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Review Article

Evolving therapeutics in acid-related disorders of the gut: is vonoprazan the drug of the next decade

Mehak Roy[1]*, Abhi Shah[2], Subham Bhowmik[3], Ishita Panchal[4], Viraj Panchal[2], Vedant Shah[2], Sanket Bharadwaj[2]

[1]Department of Medicine, School of Medical Sciences and Research, Greater Noida, Uttar Pradesh, India
[2]Department of Medicine, Smt. N.H.L Municipal Medical College and SVPISMR, Ahmedabad, Gujarat, India
[3]Department of Pathology, All India Institute of Medical Sciences, New Delhi, India
[4]Jawaharlal Nehru Medical College, Belagavi, Karnataka, India

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***Correspondence:**
Dr. Mehak Roy,
Email: mehakroy123@gmail.com

ABSTRACT

Vonoprazan a competitive potassium acid blocker (P-CAB) has been gaining traction compared to the use of traditional PPIs for the treatment of GERD and other acid-related disorders. We aim to review its comparative edge over the other widely used PPIs and its combination therapies in this article. It is also emerging to show superiority in mucosal and clinical healing rates in the already published literature. The mechanism of action of vonoprazan involves the antagonism of potassium channels present in parietal cells, thereby inhibiting gastric acid secretion. This distinctive mode of action effectively suppresses acid secretion in gastroesophageal reflux disease (GERD) and erosive esophagitis. For clinical usage, 20 mg of vonoprazan has been reported to be more effective in the management of acid-related disorders compared to conventional PPIs. This article underscores the need for continued research to fully elucidate the potential of vonoprazan in managing acid-related disorders, particularly in populations beyond Japan where its utility remains to be fully explored. It also aims to enlighten healthcare providers regarding its usage in the management of acid-related gastrointestinal disorders by providing insights into its clinical utility, practical considerations, & effective drug combinations eventually ameliorating patient outcomes and quality of life.

Keywords: Erosive esophagitis, Gastroesophageal reflux disease, Proton pump inhibitors, Potassium-competitive acid blockers, Vonoprazan

INTRODUCTION

The contemporary way of living has contributed to a rise in the prevalence of peptic ulcer disease, gastroesophageal reflux disease, and various other acid-related gastrointestinal conditions. Medications designed to prevent these ailments' function either by blocking H2 receptors or inhibiting the H+, and K+ ATPase enzymes. Proton pump inhibitors are effective, but they work slowly and may not fully relieve symptoms for most patients. In contrast, potassium-competitive acid blockers (P-CABs) bind reversibly to potassium ions and inhibit the H+, K+ ATPase enzyme reducing acid production with faster onset of action. The first P-CAB drug SCH280280 blocked the enzyme through a competitive interaction with the potassium site. However, its progress was halted due to its toxic effects on the liver.[1] The first P-CAB introduced in clinical settings was revaprazan (YH-1885, Revanex), available in the South Korean market. Despite its fast onset of action like other P-CABs, it did not demonstrate

superiority over the current proton pump inhibitors (PPIs).[2] Vonoprazan fumarate (TAK-438) was introduced in Japan in 2015 and was the second P-CAB to enter clinical use.

It is a potassium-competitive acid blocker, that works by competitively inhibiting the availability of potassium to hydrogen-potassium ATPase, reducing acid secretion. It quickly became popular due to its qualities which addressed the shortcomings of traditional Proton pump Inhibitor therapy such as short half-life, vulnerability to destruction in acidic environments, limitation to only activated proton pumps, the need for multiple doses before full effectiveness is achieved, and variability in clinical outcomes due to CYP2C19 polymorphisms. Vonoprazan fumarate is used to treat acid-related conditions in addition to eradication therapy.[2,3]

