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Physician Perceptions on Gaps in Proton Pump Inhibitor Therapy in Drug-Induced Gastritis and the Potential Role of Vonoprazan: A Cross-Sectional Survey in India (The GAP-DIG Survey)

Saurabh Mukewar [1], Kailash C. Dash [2], Mrinal Jaiswal [3], Sameer Muchhala [4], Vidhya Natarajan [5], Gauravee R. Chavan [6]

1. Gastroenterology, Midas Multispeciality Hospital, Maharashtra, IND 2. General Medicine, Muni Medical, Garage Chhak, Odisha, IND 3. Orthopedics, Agrim Hospital, varanasi, IND 4. Medical Affairs, Zydus Lifesciences Limited, Mumbai, IND 5. Medical Affairs, Zydus Healthcare Limited, Mumbai, IND 6. Medical & Regulatory Affairs, Zydus Healthcare Ltd., Maharashtra, IND

Corresponding author: Vidhya Natarajan, n15vidhya@gmail.com

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Abstract

Background

Drug-induced gastritis (DIG), particularly that associated with non-steroidal anti-inflammatory drugs (NSAIDs) and low-dose aspirin, remains a common clinical challenge. Although proton pump inhibitors (PPIs) are the standard gastroprotective therapy, their real-world effectiveness may be limited by pharmacological characteristics and dosing-related adherence issues. This survey described Indian physicians' perceptions of the limitations of PPI therapy in DIG and their views on vonoprazan, a potassium-competitive acid blocker (P-CAB). It did not evaluate the clinical efficacy of either drug class.

Methods

A cross-sectional, descriptive, web-based survey of physician perceptions was conducted between October 2025 and May 2026 among 94 Indian physicians (orthopedic surgeons, physicians, and general surgeons) who were regular prescribers of vonoprazan, identified by the sponsor's medical representatives and invited individually via WhatsApp. The 20-item questionnaire covered perceived PPI effectiveness, adherence challenges, PPI limitations, and views on vonoprazan. Data were analyzed descriptively; global assessments of vonoprazan efficacy and tolerability were secondary outcomes.

Results

Overall, 76 (80.9%) respondents rated PPIs as moderately effective for managing DIG, and 79 (84.0%) agreed that some patients continued to experience persistent symptoms or ulcer recurrence despite therapy. Among predefined response options, the most frequently selected limitations were the requirement for pre-meal dosing, 80 (85.1%), incomplete nocturnal acid suppression, 62 (66.0%), and slow onset of action, 37 (39.4%). Sixty-one (64.9%) respondents considered the empty-stomach dosing requirement difficult or very difficult for patients to follow, and 65 (69.1%) estimated poor adherence to dosing instructions in at least 30% of patients. Meal-independent dosing, 86 (91.5%), and durable 24-hour acid suppression, 69 (73.4%), were the most frequently selected potential advantages of vonoprazan. In global assessments, 68 (72.3%) and 60 (63.8%) respondents rated the efficacy and tolerability of vonoprazan, respectively, as very good or excellent compared with conventional PPIs.

Conclusion

In this sample of Indian physicians who regularly prescribe vonoprazan, respondents perceived practical limitations of conventional PPI therapy for DIG, particularly those related to pre-meal dosing and adherence, and considered the meal-independent dosing of vonoprazan to be a relevant attribute. These findings reflect physician perceptions only and do not establish the comparative effectiveness or safety of vonoprazan. Prospective patient-level studies are warranted to determine whether these perceived advantages translate into improved clinical outcomes in routine practice.

Categories: General Surgery, Gastroenterology
Keywords: drug-induced gastritis, india, nsaids, physician survey, potassium-competitive acid blocker, proton pump inhibitors, vonoprazan

Introduction

Drug-induced gastritis (DIG) represents one of the most frequently encountered gastrointestinal adverse effects associated with modern pharmacotherapy. Among the various offending medications, non-steroidal

anti-inflammatory drugs (NSAIDs) and low-dose aspirin account for the majority of clinically significant cases due to their extensive use in musculoskeletal disorders, chronic inflammatory diseases, and cardiovascular conditions [1-3]. These agents compromise gastric mucosal integrity through the inhibition of cyclooxygenase-mediated prostaglandin synthesis, reducing mucus and bicarbonate secretion and increasing susceptibility to acid-mediated injury, and also exert direct topical, acid-independent effects on the mucosa [4-6]. Superficial endoscopic mucosal injury is common among chronic NSAID users, whereas clinically significant peptic ulcers occur in approximately 15-30% of patients [2,4,6]. In this review, DIG refers to upper gastrointestinal mucosal injury and/or related dyspeptic symptoms attributed to NSAID or low-dose aspirin use. It is distinct from functional dyspepsia (symptoms without mucosal injury) and from peptic ulcer disease of other causes, chiefly *Helicobacter pylori* infection, although these conditions frequently coexist [1,7].

Proton pump inhibitors (PPIs) have remained the foundation of acid suppression therapy for over three decades. By irreversibly inhibiting the gastric H^+/K^+-ATPase proton pump, PPIs effectively suppress gastric acid secretion and reduce the incidence of NSAID-associated peptic ulcers [8-10]. However, several pharmacological and practical limitations have been described. PPIs are prodrugs requiring activation within the acidic canaliculi of stimulated parietal cells; consequently, maximal acid suppression requires repeated administration over several days [11,12]. Furthermore, for optimal efficacy, conventional PPIs should be administered 30-60 minutes before meals [11,13]. Adherence to this schedule is often poor, and interindividual variability in treatment response further complicates therapy, as most PPIs undergo hepatic metabolism through the CYP2C19 pathway, where genetic polymorphisms produce considerable variation in plasma drug concentrations [14-16]. In the Indian clinical setting, optimizing PPI therapy in patients with comorbidities receiving polypharmacy has been described as a practical challenge [17].

Despite guideline-recommended therapy, residual symptoms and nocturnal acid breakthrough remain clinical challenges, suggesting that conventional PPIs may not consistently achieve sustained 24-hour acid suppression [10,18]. These limitations have driven the development of potassium-competitive acid blockers (PCABs). Vonoprazan, the first clinically available PCAB, does not require an acidic environment for activation, binds to both active and inactive proton pumps, and is primarily metabolized by CYP3A4/5, which reduces the influence of CYP2C19 variability [19-21]. Vonoprazan has been described in recent Indian literature as a promising advancement in acid-suppressive therapy on the basis of its pharmacodynamic profile [22].

Randomized clinical trials establish efficacy under controlled conditions, whereas prescribing decisions are also shaped by physicians' perceptions of how treatments perform in routine practice. A recent systematic review and meta-analysis evaluated vonoprazan for the prevention of ulcer recurrence and gastrointestinal bleeding in patients with NSAID-induced ulcers [23], and recent Indian expert consensus statements, including the “Acid peptic disorder compass” and the Association of Physicians of India recommendations, have incorporated vonoprazan into management algorithms for acid peptic disorders [24,25]. However, data on how Indian physicians perceive the limitations of PPI therapy in DIG, and how they view P-CABs, are scarce. The objective of this survey was therefore to describe the perceptions of Indian physicians who regularly prescribe vonoprazan regarding (i) the effectiveness and practical limitations of PPI therapy in DIG and (ii) the potential advantages of vonoprazan. The study was designed as a descriptive, hypothesis-generating survey of clinician perceptions; it did not measure patient outcomes, actual prescribing, or the comparative efficacy of either drug class.

