acid-related diseases.94% of respondents opined that PPIs were the most prescribed medications for acid inhibition in non-erosive esophagitis and also for erosive esophagitis (72%).The experts opined that PPI resistance was seen in about 20% of patients. Their approach to addressing the inadequate response to PPIs was to increase the dose of the PPI, add a neuroprotective anti-ulcerate, and prescribe antacids or prokinetics. Compliance was reported to be another issue with patients undergoing long-term treatment for GERD. Noncompliance was reported to be about 50% by one-third of the experts. The unmet needs in this therapy are as follows: 1. Nocturnal acid breakthrough despite high dose PPIs, 2. Food dependent dosing, 3. Three to five days for maximal onset of action, 4. Pharmacogenomic variability due to CYP2C19 and, 5. High relapse rate despite extended therapy and double PPI dosages.

Vonoprazan is a novel potassium-competitive acid blocker (P-CAB), which has a rapid and sustained acid inhibitory effect and could be more effective than conventional proton pump inhibitors (PPIs). Vonoprazan-based therapy was more effective than PPI-based therapy as a first-line *H. pylori* eradication treatment. Vonoprazan was generally safe and well tolerated [10,11]A 5-year long safety analysis (VISION trial results) showed no increased risk as compared to PPIs despite higher gastrin levels – indicating higher gastrin levels may not translate to real-world safety.[15] A meta-analysis of 11 studies and a pooled sample of 4,108 GERD patients indicated that PCABs were significantly more effective in healing erosive esophagitis as compared to PPIs.[16]

Almost all respondents were aware of the new class of drugs – Potassium Competitive Acid Blockers (PCABs). 80.6% of respondents stated that they were eager to adopt Vonoprazan in their patients within a short span of its availability. Adopting this class of drugs has significantly changed the landscape of managing these diseases in Japan. Guidelines by the Japanese Society of Gastroenterologists recommend Vonoprazan as first-line treatment for mild and severe forms of Reflux Esophagitis. (Figure 3)[17]



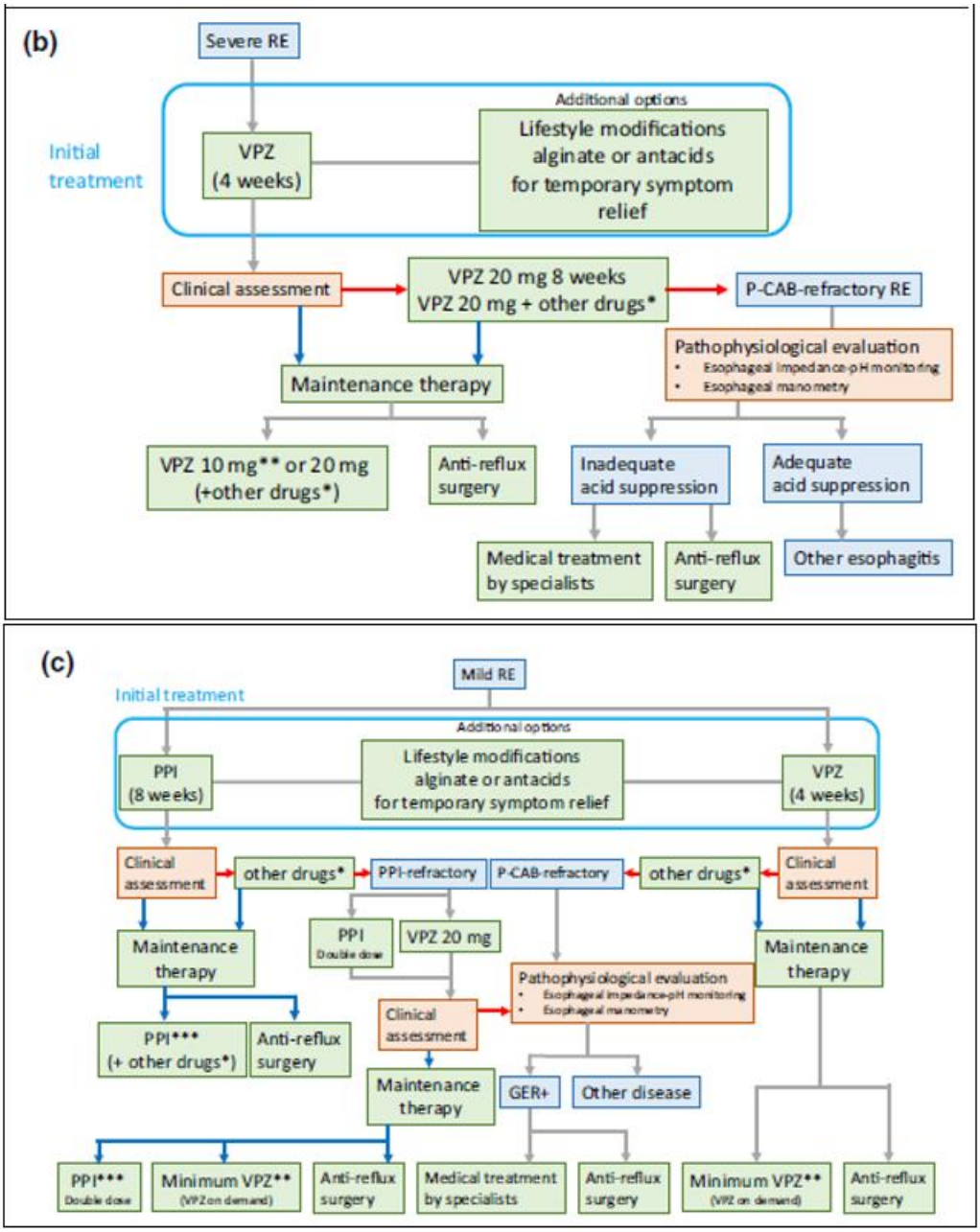


Figure 3: Adapted from Iwakiri K et al.[18]

5. Conclusion

Based on the gathered insights from Indian experts, proton pump inhibitors were considered as the cornerstone of the treatment of Gastric Acid Related Diseases. However, there are pitfalls in their use with significant unmet needs in Indian populations such as nocturnal acid breakthrough, slowly achieved maximal effect and food dependent dosing. The results also highlight the trend towards acceptance of the novel PCAB Vonoprazan based on the molecule's clinical evidence. This is a significant step forward with newer options addressing the existing unmet needs in Indian population. The findings also underscore the need for updated clinical guidelines to incorporate these new treatment options.

Author Contributions

The authors made significant contributions to the inception of the questionnaire, documented the conversations, and substantively evaluated and approved the final version for submission.

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Conflict of Interest

Mamata Amonkar did not receive any fees or honoraria for work on this study. Saurabh Patil, Vinodraj Kundapur and Jejoe Karankumar are employees of Abbott India Limited.

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