METHODS

Mechanistic insights

Conventional drugs such as PPIs work by converting non-catalytically, into an active form that forms a covalent bond with H+, K+-ATPase, inhibiting the enzyme in the canalicular spaces when the environment becomes highly acidic.[4] In contrast, H+, K+-ATPase may also be inhibited by reducing the availability of potassium ions (K+) for the enzyme. Since H+, K+-ATPase maintains an electrical balance by transporting equal amounts of hydrogen ions (H+) and K+ bidirectionally, the availability of K+ remains critical for its activity. The secretion of HCl in the gastric lumen results from conformational changes in the H+, K+-ATPase upon the binding of H+ and K+ to it, in the parietal cells. Potassium-competitive acid blockers (P-CABs) competitively and reversibly interfere with K+ binding to the enzyme. 5P-CABs, with higher pKa values and stability under low pH conditions in comparison to PPIs, accumulate in secretory canaliculi at higher concentrations, acting on H+K+-ATPase regardless of its activity status (Figure 1). Conducting molecular studies, to better understand the anatomy of the site of action of P-CABs, it has revealed a single high-affinity K+ binding site located in the transmembrane helix of the enzyme.[5] Differences in affinity and dissociation constants for H+, and K+-ATPase binding sites are the reason for the noted variations in potency and duration of action among different P-CABs. For instance, vonoprazan exhibits higher affinity and slower dissociation compared to other P-CABs, resulting in prolonged action. Studies conducted to understand vonoprazan's accumulation and clearance from the gastric pit have revealed its potential for more sustained acid suppression compared to conventional PPIs. This is on account of its significantly higher accumulation and slower clearance.[6]

Safety and tolerability

For the treatment of acid-related disorders (ARDs), the safety profile of vonoprazan is commendable yet as in the case with any other drug few concerning adverse events have been reported.[7] These have been stated as follows.

Hepatotoxicity

A major safety concern with P-CABs, including VPZ, though its incidence with VPZ remains extremely rare. These abnormalities were mostly associated with reversible elevations in serum alanine transaminase (ALT) or aspartate transaminase (AST) levels, In a few cases elevations exceeding 500 IU/l have been reported.[8]

Hypergastrinemia

Hypochlorhydria-induced hypergastrinemia remains an adverse effect induced on account of VPZ usage, elevation in serum gastrin levels is a potential concern due to its trophic effects on the epithelial cells of the stomach and intestine. Preclinical studies in rodents have suggested a possible link between sustained hypergastrinemia and the development of gastrointestinal malignancies, such as neuroendocrine tumors. Vigilant post-marketing surveillance needs to be conducted to address these concerns in humans.[9]

Gastropathy

P-CABs are related to a spectrum of gastric mucosal lesions, some shared with PPIs while others remain unique to P-CABs. Fundic gland polyps (FGPs), hyperplastic polyps (HPs), multiple white and flat elevated lesions (MWFELs), cobblestone-like mucosa (CLM), black spots (BS), gastric mucosal redness (GMR), white spots (WS), and web-like mucus are some of the mucosal lesions already reported in the literature.[10] FGPs, characterized by small size and a whitish-reddish appearance, have shown an association with long-term PPI use and P-CAB therapy, their regression has been reported with withdrawal of the concerned drug HPs, identified by their reddish color and papillary surface, have been linked to PPI and P-CAB use and have displayed a similar trend of regression post-P-CAB cessation.[11,12] MWFELs, exhibiting white, round, elevated mucosa, and CLM, displaying a cobblestone-like appearance, have also been associated with PPIs and P-CABs. P-CAB therapy remains a cause for its occurrence along with BS, WS, and GMR on account of increased gastrin levels. Other Adverse Effects: VPZ treatment has been associated with less common adverse reactions including allergic reactions, headache, nausea, dizziness and fatigue.[3] A brief overview of the same has been given in Table 1.[13,14]

Combination therapy with vonoprazan

Reduction in eradication rates of *H. pyroli* globally, on account of resistance to current combination therapies is concerning, as a result, multi-drug regimens form the cornerstone in curing this infection. Currently, the combination of metronidazole, omeprazole, and clarithromycin remains effective.[15] However, with

increasing antibiotic resistance it is paramount to have an alternate combination therapy for *H. pyroli* eradication. Vonoprazan has been tried and used in various combinations along with triple, dual, and other antimicrobials. Vonoprazan has rapid and sustained acid control, its inhibitory effect does not depend on the meal timings, with an early onset of action within 24 hours, and the gastric pH stays >4 for more than 90% of the day. Its long half-life, makes the drug bind reversibly to active H+/K+-ATPase pumps and inactive pumps, with a slower dissociation rate.[16]