Materials And Methods

Study design

This cross-sectional, descriptive, web-based physician survey was conducted between October 7, 2025, and May 31, 2026, to describe physicians' perceptions of PPI therapy for DIG and their views on vonoprazan, a P-CAB. The survey captured physician opinion and self-reported clinical experience only; no patient-level data were collected, and actual prescribing was not measured. The survey was sponsored by Zydus Healthcare Ltd, which markets vonoprazan in India. The survey was programmed, hosted, and analyzed independently, with medical writing assistance provided by Medeva Healthtech Pvt Ltd, Hyderabad, Telangana, India. Reporting follows the Checklist for Reporting Results of Internet E-Surveys (CHERRIES), where applicable [26].

Case definition

For the purposes of this survey, DIG referred to upper gastrointestinal mucosal injury and/or related dyspeptic symptoms that the treating physician attributed to NSAID or low-dose aspirin use. The questionnaire did not provide a formal case definition or require endoscopic confirmation; responses therefore reflect each physician's working clinical definition, which may have encompassed symptomatic dyspepsia, endoscopic gastropathy (erosions), and NSAID- or aspirin-associated peptic ulcers. These entities are not interchangeable, and this is considered in the Limitations.

Survey development

The questionnaire was developed following a review of published literature on DIG, PPI therapy, and P-CAB blockers. Draft questions were reviewed for content and clarity by clinicians experienced in the management of acid-related disorders, and the final questionnaire was pilot-tested for clarity among physicians before circulation. No formal psychometric validation (e.g., reliability or construct-validity testing) was performed. The final instrument comprised 20 items (Appendix A) and was administered in English on a web-based electronic data-capture platform operated by Medeva Healthtech Pvt Ltd. All items were mandatory. The PPI effectiveness item (Q5) offered four response options, including "Not effective at all"; the global assessment items for vonoprazan (Q18 and Q19) offered five options, including "Poor"; and the item on the most compelling reason to consider vonoprazan (Q17) included the option "I see no compelling reason to switch."

Survey participants

Eligible participants were practicing clinicians who manage patients with DIG, including those receiving NSAIDs or low-dose aspirin. Orthopedic surgeons, physicians (consultant and general physicians), and general surgeons were targeted because they are the principal prescribers of long-term NSAIDs and low-dose aspirin, and therefore of co-prescribed gastroprotection, in Indian practice; gastroenterologists were not targeted. A purposive (non-probability) sampling approach was used. The sponsor's medical representatives identified physicians who regularly prescribe vonoprazan from the field force's lists of regular prescribers of the brand, and the survey link was sent individually to these physicians via WhatsApp. Prescriber status was established by the field force and was not separately confirmed by a question in the survey. The number of physicians who received the link was not recorded; therefore, the number of invitees and the response rate cannot be calculated. Responses were received in two periods (October 2025 to January 2026, n = 26; April to May 2026, n = 68). Eligibility was based on regular vonoprazan prescribing (as identified by the field force), self-reported specialty (Q2), and having treated patients with DIG with PPIs in the preceding six months (Q4). Names and practice locations were used to check for duplicate submissions, and none were identified. A total of 94 physicians completed the survey, and all completed responses were included in the analysis. Some participants received an honorarium from the sponsor under a written agreement, whereas others received no payment. Honoraria were provided for participants' time and were not contingent on the content of their responses.

Data collection

Data were collected via a structured, self-administered online questionnaire. The survey instrument comprised a practice-profile block and five thematic sections: (A) clinical experience with PPI therapy; (B) patient adherence and real-world challenges; (C) the importance of food-timing-independent dosing; (D) perceived limitations of PPI therapy; and (E) perceptions of vonoprazan relative to conventional PPIs, including a global assessment of its efficacy and tolerability.

Each section comprised single-select and multi-select questions with predefined response options. Physician-reported items included estimates of the proportion of NSAID/aspirin-treated patients who experienced breakthrough gastrointestinal symptoms despite PPI prophylaxis, perceived onset of PPI symptom relief, frequency of adjunctive therapy use, and feasibility of empty-stomach dosing. Perceptions of vonoprazan were assessed using items addressing meal-independent dosing, duration of acid suppression, speed of onset, and metabolic consistency (CYP3A4/5 vs. CYP2C19). The survey invitation, which was displayed before the first question, is reproduced in Appendix A. Survey responses were collected electronically, exported, and verified for completeness prior to analysis.

Data confidentiality and handling

The survey invitation stated that responses would remain confidential. Respondents' names and practice affiliations were requested to verify that respondents were practicing clinicians, to identify duplicate submissions, and to classify practice location. Data were stored on the survey platform with access restricted to the study team (Medeva study team only; whether the sponsor had access to identifiable responses), identifying fields were removed before analysis, and results are reported only in aggregate. No patient-identifiable information was requested or collected.

Outcome measures

The primary outcome measures were as follows: (1) physician-rated effectiveness of current PPI therapy in managing DIG symptoms, assessed on a four-point scale (Very effective, Moderately effective, Minimally effective, Not effective at all); (2) the estimated proportion of patients on chronic NSAID or low-dose aspirin therapy who continued to experience gastrointestinal symptoms despite PPI prophylaxis; and (3) physician-perceived unmet clinical need for a faster-acting and more consistent acid suppressant, evaluated on a four-point agreement scale (Strongly agree, Agree, Disagree, Strongly disagree) without a neutral option. The global assessments of vonoprazan efficacy and tolerability compared with conventional PPIs, rated on a five-point ordinal scale (Poor, Fair, Good, Very Good, Excellent), were secondary outcomes. Because all respondents were regular prescribers of vonoprazan, these ratings reflect respondents' clinical experience; however, the scale did not include explicit comparative anchors (e.g., worse than, similar to, or better than PPIs).

Other secondary outcomes included the most common reasons for patient non-adherence to PPI dosing instructions, the principal pharmacological and practical limitations of PPI therapy selected from predefined options, and the vonoprazan pharmacological attributes considered most relevant to the respondents' clinical setting (e.g., meal-independent acid suppression, durable 24-hour coverage including nocturnal control, rapid onset within approximately two hours, and binding to both active and inactive proton pumps).

Statistical analysis

All analyses were descriptive, consistent with the study's cross-sectional, hypothesis-generating design. Categorical variables were summarized as absolute frequencies and percentages (n [%]). Results are reported for the overall study sample (N = 94) and by physician specialty (Physician, Orthopedic Surgeon, General Surgeon, Other; Appendix B); no inferential testing was performed, given the non-probability sample and small subgroup sizes. Geographic zones were assigned from the respondent-reported practice state using a standard four-zone grouping: North (Uttar Pradesh, Rajasthan, Delhi, Madhya Pradesh), West (Maharashtra, Goa), South (Karnataka, Telangana, Tamil Nadu, Andhra Pradesh, Kerala), and East (West Bengal, Odisha, Jharkhand, Assam).

For multi-select survey items, including reasons for PPI non-adherence, observed limitations of PPI therapy, and perceived clinical advantages of vonoprazan, individual response options were summarized independently, as respondents could select more than one option. For mutually exclusive, single-select items, frequency distributions across response categories are presented, and the percentages sum to 100% (subject to rounding). Because all items were mandatory, there were no missing data. All statistical computations were performed using standard analytical software.

Results

Sample profile

A total of 94 clinicians completed the survey and were included in the analysis. Orthopedic surgeons comprised the largest specialty group (n = 44; 46.8%), followed by physicians (n = 37; 39.4%), general surgeons (n = 11; 11.7%), and other specialists (n = 2; 2.1%). Respondents practiced at hospitals and clinics in 15 states and union territories of India.

