Vonoprazan – A New Drug for Acid Peptic Disorders

Vonoprazan represents a novel potassium-competitive acid blocker with a different mechanism of action compared to the traditional proton-pump inhibitors (PPIs). Chemically, it acts by reversibly inhibiting the enzyme H^+/K^+-ATPase in the stomach, blocking acid secretion directly without the need of activated proton pumps.

Why the Need – Limitations of Proton-Pump Inhibitors

PPIs present several limitations in their clinical use. First, they have a short half-life, which means their action is temporary and requires frequent dosing. In addition, they are unstable in acidic environments, necessitating enteric coatings or other forms of protection to ensure absorption in the small intestine. PPIs only inhibit active proton pumps, so they are not fully effective until after multiple doses (usually 3–5 cycles), which may delay clinical benefits. The drug gets absorbed in the small intestine gets into the bloodstream and comes back to the parietal cell to decrease acid suppression, especially in active pumps. For active pumps, we need food in the stomach. This forces the patients to take it preferably before food where an acidic environment can destabilize the drug. We need gastro-resistant forms or any coating to increase the transit in the stomach for it to get absorbed in the small intestine. The pKa of rabeprazole is around 5 while that of lansoprazole is 3.5: the decreased pKa can decrease active forms of the drug. Furthermore, the effectiveness of PPIs can vary based on genetic differences, especially those relating to CYP2C19 polymorphisms. CYP2C19 is an enzyme that metabolizes PPIs, and certain genetic variants can cause patients to metabolize the drug either too quickly or too slowly, leading to reduced effectiveness or increased side effects. This variability can make it difficult to achieve consistent treatment benefits across a varied patient population. Long-term PPI use may reduce stomach acid output, particularly during the daytime postprandial period, lowering iron, calcium, and vitamin B12 absorption and potentially producing a pathological state linked with nutrient deficiency.[1] There are rare studies of auditory impairment and increased likelihood of getting diabetes mellitus[2,3] in patients undergoing long-term PPI treatment.

Overall, these factors combine to limit the efficacy and predictability of PPIs in clinical practice.

Advantages of Vonoprazan

- Quicker onset of activity: Vonoprazan rapidly inhibits the secretion of acid by competitively blocking the enzyme H^+/K^+-ATPase in a direct manner
- Longer duration: It possesses a longer half-life compared with conventional PPIs and thus provides an extended inhibition of acid secretion
- Stability to acid: Unlike PPIs, vonoprazan has stability to acid and therefore does not require any enteric coating
- No dependency on proton-pump activation: Vonoprazan is independent of pump activation and thus offers faster effects
- Less variability in dosage: Most of them are less dependent on genetic polymorphisms, like CYP2C19; thus, their effect is quite predictable
- Fewer administration cycles required: Full therapeutic effect after fewer doses compared to PPIs
- More efficacy: It attains better control of acid-related diseases such as gastro esophageal reflux disease (GERD).[4]

Clinical Studies with Vonoprazan

The clinical studies in adult patients were done for several gastrointestinal conditions and proved that vonoprazan is effective and safe for:

- *Helicobacter pylori* eradication: Vonoprazan has shown efficacy against *H. pylori* and is noninferior to PPIs in an eradication regimen. In the same mentioned above study, the vonoprazan triple therapy eradication rate was 84.7% against nonresistant strains, versus 78.8% for lansoprazole triple therapy
- Heated esophagitis: Vonoprazan does not have inferiority to lansoprazole for healing esophagitis and is superior for healing Los Angeles Classification Grade C/D esophagitis
- Heartburn: Vonoprazan is noninferior to lansoprazole for heartburn-free days
- Duodenal ulcers: Vonoprazan may be useful in the healing of duodenal ulcers.

Side Effects of Vonoprazan

In general, vonoprazan is well tolerated, but like any medication, it does have some side effects. These commonly include diarrhea, nausea, and abdominal pain; constipation and headache are less frequently reported. Of greater concern, however, are long-term risks such as hypomagnesemia, Vitamin B12 deficiency, and increased susceptibility to infections, including *Clostridium difficile*, related to reduced stomach acid.[5-7] Careful monitoring should be considered in patients undergoing prolonged therapy to minimize these risks. The abovementioned two studies included around 1900 adults more than 18 years of either sex.

Conclusion

As such, vonoprazan represents an important step forward in the development of the current PPIs in the treatment of acid-related diseases of the gastrointestinal tract. Because its

start of activity was rapid, with a longer duration of action, acid stability, and lesser reliance on genetic polymorphism, thereby giving a number of clinical advantages. Besides, faster and more predictable action of vonoprazan makes it highly suitable in GERD, eradication of *H. pylori*, and esophagitis treatment. In general, well-tolerated, careful monitoring is required regarding long-term use due to associated risks of nutritional deficiencies and infection susceptibility.

Srinivasan Parthasarathy

Professor, Department of Anesthesiology, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Puducherry, India

Address for correspondence: Prof. Srinivasan Parthasarathy, Department of Anesthesiology, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Puducherry, India.
E-mail: painfreepartha@gmail.com

References

1. Brisebois S, Merati A, Giliberto JP. Proton pump inhibitors: Review of reported risks and controversies. Laryngoscope Investig Otolaryngol 2018;3:457-62.
2. Yee J, Han HW, Gwak HS. Proton pump inhibitor use and hearing loss in patients with type 2 diabetes: Evidence from a hospital-based case-control study and a population-based cohort study. Br J Clin Pharmacol 2022;88:2738-46.
3. Czarniak P, Ahmadizar F, Hughes J, Parsons R, Kavousi M, Ikram M, *et al.* Proton pump inhibitors are associated with incident type 2 diabetes mellitus in a prospective population-based cohort study. Br J Clin Pharmacol 2022;88:2718-26.
4. Abdel-Aziz Y, Metz DC, Howden CW. Review article: Potassium-competitive acid blockers for the treatment of acid-related disorders. Aliment Pharmacol Ther 2021;53:794-809.
5. Chey WD, Mégraud F, Laine L, López LJ, Hunt BJ, Howden CW. Vonoprazan triple and dual therapy for *Helicobacter pylori* infection in the United States and Europe: Randomized clinical trial. Gastroenterology 2022;163:608-19.
6. St Onge E, Phillips B. Vonoprazan: A new potassium-competitive acid blocker. J Pharm Technol 2023;39:139-46.
7. Murakami K, Sakurai Y, Shiino M, Funao N, Nishimura A, Asaka M. Vonoprazan, a novel potassium-competitive acid blocker, as a component of first-line and second-line triple therapy for *Helicobacter pylori* eradication: A phase III, randomised, double-blind study. Gut 2016;65:1439-46.

Access this article online

Quick Response Code:

Website: https://journals.lww.com/sbvj/

DOI: 10.4103/SBVJ.SBVJ_42_24

How to cite this article: Parthasarathy S. Vonoprazan – A new drug for acid peptic disorders. SBV J Basic Clin Appl Health Sci 2024;7:103-4.

Received: 13-09-2024, **Revised:** 16-09-2024,
Accepted: 18-09-2024, **Published:** 26-11-2024.