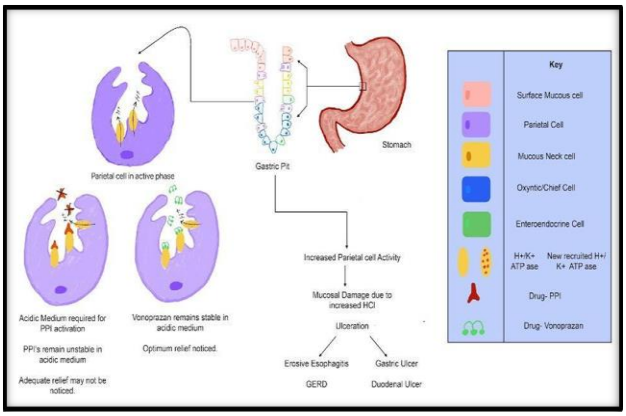

Figure 1: Mechanistic insights comparing the action of PPIs v/s vonoprazan in a gastric environment.

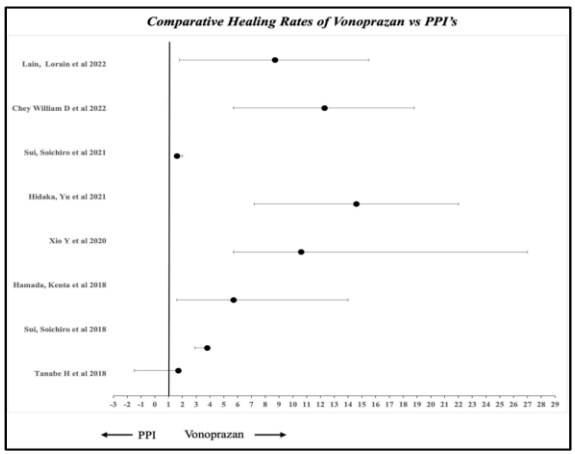

Figure 2: The k Forest plot depicting clinical efficacy of Vonoprazan in comparison with PPIs.

DUAL THERAPY

Furuta et al concluded that dual therapy with only vonoprazan and amoxicillin is just as effective as triple therapy, 92.9% and 91.9%, respectively. This made it clear that neither clarithromycin nor metronidazole as a second antibiotic contributes that much to the eradication rate of H. pylori. Research conducted in Japan on vonoprazan dual therapy found efficacy rates close to 93%, which was similar to those with triple therapy.[17] Additionally, a meta-analysis revealed improved eradication rates in vonoprazan dual therapy, compared to triple regimens containing a PPI and clarithromycin or rifabutin. It was also noted that vonoprazan dual therapy had an equal efficacy to bismuth-based quadruple therapy, despite utilizing fewer antimicrobials.

A study by Zuberi et al, where vonoprazan amoxicillin dual therapy was used for 14 days showed a significantly higher eradication rate of *H. pyroli* bacteria of up to 93.5% compared to PPI-based therapy which showed 83.9% eradication rate ($p<0.05$).[18] It is also seen repeatedly that whenever vonoprazan was used in either 7 day dual or triple therapy along with amoxicillin or amoxicillin and clarithromycin, a higher rate of eradication of 85% to 87% was observed.[19] In addition to vonoprazan to dual therapy to eradicate *H. pylori*, many studies have demonstrated better tolerability than PPI-based triple therapy with significantly lower incidence of adverse effects like nausea vomiting, bloating, and diarrhea without stopping the regimen.[18]

Similarly, a meta-analysis focusing on the efficacy and safety of vonoprazan-based therapy showed a significantly lower incidence of adverse events with the vonoprazan-based dual therapy (32.7%) compared to traditional PPI-based therapy (40.5%). It also showed an odds ratio of 0.71 with a highly significant 95% CI of 0.53-0.95 and a $p<0.05$, providing more knowledge on the better tolerability of vonoprazan-based dual therapy.[20] Peng X et al, conducted a study focusing on the eradication rate of H. Pyroliusing a 14-day combination therapy of VA-dual group (vonoprazan 20 mg b.i.d + amoxicillin 750 mg q.i.d) or EACP-quadruple group (esomeprazole 20 mg+amoxicillin 1000 mg+clarithromycin 500 mg+colloidal bismuth subcitrate 220 mg bid). Their findings were assessed using a 13C-urea breath test (UBT) and found eradication rates of 89.9% and 81% respectively in both groups. ($p=0.037$).[21] Hence this study was able to signify antimicrobial stewardship and the idea of using fewer antimicrobials to achieve higher eradication rates.