Geographic zone

Based on the respondent-reported practice state, the South zone contributed the largest share (n = 45; 47.9%), encompassing Karnataka, Telangana, Tamil Nadu, Andhra Pradesh, and Kerala. The North zone accounted for 23 (24.5%) respondents and included Uttar Pradesh, Rajasthan, Delhi, and Madhya Pradesh. The West zone accounted for 18 (19.1%) respondents and spanned Maharashtra and Goa. The East zone had the smallest representation (n = 8; 8.5%), with respondents from West Bengal, Odisha, Jharkhand, and Assam (Figure *1*; Table *1*).

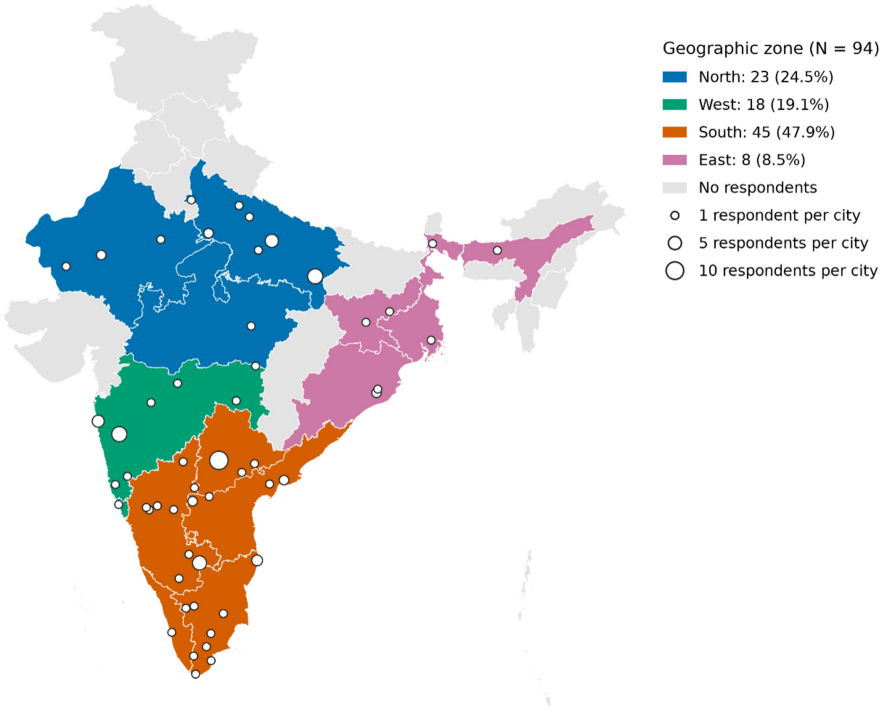


FIGURE 1: Geographic distribution of the 94 survey respondents by state and zone of India (North, West, South, East), with respondents' practice cities marked.

States with at least one respondent are shaded by zone; states without respondents are shown in grey. Circles mark respondents' practice cities, with circle area proportional to the number of respondents per city. Zones were assigned from respondent-reported practice state using a standard four-zone grouping (see the Statistical Analysis section); zone totals (n [%]) correspond to Table 1.

This is an original figure created by the authors directly from the study's own aggregated survey data (respondent-reported practice city and state; N = 94 physicians). It has not been reproduced or adapted from any previously published source. State boundaries are from DataMeet (Creative Commons Attribution 2.5 India). No generative artificial intelligence tool was used to create this figure; it was produced in Python using the matplotlib library.

Characteristic	Overall (N=94)
Specialty	
Physician	37 (39.4)
Orthopedic Surgeon	44 (46.8)
General Surgeon	11 (11.7)
Other	2 (2.1)
Geographic zone	
North	23 (24.5)
South	45 (47.9)
West	18 (19.1)
East	8 (8.5)
Patient volume (DIG treated with PPIs, past 6 months)	
Less than 50	10 (10.6)
51-100	41 (43.6)
101-200	35 (37.2)
More than 200	8 (8.5)

TABLE 1: Respondent profile by specialty, geographic zone, and patient volume (N = 94)

Values are presented as n (%)

DIG, drug-induced gastritis; PPI, proton pump inhibitor

Patient volume

Most respondents managed a high DIG caseload: 41 (43.6%) had treated 51-100 patients with PPIs in the preceding six months, and 35 (37.2%) had treated 101-200 patients. Only 10 (10.6%) reported treating fewer than 50 patients, and 8 (8.5%) reported treating more than 200 (Table *1*).

PPI Effectiveness and clinical performance

Overall Effectiveness

Overall, 76 (80.9%) of respondents rated PPI therapy as moderately effective in managing DIG, 13 (13.8%) as very effective, and 5 (5.3%) as minimally effective; no respondent selected “Not effective at all” (Figure *2A*).

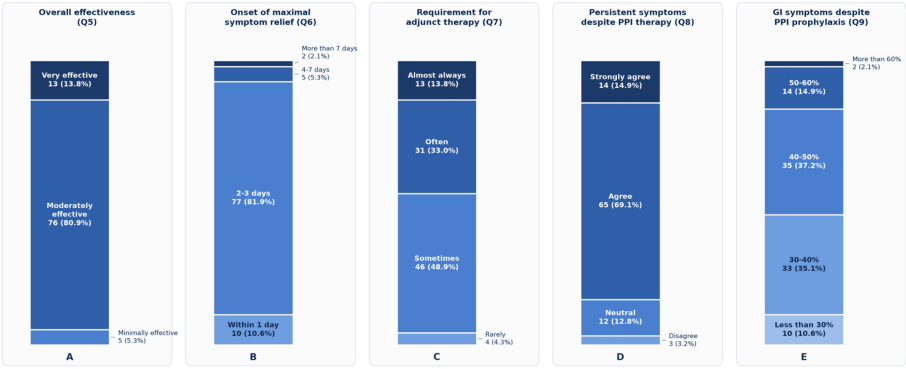


FIGURE 2: Distribution of responses to five survey items on PPI therapy in DIG and in patients receiving NSAIDs or low-dose aspirin.

Each stacked bar represents the percentage of respondents selecting each response option. Panels correspond to Q5 (A), Q6 (B), Q7 (C), Q8 (D), and Q9 (E) of the questionnaire (Appendix A). Segment heights are proportional to the percentage of respondents; options selected by no respondent ("Not effective at all" for Q5 and "Strongly disagree" for Q8) are not shown.

DIG, drug-induced gastritis; GI, gastrointestinal; NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor

Onset of Symptom Relief

Most respondents (77; 81.9%) reported that maximal symptom relief occurred within 2-3 days after PPI initiation; 10 (10.6%) reported relief within 1 day and 7 (7.4%) after more than 3 days (Figure *2B*).

Requirement for Adjunct Therapy

Most physicians (90; 95.7%) indicated that adjunctive therapy was required at least sometimes (sometimes, 46 [48.9%]; often, 31 [33.0%]; almost always, 13 [13.8%]) (Figure *2C*).

Persistent Symptoms Despite PPI Therapy

Overall, 79 (84.0%) of respondents agreed or strongly agreed that a subset of their patients continued to experience persistent symptoms or ulcer recurrence despite PPI therapy, 12 (12.8%) were neutral, and 3 (3.2%) disagreed (Figure *2D*).

Gastrointestinal Symptom Breakthrough Despite PPI Prophylaxis

Most respondents (68; 72.3%) estimated that approximately 30-50% of their patients on NSAIDs or low-dose aspirin continued to experience gastrointestinal symptoms despite PPI prophylaxis (Figure *2E*). These figures are physician estimates and do not represent measured prevalence.