TRIPLE THERAPY

Studies have been conducted for assessing triple therapies with Vonoprazan-Amxocillin-Clarithromycin (VAC) or metronidazole in place of clarithromycin. They showed a universally high eradication rate. Mahrous et al. found a 90% cure rate using 500 mg metronidazole.[22] Similarly, Katayama et al found a cure rate of 87% using 250 mg of metronidazole. To date, there is controversy over using clarithromycin over metronidazole in triple therapy. Katayama et al concluded a similar cure rate as compared to metronidazole i.e, 90.6%.[23] Tanabe et al found an eradication rate of 94.4% with clarithromycin triple therapy and a slightly higher rate of 97.1% with metronidazole in the triple therapy.[24] The superior efficacy of metronidazole can be explained by the increased resistance to clarithromycin. Various studies have been conducted demonstrating the higher cure rates with vonoprazan triple therapy as compared to the traditional PPI triple therapy. In a study conducted by Chey et al

vonoprazan triple therapy eradicated *H. pyroli* 84.7% (222 of 262) of patient's vs 78.8% (201 of 255) for lansoprazole triple therapy. In the same study, a sub-analysis with clarithromycin-resistant strains was conducted. Vonoprazan triple therapy eradicated *H. pyroli* in 65.8% of patients (48 of 73) within the full analysis set compared with 31.9% (23 of 72) on lansoprazole triple therapy.[25] H. Pyrolieradication requires high-efficacy gastric acid suppression. In a study titled SAMURAI pH, conducted by Takeuchi et al, vonoprazan produces more substantial suppression of gastric acidity than PPIs.[26] These results from the United States and Europe support previous Japanese studies that reported higher eradication rates with vonoprazan-based regimens than with PPI-clarithromycin–based triple therapy. Vonoprazan tripletherapy was successful in up to 96% of patients in these Japanese studies, including up to 83% with clarithromycin-resistant strains, vs 70% to 77% of patients who received PPI-based triple therapy.[27]

Table 1: Adverse effects observed in patients treated with PPI's and vonoprazan.

Adverse Events	
Proton pump inhibitors[2]	**Vonoprazan**[3]
Hypergastrinemia	Hypergastrinemia
Malabsorption	Diarrhoea
Hypochlorhydria	Constipation
Interstitial nephritis	Flatulence
Collagenous colitis	Hepatotoxicity
Dementia	Gastropathy
Myocardial infarction	Skin reactions

Table 2: Superior healing rates of vonoprazan compared to PPIs evaluated through RCTs conducted in the last 6 years.

S. No	RCT study	Year	Comparative healing rates of vonoprazan Vs PPI	Lower 95% CI	Upper 95% CI
1	**Tanabe H et al**[55]	2018	1.7*	-4.9	1.7
2	**Sui, Soichiro et al**[29]	2018	3.8*	2.9	3.8
3	**Hamada, Kenta et al**[56]	2018	5.7*	1.6	14
4	**Xio Y et al**[51]	2020	10.6*	5.7	27
5	**Hidaka Yu et al**[57]	2021	14.6*	7.2	22
6	**Sui, Soichiro et al**[27]	2021	1.6*	1.5	2
7	**Chey William D et al**[25]	2022	12.3*	5.7	18.8
8	**Lain Lorain et al**[58]	2022	8.7*	1.8	15.5

*p value<0.05 is significant

Lesser used combinations

Sitafloxacin

The standard treatment regimens of PPI with clarithromycin or triple therapy, even including vonoprazan, are sometimes insufficient for maintaining the required round-the-clock acid suppression for successful eradication of *H. Pyroli* in a few patients. In those circumstances, sitafloxacin (STFX) has been tried and has shown efficient capability when combined with other first-line therapies. It is a quinolone antibiotic that, is an effective third-line alternative in clarithromycin and metronidazole resistance or intolerance. STFX inhibits DNA gyrase and topoisomerase IV, enzymes that are essential for microbial DNA repair and replication. Topoisomerase IV is more sensitive to the antimicrobial effects of STFX as compared to other fluoroquinolones such as levofloxacin (LVFX) or ciprofloxacin. STFX is found to be more efficacious for LVFX-resistant H. Pyrolistrains. The prevalence of STFX resistance in H. Pyroliis less than 10%, which serves as a significant incentive for its use in its treatment.[28] Sitafloxacin has a very low MIC and is a very acid-sensitive antimicrobial, whose activity greatly increases in environments with potent acid suppression. Therefore, its efficacy becomes compounded more with vonoprazan as compared to the standard PPI regimen, as shown in an RCT conducted by Sue et al., patients were divided into two treatment groups, one receiving VPZ/AMX/STFX bid for 7 days and another receiving PPI/AMX/STFX bid for 7 days. ITT analysis for both groups was concluded to be 75.8% (95% CI: 57.7–88.9%) and 53.3% (95% CI: 34.3–71.7%) respectively.[29] Although an eradication rate close to 75% is not ideal, it reinforces an acceptable scenario for metronidazole or clarithromycin-resistant cases. STFX has also been tried successfully as an alternative in patients with penicillin/amoxicillin allergy. PPI/STFX/MNZ may be used which not only addresses the penicillin allergy but also the component of clarithromycin resistance which is widely prevalent.[30]

Bismuth

Various studies have assessed the use of bismuth-based quadruple therapy with vonoprazan. Of note, in a study conducted on the Chinese population by Lu et al, patients (n=234) were divided into three groups of 1:1:1 ratio to receive vonoprazan 20 mg daily+amoxicillin 1000 mg+furazolidone 100 mg twice a day+colloidal bismuth 200 mg twice a day for 10 days (V10) or 14 days (V14), or esomeprazole 20 mg+amoxicillin 1000 mg +

furazolidone 100 mg twice a day+colloidal bismuth 200 mg twice a day for 14 days (E14). The eradication rates in the V10, V14, and E14 groups were 96.2% (89.2-99.2%), 94.9% (87.4-98.6%), and 93.6% (85.7-97.9%).[31] Bismuth-based combination therapy is used given its cost-effectiveness. Dore et al also showed that the addition of bismuth to the *H. Pyroli* eradication therapy increased the rate by 30% in antibiotic-resistant strains.[32] However, bismuth being a heavy metal is known to harm the central nervous system, kidneys and may also cause bismuth-related osteoarthropathy and toxic encephalopathy.[33] Similarly, Chen et al, when evaluated a new triple therapy avoiding bismuth, showed a higher efficacy rate similar to that of bismuth-based quadruple therapy.[34] Hence, using bismuth-based therapy needs surveillance for better tolerability.

DISCUSSION

Expected challenges with its usage in daily practice

With the rising usage of this novel drug for GERD and other ailments, bacterial resistance to it is bound to develop. Vonoprazan is hailed for reducing the load of clarithromycin-resistant strains. In combination with amoxicillin, it allows the latter to clear these clarithromycin-resistant strains effectively. Hence, it has become a viable option to replace triple therapy with dual vonoprazan-amoxicillin therapy. The long-term effectiveness of vonoprazan remains to be analyzed. Sufficient data is not available to calculate the resistance developing to this novel drug, much of its efficacy when used in a triple or dual therapy relies on the dose of the other acting antibiotic and the duration of therapy itself. With the increasing resistance to clarithromycin, the effectiveness of triple therapy with either the novel vonoprazan-based combination or the traditional PPI-based combination is declining.[35] Over-prescribing triple therapy containing VAC (Vonoprazan, Amoxicillin, Clarithromycin) is contributing to increased clarithromycin resistance. Remedies include substitution of clarithromycin with metronidazole or rifabutin, but this is at the cost of optimal medical therapy.