PPI therapy: observed limitations

Respondents most frequently selected the requirement for pre-meal dosing (80; 85.1%) and incomplete night-time acid suppression (62; 66.0%) as limitations of conventional PPI therapy, followed by slow onset of action (37; 39.4%), breakthrough symptoms despite twice-daily dosing (35; 37.2%), and variable response attributed to CYP2C19 metabolic differences (26; 27.7%); 2 (2.1%) reported no major limitations. Overall, 91 (96.8%) respondents agreed or strongly agreed that there is a clinical need for alternatives to PPIs that provide faster and more consistent acid suppression (Figure *3*; Table *2*). Because these limitations were presented as predefined response options, the frequencies indicate endorsement of the options offered rather than spontaneously reported observations.

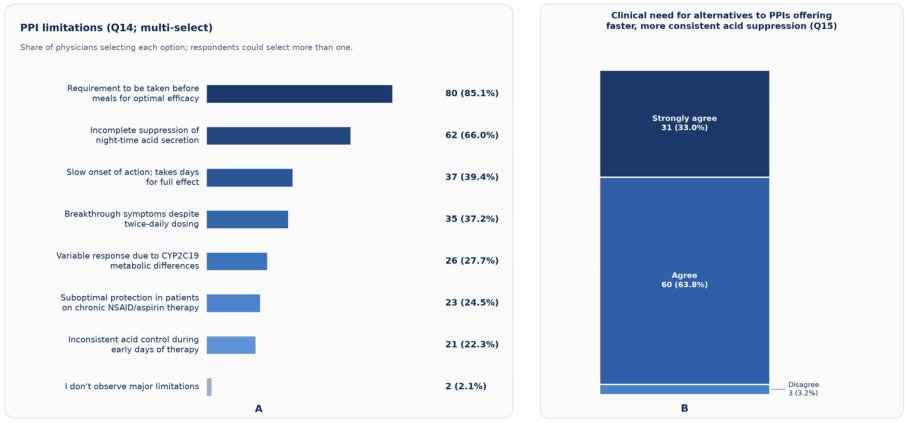


FIGURE 3: Distribution of responses to two survey statements evaluating perceptions of PPI limitations and the need for alternative therapies.

(A) Left panel: respondents could select multiple limitations of PPI therapy. Percentages represent the proportion selecting each option. (B) Right panel: responses were collected on a four-point agreement scale (Strongly agree, Agree, Disagree, Strongly disagree) without a neutral option. No respondent selected “Strongly disagree”. Percentages represent the proportion selecting each option.

NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor

Clinician-reported item	n (%)
PPI limitations (multi-select; respondents could select more than one)	
Requirement to be taken before meals for optimal efficacy	80 (85.1)
Incomplete suppression of night-time acid secretion	62 (66.0)
Slow onset of action; takes days for full effect	37 (39.4)
Breakthrough symptoms despite twice-daily dosing	35 (37.2)
Variable response due to CYP2C19 metabolic differences	26 (27.7)
Suboptimal protection in patients on chronic NSAID/aspirin therapy	23 (24.5)
Inconsistent acid control during early days of therapy	21 (22.3)
I don't observe major limitations	2 (2.1)
Clinical need for faster, more consistent acid suppression (four-point agreement scale; no neutral option)	
Strongly agree	31 (33.0)
Agree	60 (63.8)
Disagree	3 (3.2)

TABLE 2: Clinician-reported PPI limitations and perceived unmet need (multi-select; n = 94)

NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor

PPI adherence challenges and dosing preferences

Reasons for Non-adherence

Timing-related inconvenience (the requirement to take PPIs before meals) was the most frequently selected reason for poor adherence to PPI therapy (80; 85.1%), followed by the need for twice-daily doses in some cases (60; 63.8%), incomplete control of symptoms (43; 45.7%), and delayed onset of symptom relief (30;

31.9%) (Figure 4).

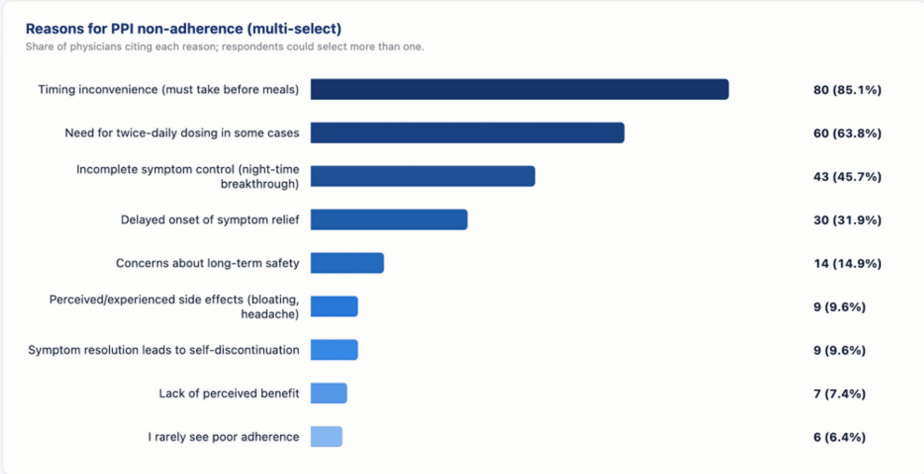


FIGURE 4: Distribution of respondents selecting reasons contributing to non-adherence with PPIs.

Respondents could select multiple reasons. Percentages represent the proportion of respondents selecting each reason.

PPI, proton pump inhibitor

Feasibility of Empty-Stomach Dosing

Overall, 61 (64.9%) physicians considered the empty-stomach requirement for PPI administration difficult (48; 51.1%) or very difficult (13; 13.8%) for their patients to follow consistently. This proportion was similar across the three main specialties (63.6% to 67.6%; Appendix B) (Figure 5A).

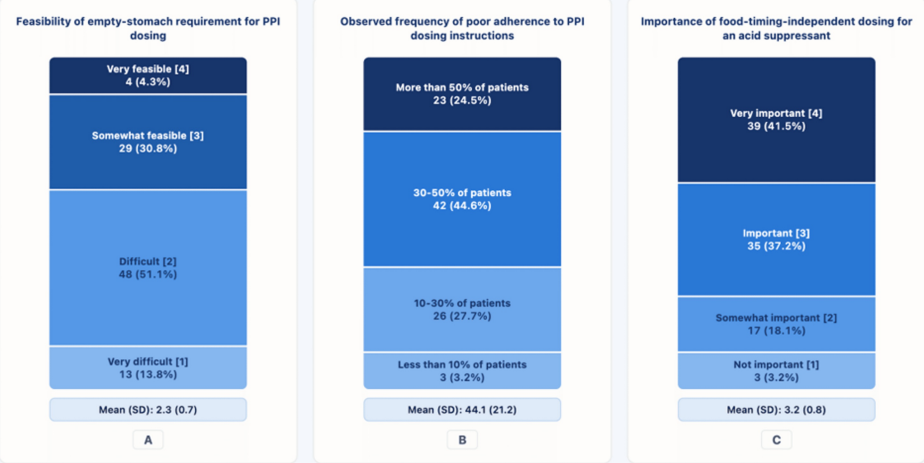


FIGURE 5: Distribution of responses to three survey statements evaluating perceptions of PPI dosing requirements and preferences.

Each stacked bar represents the percentage of respondents selecting each response option. Numbers in brackets [] indicate the score assigned to each response option. Bracketed percentages to the right indicate the cumulative percentage at each level.

PPI, proton pump inhibitor; SD, standard deviation

Observed Non-adherence Frequency

Overall, 65 (69.1%) physicians estimated that at least 30% of their patients did not consistently follow the

recommended PPI dosing instructions (30-50% of patients, 42 [44.7%]; more than 50% of patients, 23 [24.5%]) (Figure 5B).

Importance of Food-Timing-Independent Dosing

Overall, 74 (78.7%) of respondents considered food-timing-independent dosing important or very important when selecting an acid suppressant (Figure 5C).

Vonoprazan: perceived advantages and clinician satisfaction

Perceived Clinical Advantages Over PPIs

Meal-independent acid suppression (86; 91.5%) and a longer half-life enabling more durable 24-hour acid control (69; 73.4%) were the most frequently selected potential advantages of vonoprazan, whereas rapid onset (33; 35.1%), binding to both active and inactive proton pumps (33; 35.1%), more consistent response due to CYP3A4/5 metabolism (28; 29.8%), and stronger healing efficacy (24; 25.5%) were selected less often (Figure 6A).

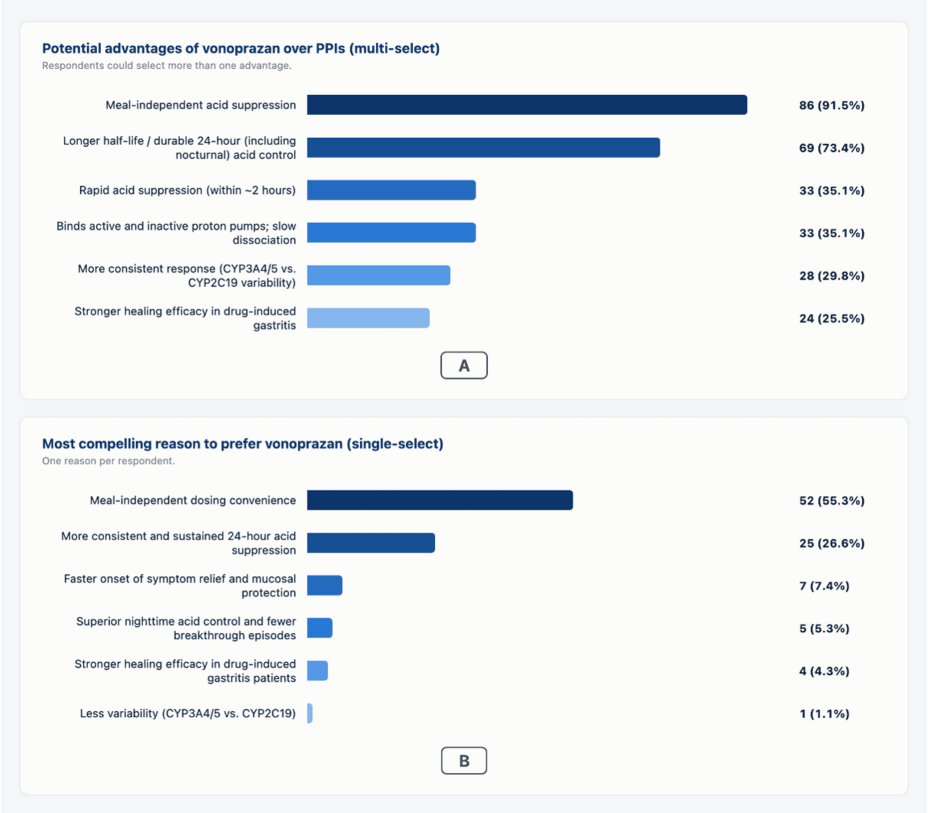


FIGURE 6: Distribution of responses evaluating the perceived advantages of vonoprazan over PPIs and the most compelling reason for preferring vonoprazan.

(A) Upper panel: respondents could select multiple perceived advantages of vonoprazan over PPIs. Percentages represent the proportion selecting each option. (B) Lower panel: respondents selected the single most compelling reason for preferring vonoprazan over PPIs. Percentages represent the proportion selecting each option. Percentages may not total exactly 100% because of rounding.

PPI, proton pump inhibitor

Most Compelling Reason to Prefer Vonoprazan

When asked to select the single most compelling reason to consider vonoprazan over conventional PPIs, 52 (55.3%) respondents chose meal-independent dosing convenience and 25 (26.6%) chose more consistent and sustained 24-hour acid suppression; no respondent selected "I see no compelling reason to switch" (Figure 6B). The advantages listed were predefined, pharmacologically framed options; their selection indicates which proposed attributes respondents considered relevant rather than observed clinical benefit.

Secondary outcome: global assessment of vonoprazan

Global Efficacy

Compared with conventional PPIs, 68 (72.3%) respondents rated the overall efficacy of vonoprazan as very good (46; 48.9%) or excellent (22; 23.4%), 23 (24.5%) as good, and 3 (3.2%) as fair; no respondent selected "Poor" (Figure 7A).



FIGURE 7: Distribution of responses comparing the global efficacy and global tolerability of vonoprazan with conventional PPIs.

(A) Global efficacy panel. (B) Global tolerability panel.

Response options were Poor, Fair [1], Good [2], Very Good [3], and Excellent [4]; no respondent selected "Poor." Numbers in brackets are the scores assigned for analysis.

PPI, proton pump inhibitor

Global Tolerability

For tolerability, 60 (63.8%) respondents rated vonoprazan as very good (37; 39.4%) or excellent (23; 24.5%), 26 (27.7%) as good, and 8 (8.5%) as fair; no respondent selected "Poor" (Figure 7B). Across the three main specialties, ratings of very good or excellent ranged from 64.9% (physicians) to 79.5% (orthopedic surgeons) for efficacy and from 56.8% to 72.7% for tolerability (Appendix B). These ratings reflect the perceptions of regular prescribers of vonoprazan; because the scale did not include explicit comparative anchors, they should not be interpreted as evidence of comparative efficacy or tolerability.

Discussion

This survey describes the perceptions of 94 Indian physicians, predominantly orthopedic surgeons and physicians who regularly prescribe vonoprazan and were identified through the sponsor's field force, regarding PPI therapy for DIG and the potential role of vonoprazan. Three principal findings emerged. First, most respondents rated PPIs as moderately, rather than very, effective and agreed that a subset of their patients had persistent symptoms despite PPI therapy. Second, respondents most frequently attributed suboptimal real-world performance to practical issues related to pre-meal dosing and adherence. Third, respondents considered meal-independent dosing and sustained acid suppression to be the most relevant proposed attributes of vonoprazan. These are physician perceptions; they do not establish the prevalence of PPI failure or non-adherence, or the comparative effectiveness of vonoprazan. Below, we place these perceptions in the context of published evidence, which provides background but does not confirm the survey findings.

PPI effectiveness and persistent symptoms in context

The finding that most physicians rated PPI therapy as moderately effective, and that most had encountered persistent symptoms or ulcer recurrence despite therapy, should be interpreted cautiously. Randomized trials and meta-analyses show that PPIs substantially reduce NSAID- and aspirin-associated ulcers compared with no gastroprotection [8,9,27], and in the present survey, 89 (94.7%) respondents rated PPIs as at least moderately effective. Several explanations for residual symptoms despite PPI therapy are plausible. Some relate to acid suppression, including delayed onset, nocturnal acid breakthrough, CYP2C19-dependent

variability, and missed or mistimed pre-meal doses [11,13,14,18]. Others are acid-independent and would not be expected to respond to more potent acid suppression: concomitant *H. pylori* infection, which acts synergistically with NSAIDs to increase ulcer risk and is highly prevalent in India [7,28]; direct topical and prostaglandin-mediated mucosal injury, including small-bowel injury that PPIs do not prevent [5,6]; and overlap with functional dyspepsia. The present survey did not distinguish among these mechanisms. In particular, mechanisms such as nocturnal breakthrough and CYP2C19 variability were offered to respondents as predefined options, and their role cannot be inferred from the responses.