Insights on comparative efficacy to traditional PPIs

For the Department of Gastroenterology in the United States, the most common outpatient complaint with its subsequent diagnosis remains Gastroesophageal reflux disease (GERD); affecting 20% of the adult population by the week with 7% occurring daily.[36] non-erosive reflux disease (NERD), Erosive Esophagitis (EE) and Barrett's esophagus are the 3 categories within the GERD. Of these non-erosive reflux's disease and Erosive esophagitis, both have varied treatment responses to anti-reflux medication.[37] In a randomized open-label cross-over study conducted by Sakurai Y et al in 2015 in Japan, the acid-inhibitory effects of vonoprazan 20 mg were compared with esomeprazole 20 mg and 10 mg of rabeprazole in the healthy adult population. The clinical endpoint of this cross-over study was to measure change or reduction in gastric pH at the end of 24 hours and variations in mean gastric pH observed over a week post-administration of these drugs. The findings in this study noted that on days 1 and 7, vonoprazan's acid-inhibitory effect was significantly higher than esomeprazole or rabeprazole. At the end of the week reduction in gastric pH levels was about 25% more in the vonoprazan cohort compared to the esomeprazole group; similarly, it was nearly 29% less when compared to the group administered with rabeprazole. In stark contrast, the reduction in gastric pH levels was only 0.37 for the esomeprazole and 0.39 for the rabeprazole group. Compared to esomeprazole (20 mg) or rabeprazole (10 mg), this study showed that vonoprazan (20 mg) had a more fast and prolonged acid-inhibitory action.[38] An additional advantage of vonoprazan compared to PPIs is that its absorption is not dependent on the food intake, thus its intake is independent of meal timings, providing better compliance than PPIs.[39] Furthermore, it was also demonstrated on esophageal impedance-pH testing that PPI treatment twice daily failed to completely decrease acidic suppression, especially during nighttime.[40] A recent Systematic Review with meta-analysis published by Sinadibrata DM et al in January 2024 compared the efficacy and safety of vonoprazan with PPIs to treat PPI-resistant GERD.

It primarily evaluated the maintenance rates and endoscopic mucosal healing achieved. The improvements if any were scaled per the Frequency Scale for Symptoms of GERD (FSSG) scores. Serious Adverse events if any had also been considered in this study. The present meta-analysis comprised twelve studies. PPI-resistant EE when compared with vonoprazan was found to be more efficacious than PPIs endoscopic mucosal healing was achieved in about 90% of the cases within 8 weeks. The study further evaluates the remission rates on maintenance regimen and vonoprazan was found to be highly efficacious as at 48 months around 94% of the patients who had achieved symptomatic and endoscopic remission continued to be in remission. The study documented patients reporting symptomatic resolution in around 75% of the cases under the Frequency Scale for Symptoms of GERD (FSSG) scores. A comprehensive review of RCTs conducted within the last 6 years noted a significant improvement in the resolution of symptoms when treated with vonoprazan (Table 2, Figure 2). The safety record of the drug was excellent as no serious adverse events had been reported. Minor events have been enlisted in Tables.

RCTs and the evidence they provide

Compared with present first-line regimens, P-CABs have displayed prolonged gastric acid inhibitory effects.[26] In a study published by Ota K et al on Japanese healthy adults in 2021, for the first time slowing of gastric emptying was demonstrated when vonoprazan was administered at a dosage of 20 mg per day, it has better acid suppression abilities than conventional dosing regimens.[26,42] In this study, complete suppression of gastric acid secretion was