Although international and Indian clinical guidelines continue to recommend PPIs as the standard first-line gastroprotective therapy for NSAID- and aspirin-associated gastric injury, physicians in routine clinical practice often evaluate treatment effectiveness differently from efficacy demonstrated in randomized clinical trials. Clinical trials are conducted under carefully controlled conditions with high treatment adherence, structured follow-up, and standardized dosing schedules, whereas routine practice involves heterogeneous patient populations, polypharmacy, irregular meal patterns, self-medication with NSAIDs, and variable adherence to dosing instructions. Consequently, physicians may encounter persistent symptoms despite guideline-concordant prescribing, not necessarily because PPIs lack intrinsic efficacy, but because their real-world effectiveness can be influenced by practical challenges such as incorrect timing of administration, poor adherence, delayed onset of maximal acid suppression, and inter-patient variability in response. Such factors may contribute to the perception, held by most respondents, that PPIs are moderately rather than very effective, although they were not measured directly in this survey.

Pharmacological and practical limitations of PPIs

Conventional PPIs are prodrugs that require an acidic microenvironment for activation, accumulate covalently on actively secreting H+/K+-ATPase pumps over several days, and are metabolized predominantly via CYP2C19 [11,12]. These properties correspond to several of the predefined limitations most frequently endorsed by respondents.

First, because only pumps actively secreting acid at the time of dosing are irreversibly bound, PPIs must be timed 30-60 minutes before a meal to coincide with meal-stimulated pump activation; pumps recruited later in the day, or overnight, remain unblocked. This mechanistic constraint may contribute to both the delayed onset to maximum effect (typically requiring several days of consecutive dosing to inhibit a sufficient proportion of the total pump pool) and nocturnal acid breakthrough, as twice-daily PPI dosing does not achieve continuous pump saturation through the overnight period [11,18]. For patients on continuous NSAID or low-dose aspirin therapy who require uninterrupted 24-hour mucosal protection, this incomplete and time-limited coverage may be clinically relevant.

Second, CYP2C19 polymorphism introduces inter-individual variability in PPI exposure: rapid metabolizers clear the drug faster and achieve substantially less acid suppression than poor metabolizers receiving the same dose, a difference demonstrated in pharmacodynamic and real-world studies comparing genotype strata [14,15,29,30]. Because CYP2C19 poor-metabolizer frequency varies by population (reported at roughly 2-6% in Caucasian and 9-23% in East Asian cohorts) [16], and data specific to Indian populations are limited, some Indian patients receiving standard PPI doses could be under-treated; this was not assessed in the present survey.

Vonoprazan and other P-CABs act by a mechanistically distinct route: reversible, potassium-competitive binding to the H+/K+-ATPase that does not require acid activation and is not dependent on the pump being in its active secretory state. This allows rapid acid suppression from the first dose, independent of meal timing, and metabolism is predominantly via CYP3A4 rather than CYP2C19, which reduces genotype-driven variability [19-21]. In a crossover pharmacodynamic study, vonoprazan achieved a pH ⩾4 holding-time ratio of 100% (twice-daily) versus 91% for esomeprazole twice-daily, and a pH ⩾5 holding-time ratio of 99% versus 84%, with greater acid inhibition across CYP2C19 poor, intermediate, and rapid metabolizer strata [29]. In a separate crossover study in healthy volunteers, vonoprazan 20 mg produced faster and greater acid inhibition than esomeprazole 20 mg or rabeprazole 10 mg [31]. These pharmacodynamic characteristics are consistent with the attributes that respondents considered relevant; because respondents were regular prescribers of vonoprazan, their views are likely to reflect clinical experience as well as familiarity with this literature.

Adherence challenges and dosing complexity

Respondents perceived poor adherence to PPI dosing instructions as common: 61 (64.9%) considered the empty-stomach requirement difficult or very difficult for patients to follow, and 65 (69.1%) estimated poor adherence in at least 30% of patients. These are physician estimates rather than measured adherence. Studies of PPI users have shown that many patients do not take PPIs as directed in relation to meals [13], and medication adherence generally decreases as dosing complexity increases [32,33]. Mistimed pre-meal dosing may reduce the pharmacodynamic effect of PPIs [11], although its clinical impact on NSAID- or aspirin-associated injury was not assessed in this survey.

The Indian prescribing context

The relevance of these considerations may be amplified in Indian practice, where NSAIDs are widely used for musculoskeletal conditions and are available without a prescription. Over-the-counter access reduces the opportunity for a physician to reinforce correct timing of co-prescribed gastroprotection. The International Consensus on Guiding Recommendations for Management of Patients with NSAID-Induced Gastropathy (ICON-G), developed with Indian gastroenterology input, recognizes NSAID-induced gastropathy as an important public health concern and endorses risk-stratified gastroprotection [34], and Indian practice-based reviews have highlighted the challenges of optimizing PPI therapy in patients with comorbidities and polypharmacy [17]. Our respondents' endorsement of an unmet need for alternatives, and their preference for meal-independent dosing, are consistent with these practical considerations; however, the near-unanimous agreement with the unmet-need item (96.8%) should be interpreted in light of its wording and the absence of a neutral option.

Vonoprazan: clinical evidence in NSAID and aspirin users

Vonoprazan's effect on NSAID- and aspirin-associated ulcer recurrence has been assessed in randomized non-inferiority trials conducted in Japan. In a phase 3, double-blind, lansoprazole-controlled trial involving 642 patients requiring long-term NSAID therapy who had a history of peptic ulcer, the 24-week rate of endoscopically confirmed ulcer recurrence was 3.3% with vonoprazan 10 mg, 3.4% with vonoprazan 20 mg, and 5.5% with lansoprazole 15 mg. Both vonoprazan doses demonstrated non-inferiority to lansoprazole, with differences in recurrence rates of −2.2% (95% CI, −6.2 to 1.8) for vonoprazan 10 mg and −2.1% (95% CI, −6.1 to 2.0) for vonoprazan 20 mg ($p<0.001$ for non-inferiority for both comparisons). Ulcer recurrence rates remained low during the subsequent single-blind extension [35]. In a parallel phase 3 trial of 621 patients requiring long-term low-dose aspirin, the 24-week peptic ulcer recurrence rate was 2.8% with lansoprazole 15 mg versus 0.5% with vonoprazan 10 mg and 1.5% with vonoprazan 20 mg; both vonoprazan doses were non-inferior to lansoprazole [36]. Twelve-month post-marketing surveillance data from Japan have reported a consistent safety and effectiveness profile for vonoprazan in preventing gastric and duodenal ulcer recurrence during ongoing NSAID therapy [37]. Importantly, these trials demonstrated non-inferiority, not superiority, to low-dose lansoprazole and were conducted exclusively in Japanese patients; their generalizability to Indian patients, who may differ in *H. pylori* prevalence, CYP2C19 genotype distribution, and patterns of NSAID use, has not been established. These data therefore provide context for, but do not validate, the favorable efficacy ratings given by respondents.

Comparative evidence: vonoprazan versus PPIs

In a randomized crossover pharmacodynamic study, vonoprazan 20 mg twice daily achieved a 24-hour intragastric pH ⩾4 holding-time ratio of 100% and a pH ⩾5 holding-time ratio of 99%, compared with 91% and 84%, respectively, for esomeprazole 20 mg twice daily, irrespective of CYP2C19 genotype [29]. In two phase 3 non-inferiority trials of gastric and duodenal ulcer healing, vonoprazan 20 mg was non-inferior to lansoprazole 30 mg at 8 weeks (93.5% versus 93.8% for gastric ulcer healing; difference -0.3%, 95% CI -4.75 to 4.21) [38]. A recent network meta-analysis of P-CABs versus PPIs for peptic ulcer found broadly comparable healing efficacy between the classes [39]. Thus, any potential advantage of vonoprazan in DIG would be expected to relate to the predictability, speed, and meal-independence of acid suppression rather than to higher healing rates, which are the attributes our respondents prioritized; whether these pharmacodynamic properties translate into better clinical outcomes in routine Indian practice remains to be demonstrated.

Considerations for specific patient groups

The pharmacological profile of vonoprazan raises hypotheses about its use in patient groups at high risk of DIG, which require prospective evaluation.

Elderly Patients

The elderly often have reduced hepatic function and polypharmacy. Vonoprazan's CYP3A4/5 metabolism and lack of acidic activation requirement may make its pharmacokinetics less susceptible to CYP2C19-related variability than those of CYP2C19-metabolized PPIs, although clinical data in elderly Indian patients are lacking.

Cardiovascular Patients on Aspirin

Patients on low-dose aspirin require continuous gastroprotection. In a randomized trial in Japanese patients receiving long-term low-dose aspirin, vonoprazan was non-inferior to lansoprazole for the prevention of ulcer recurrence [36]. Data on interactions between vonoprazan and P2Y12 inhibitors such as clopidogrel are limited, and the absence of the interaction concerns previously raised for PPIs [40] should not be assumed for P-CABs.

Chronic NSAID Users and Polypharmacy

Patients with rheumatological or musculoskeletal conditions on chronic NSAIDs often have irregular meal

schedules, and vonoprazan's meal-independent dosing may reduce one adherence barrier. Consistent with this, 31 (70.5%) of orthopedic surgeons, compared with 12 (32.4%) of physicians, selected meal-independent dosing as the most compelling reason to consider vonoprazan (Appendix B).

Interpretation and Implications

In this sample, Indian physicians reported awareness of practical limitations of PPIs. Respondents managing chronic NSAID users, particularly orthopedic surgeons, considered meal-independent dosing to be the most relevant potential advantage of vonoprazan. Whether rapid, meal-independent, and sustained acid suppression with vonoprazan translates into improved adherence or fewer clinical events in Indian patients with NSAID- or aspirin-associated gastric injury requires evaluation in prospective, patient-level studies, ideally including comparative effectiveness designs.

Limitations

The findings should be interpreted in light of several important limitations. First, this was a cross-sectional survey of physician perceptions; it did not measure patient-level outcomes, actual prescribing, adherence, or the prevalence of persistent symptoms, and physician estimates are subject to recall and other cognitive biases.

Second, the sample comprised regular prescribers of vonoprazan identified by the sponsor's medical representatives and invited via WhatsApp. Prescriber status was based on field-force lists and was not confirmed within the survey, and the number of physicians invited was not recorded, and thus the response rate cannot be calculated. Because all respondents already prescribed the sponsor's product, their views are likely to be more favorable toward vonoprazan than those of physicians in general, and the findings cannot be generalized to physicians who do not prescribe it; physicians with an interest in the topic may also have been more likely to respond. Some respondents received an honorarium from the sponsor, which may also have influenced participation or responses. The sample was unevenly distributed (47.9% from the South zone and 8.5% from the East zone) and comprised mainly orthopedic surgeons and physicians; gastroenterologists, who manage refractory and complicated cases, were not included. The findings therefore cannot be generalized to all Indian physicians and should not be regarded as nationally representative.

Third, the questionnaire was not formally validated, and its design may have biased responses. The survey invitation described its purpose as understanding the practical limitations of PPI therapy and the role of newer therapies such as P-CABs, and several items presented PPI limitations and the proposed advantages of vonoprazan as predefined response options; this framing may have primed respondents and encouraged agreement. In addition, the item on the need for alternatives to PPIs had no neutral option, and the multi-select items did not invite respondents to report advantages of PPIs. Responses to these items should therefore be regarded as endorsement of the options offered rather than as independent observations.

Fourth, no formal case definition of DIG was provided, and respondents may have applied different definitions encompassing dyspepsia, endoscopic gastropathy, and peptic ulcer; these outcomes are not interchangeable. The survey also did not capture *H. pylori* status or testing practices, NSAID type and dose, or concomitant antithrombotic therapy.

Fifth, although all respondents were regular prescribers of vonoprazan, the duration of each respondent's experience and the number of patients they had treated with it were not recorded. In addition, the global rating scale lacked explicit comparative anchors (e.g., worse than, similar to, or better than PPIs); thus, the ratings cannot be interpreted as evidence that respondents regard vonoprazan as superior to PPIs.

Finally, the study was sponsored by the company that markets vonoprazan in India, three authors are employees of the sponsor, and the survey was programmed and analyzed by a contract research organization funded by the sponsor. Although all data are reported in full, these relationships represent a potential source of bias. Despite these limitations, the survey provides descriptive, hypothesis-generating information on how a sample of Indian physicians who frequently prescribe NSAIDs perceive the practical limitations of PPI therapy, an area in which Indian data are scarce.

Conclusions

In this sponsor-supported sample of 94 Indian physicians who regularly prescribe vonoprazan, most respondents rated PPIs as moderately effective for DIG and reported perceived practical limitations related to pre-meal dosing, adherence, and sustained acid suppression. Respondents most frequently identified meal-independent dosing and durable acid suppression as relevant potential attributes of vonoprazan and rated its efficacy and tolerability favorably in global assessments. These findings reflect physician perceptions only and do not establish the comparative effectiveness or safety of vonoprazan. Prospective, patient-level studies in Indian patients receiving NSAIDs or low-dose aspirin are needed to determine whether these perceived advantages translate into improved adherence and clinical outcomes.

Appendices

The GAP-DIG survey instrument comprised 20 items organized into a screening/practice-profile block and five thematic sections (A-E), administered as a structured, self-administered online questionnaire. Item wording, response format, and full response options are reproduced in the table below, with section headings as displayed to respondents. All items were mandatory. Question 20 constituted the participant self-declaration and informed-consent item.

Survey invitation (displayed to respondents before Question 1): "Dear Doctor, We invite you to participate in this survey designed to capture your valuable clinical insights. The purpose of this study is to understand the practical limitations of proton pump inhibitor (PPI) therapy in patients with drug-induced gastritis (DIG), particularly those related to NSAID and aspirin use. Despite being a mainstay of acid suppression for the past 25+ years, PPIs may not always provide optimal protection in real-world practice in the management of DIG. Your first-hand experiences in managing such patients are essential to identify existing challenges, unmet needs, and the role of newer emerging therapies like P-CABs. Your responses will remain confidential and will contribute to a better understanding of clinical practice patterns and potential opportunities for improving patient care. We greatly appreciate the time and expertise you are investing in this initiative. Thank you for your participation."