not observed at 10 mg of VPZ, extrapolated further a dose-dependent nature was noted, on a dosage of 20 mg of VPZ, and near-total suppression of gastric acid was observed.[43] The relation between gastric acid secretion & gastric emptying is not a linear one. If studied with proton pump inhibitors a delay is noted, particularly with solids as an acidic environment is a precondition for the hydrolysis of peptide linkages. With liquids, studies have remained inconclusive.[44] For vonoprazan gastric emptying time on a routine dosage remains delayed but could be both accelerated or decelerated. On a routine basis, it is administered at 20 mg but it can also be given at 10 mg doses, therefore it was found that the process of stomach emptying may speed up if there is a slight suppression of gastric acid output. In contrast, delayed stomach emptying may occur when gastric acid secretion is significantly reduced to levels of complete absence. It is uncertain how much the inhibition of stomach acid secretion affects the timing of gastric emptying, significant individual variations would be present. This may have resulted in variation in stomach emptying, more prominently seen with 10 mg of VPZ.[43] Vonoprazan though efficacious and in certain contexts has been proven to be better than the existing first-line drugs. These findings remain more consistent when the cohort is a Japanese adult population. These results cannot be extended to other demographics within Asia itself as the findings become more inconsistent. An RCT was conducted by Sarita RA et al in 2023. The study provided insights into the effectiveness of vonoprazan in eradicating *H. Pyroli* in the Thai population. At the end of the trial, a week's and even 2 weeks of high-dose dual regimen treatment with VPZ was found to be ineffective in alleviating symptoms and eradicating H. pylori. The trial further recommended the addition of bismuth to both vonoprazan-based dual therapy and high dose vonoprazan dual therapy for achieving desirable cure rates. These findings were more consistent with the US than Japan.[45] Chinese literatures were not encouraging enough including a study performed by Hu Yi et al in 2022. The trial noted that in the Chinese population a 7 or 10-day vonoprazan dual therapy, co-administered with amoxicillin b.i.d or even t.i.d fails to treat satisfactorily H. pylori-based conditions and necessary optimization with other known treatment regimens was necessary.[46] A Study by Laine Loren et al in 2022 based on the American population reported findings in line with Japanese research papers on improved inhibition of intragastric acidity and better efficacy than standard treatment schedules currently present.[47]

Its role in erosive esophagitis

One of the mainstays of therapies used in erosive esophagitis (EE) is to suppress the acid secretion for which PPIs are the mainstay.[48] Yet about 10-20% of the patients with Los Angeles (LA) C and D grades in EE have shown no successful healing with 8-week-long PPI therapy.[49] Hence, exploring newer medications like vonoprazan becomes important in EE. The treatment guideline of EE focuses on targeting medication that can relieve symptoms, healing, and maintaining the patient in remission for EE which further prevents the complication. According to the ACG guidelines, treatment regimens should focus on healing and then shift to the maintenance phase.[50]

Till now, Vonoprazan has shown clinical efficacy in both these phases. A phase 3 randomized double-blinded study done by Xiao et al on the Asian population to show non-inferiority of vonoprazan versus lansoprazole in EE showed that patients with LA classification grade C/D, showed a higher rate of healing with vonoprazan compared to lansoprazole, with similar safety outcomes in EE.[51] These findings were similar to another phase 3 clinical trial where vonoprazan showed 92.4% healing rates versus lansoprazole with 91.3% healing rates.[52] In both these studies, vonoprazan was able to show higher healing rates compared to traditional PPIs in patients with LA grade C/D, showing the superiority of vonoprazan, a novel potassium-competitive acid blocker (P-CAB).

However, all PPIs do not have similar efficacy and potency and both the studies used lansoprazole as a control arm hence it becomes imperative to have further studies that show comparison with various PPIs. A Bayesian network meta-analysis done by Miyazaki H et al, compared vonoprazan with various PPIs for patients with severe EE, it showed a significantly high OR with vonoprazan compared to PPIs.[53] Similar results were obtained by a meta-analysis using six RCTs where vonoprazan showed superiority to PPIs for severe EE.[54] One of the reasons for higher healing with vonoprazan in LA grade C/D may be that the healing of EE directly correlates with intragastric pH and the superiority of vonoprazan has higher acidic suppression compared to PPIs.[26,38,47]

The use of vonoprazan is also explored in the maintenance phase of EE, comparing it with PPIs, where a study by Ashida et al, showed that vonoprazan was well-tolerated as well as showed less than 10% of patients treated showed recurrence of EE with vonoprazan 10 or 20 mg till 52-week maintenance therapy. The most commonly occurring treatment-related emergency adverse event with vonoprazan was nasopharyngitis.[52] Similarly, another phase 3 randomized controlled trial showed that vonoprazan was superior and had less recurrence of EE at the end of 24 weeks compared to lansoprazole.[39]

CONCLUSION

Most unmet requirements in GERD care would be satisfied, if not entirely, by introducing a more potent, long-acting vonoprazan into clinical use. Its clinical efficacy remains excellent in a small cohort of the Japanese population. Extensive trials and studies need to be conducted worldwide, though very recently it has been approved by the US FDA. Considering these short comings, it remains a valuable drug for the resolution of gastric ailments remaining refractory to treatment by conventional drug regimens.

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