Appendix A

Q#	Question	Response type / options
Screening & Practice Profile (Q1-Q4)		
Q1	Please enter your full name.	Short answer (required)
Q2	Please indicate your area of specialization.	Single-select: General Surgeon; Orthopedic Surgeon; Consultant Physician; General Physician; Other (specify)
Q3	Please specify your current practice location and affiliation (Hospital/Clinic, City, State).	Short answer (required)
Q4	Please indicate how many patients with drug-induced gastritis you have treated with PPIs in the past 6 months.	Single-select: Less than 50; 51-100; 101-200; More than 200
Section A: Clinical Experience with PPI Therapy (Q5-Q9)		
Q5	How effective do you find PPIs in managing symptoms of drug-induced gastritis in your daily practice?	Single-select: Very effective; Moderately effective; Minimally effective; Not effective at all
Q6	After initiation of PPI therapy, when is maximum symptom relief usually noticed in patients with drug-induced gastritis?	Single-select: Within 1 day; 2-3 days; 4-7 days; More than 7 days; Relief is often inconsistent or delayed
Q7	In drug-induced gastritis cases, how often do PPIs require adjunct/additional therapy to manage symptoms?	Single-select: Rarely; Sometimes; Often; Almost always
Q8	To what extent do you agree: “Despite PPI therapy, a subset of my patients with drug-induced gastritis continue to experience persistent symptoms or ulcer recurrence”?	Single-select: Strongly agree; Agree; Neutral; Disagree; Strongly disagree
Q9	What percentage of patients on NSAIDs or low-dose aspirin still experience GI symptoms despite being on PPI prophylaxis?	Single-select: Less than 30%; 30-40%; 40-50%; 50-60%; More than 60%
Section B: Patient Adherence and Real-World Challenges (Q10-Q12)		

Q10	What are the main reasons drug-induced gastritis patients discontinue or poorly adhere to PPI therapy?	Multi-select: Requirement to take before meals (timing inconvenience); Delayed onset of symptom relief; Incomplete control of symptoms (e.g., night-time breakthrough); Need for twice-daily doses in some cases; Perceived/experienced side effects (e.g., bloating, headache); Concerns about long-term safety; Lack of perceived benefit; Symptom resolution leads to discontinuation; I rarely see poor adherence; Other (specify)
Q11	How feasible is it for your patients to follow the 'empty stomach' requirement for PPI dosing consistently?	Single-select: Very feasible; Somewhat feasible; Difficult; Very difficult
Q12	How often do you observe poor adherence to PPI dosing instructions (once daily, ideally 30-60 minutes before the first meal) among your patients?	Single-select: Less than 10% of patients; 10-30% of patients; 30-50% of patients; More than 50% of patients
Section C: Pharmacological Limitations of PPIs (Q13)		
Q13	How important is it to you that an acid suppressant works independently of food timing (i.e., can be taken with or without meals)?	Single-select: Not important; Somewhat important; Important; Very important
Section D: Therapy Gaps (Q14)		
Q14	What are the common limitations you observe with PPI therapy in managing drug-induced gastritis?	Multi-select: Slow onset of action; takes days for full effect; Requirement to be taken before meals for optimal efficacy; Incomplete suppression of night-time acid secretion; Breakthrough symptoms despite twice-daily dosing; Variable response due to CYP2C19 metabolic differences; Inconsistent acid control during early days of therapy; Suboptimal protection in patients on chronic NSAID/aspirin therapy; I don't observe major limitations
Section E: Vonoprazan (Q15-Q20)		
Q15	Please indicate your level of agreement: "There is a clinical need for alternatives to PPIs that offer faster, more consistent acid suppression in NSAID/aspirin-induced gastritis."	Single-select: Strongly agree; Agree; Disagree; Strongly disagree
Q16	Which potential advantages of vonoprazan over PPIs are relevant in your clinical setting?	Multi-select: Achieves target acid suppression rapidly (within ~2 hours); Acid suppression independent of meal/timing of dosing; Binds both active and inactive proton pumps and has slow dissociation; Longer half-life, enabling more durable 24-hour (including nighttime) acid control; More consistent response (CYP3A4/5 metabolism; less genetic variability vs CYP2C19); Stronger healing efficacy in drug-induced gastritis patients
Q17	In your opinion, what is the most compelling reason to consider vonoprazan over conventional PPIs in NSAID/aspirin-induced gastritis?	Single-select: Faster onset of symptom relief and mucosal protection; Meal-independent dosing convenience; More consistent and sustained 24-hour acid suppression; Superior night-time acid control and fewer acid breakthrough episodes; Less variability in response due to CYP3A4/5 metabolism (vs CYP2C19 for PPIs); Stronger healing efficacy in drug-induced gastritis patients; I see no compelling reason to switch
Q18	Global Assessment of Efficacy: Compared to conventional PPIs, how would you rate the overall efficacy of vonoprazan in managing drug-induced gastritis?	Single-select: Excellent; Very Good; Good; Fair; Poor
Q19	Global Assessment of Tolerability: Compared to conventional PPIs, how would you rate the overall tolerability of vonoprazan in managing drug-induced gastritis?	Single-select: Excellent; Very Good; Good; Fair; Poor
Q20	Self-declaration of research-only use, de-identified responses, and consent to aggregate publication.	Confirmation checkbox (required)

TABLE 3: GAP-DIG survey questionnaire (20 items; n = 94 respondents)

GI, gastrointestinal; NSAID, non-steroidal anti-inflammatory drug; PPI, proton pump inhibitor

Appendix B

Item	Physician (n=37)	Orthopedic Surgeon (n=44)	General Surgeon (n=11)	Other (n=2)	Overall (N=94)
PPIs moderately effective (Q5)	30 (81.1)	34 (77.3)	11 (100.0)	1 (50.0)	76 (80.9)
PPIs very effective (Q5)	4 (10.8)	8 (18.2)	0 (0.0)	1 (50.0)	13 (13.8)
Agree/strongly agree: persistent symptoms or recurrence despite PPI (Q8)	34 (91.9)	35 (79.5)	9 (81.8)	1 (50.0)	79 (84.0)
Empty-stomach dosing difficult/very difficult (Q11)	25 (67.6)	28 (63.6)	7 (63.6)	1 (50.0)	61 (64.9)
Poor adherence observed in ≥30% of patients (Q12)	24 (64.9)	30 (68.2)	9 (81.8)	2 (100.0)	65 (69.1)
Food-timing independence important/very important (Q13)	28 (75.7)	35 (79.5)	10 (90.9)	1 (50.0)	74 (78.7)
Agree/strongly agree: need for alternatives to PPIs (Q15)	35 (94.6)	43 (97.7)	11 (100.0)	2 (100.0)	91 (96.8)
Meal-independent acid suppression relevant (Q16)	34 (91.9)	39 (88.6)	11 (100.0)	2 (100.0)	86 (91.5)
Meal-independent dosing as most compelling reason (Q17)	12 (32.4)	31 (70.5)	7 (63.6)	2 (100.0)	52 (55.3)
Vonoprazan efficacy rated very good/excellent (Q18)	24 (64.9)	35 (79.5)	7 (63.6)	2 (100.0)	68 (72.3)
Vonoprazan tolerability rated very good/excellent (Q19)	21 (56.8)	29 (65.9)	8 (72.7)	2 (100.0)	60 (63.8)

TABLE 4: Selected survey responses by physician specialty

Values are presented as n (%). Percentages for the “Other” group (n = 2) should be interpreted with caution.

No inferential statistical testing was performed.

PPI, proton pump inhibitor; Q, questionnaire item number (Appendix A)

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Vidhya Natarajan, Sameer Muchhala, Gauravee R. Chavan, Saurabh Mukewar, Kailash C. Dash, Mrinal Jaiswal

Acquisition, analysis, or interpretation of data: Vidhya Natarajan, Sameer Muchhala, Gauravee R. Chavan, Saurabh Mukewar, Kailash C. Dash, Mrinal Jaiswal

Drafting of the manuscript: Vidhya Natarajan, Sameer Muchhala, Gauravee R. Chavan, Saurabh Mukewar, Kailash C. Dash, Mrinal Jaiswal

Critical review of the manuscript for important intellectual content: Vidhya Natarajan, Sameer Muchhala, Gauravee R. Chavan, Saurabh Mukewar, Kailash C. Dash, Mrinal Jaiswal

Supervision: Vidhya Natarajan, Sameer Muchhala, Kailash C. Dash

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