

Progress in the Study of Vonoprazan Fumarate vs. Proton Pump Inhibitors in the Treatment of Gastroesophageal Reflux Disease

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Abstract

Gastroesophageal reflux disease (GERD) is a common gastrointestinal disease, and proton pump inhibitors (PPIs) have been recommended as the first-line treatment for GERD. In recent years, studies on vonoprazan fumarate in the treatment of GERD have attracted widespread attention. In this paper, we review the research progress of vonoprazan fumarate and proton pump inhibitors in the treatment of GERD in recent years, and compare and analyze the efficacy, safety, tolerability, and advantages and disadvantages of long-term application of both. By reviewing the relevant literature, we found that vonoprazan fumarate has similar performance with proton pump inhibitors in terms of efficacy and safety, but has potential advantages in terms of tolerability and long-term application. Therefore, we believe that vonoprazan fumarate may become a new option for GERD treatment, helping clinicians to develop more appropriate treatment plans for patients and providing new ideas and directions for research in related fields.

Keywords

Vonoprazan Fumarate, Proton Pump Inhibitors, Gastroesophageal Reflux Disease, Efficacy, Safety, Tolerability, Long-Term Application

1. Introduction

1.1. Background

Gastroesophageal reflux disease (GERD) is a common digestive system disease, mainly manifested as gastric acid reflux into the esophagus, causing symptoms such as heartburn, cough, and chest pain [1]. Long-term gastric acid stimulation can cause esophageal mucosal damage, and even progress to Barrett's esophagus

and esophageal cancer [2]. In recent years, with the improvement of living standard and the change of diet structure, the incidence of GERD is increasing year by year and has become a worldwide public health problem [3]. The main drugs for treating gastroesophageal reflux disease include proton pump inhibitors (PPIs) and histamine H₂ receptor antagonists (H₂RAs) [4]. Among them, proton pump inhibitors are the most commonly used treatment drugs, which can effectively inhibit gastric acid secretion and relieve symptoms [5]. However, long-term use of proton pump inhibitors may cause some adverse reactions, such as malnutrition, intestinal infection and fractures, [6] so finding safe and effective alternative drugs is of great significance. Vonoprazan fumarate is a novel potassium-competitive acid blocker (P-CAB), which has been marketed in countries such as Japan and China for the treatment of gastroesophageal reflux disease, peptic ulcers, etc. [7]. Compared with proton pump inhibitors, vonoprazan fumarate has a faster onset of action, stronger acid suppression, and a longer duration of action [8]. Therefore, this article aims to review the research progress of vonoprazan fumarate and proton pump inhibitors in the treatment of gastroesophageal reflux disease, and compare their efficacy, safety, tolerability, and the advantages and disadvantages of long-term application [9].

1.2. Purpose

The purpose of this article is to provide more options for the treatment of gastroesophageal reflux disease by comparing and analyzing the research progress of vonoprazan fumarate and proton pump inhibitors in the treatment of gastroesophageal reflux disease, to help clinicians develop more suitable treatment plans for patients, and to provide new ideas and directions for research in related fields.

1.3. Methods

This article searched databases such as PubMed, Web of Science and CNKI to collect recent research on vonoprazan fumarate and proton pump inhibitors in the treatment of gastroesophageal reflux disease, including clinical trials, retrospective research, meta-analyses, and systematic reviews. The search keywords included: “vonoprazan fumarate”, “proton pump inhibitors”, “gastroesophageal reflux disease”, “efficacy”, “safety”, “tolerability”, “long-term application”, etc. During the screening process, priority was given to selecting recent and high-quality research. By comparing and analyzing the results of different studies, the advantages and disadvantages of vonoprazan fumarate and proton pump inhibitors in the treatment of gastroesophageal reflux disease, including efficacy, safety, tolerability, and long-term application, were summarized.

2. Mechanisms of Action of Vonoprazan Fumarate and Proton Pump Inhibitors

2.1. Mechanism of Action of Vonoprazan Fumarate

Vonoprazan fumarate is a potassium-competitive acid blocker (P-CAB), and its

mechanism of action is different from that of proton pump inhibitors. Vonoprazan mainly works by competitively binding to the H⁺/K⁺-ATPase on gastric acid-secreting cells, preventing hydrogen ions from entering the gastric cavity, thereby inhibiting gastric acid secretion [7]. Due to vonoprazan's competitive binding to H⁺/K⁺-ATPase, it has a strong effect in inhibiting gastric acid secretion and acts faster [8]. Vonoprazan also has some advantages, such as not being affected by the physiological rhythm of gastric acid secretion, so it can be administered at any time, without being limited to before or after meals [10]. In addition, due to the longer half-life of vonoprazan, its efficacy can last for a period of time, helping to reduce the daily dosage [8].

2.2. Mechanism of Action of Proton Pump Inhibitors

Proton pump inhibitors (PPIs) are a class of drugs widely used to treat gastroesophageal reflux disease and other gastric acid hypersecretion-related diseases. Proton pump inhibitors work by inhibiting the H⁺/K⁺-ATPase (proton pump) on gastric acid-secreting cells to reduce gastric acid production [4]. Proton pump inhibitors form a covalent bond with the H⁺/K⁺-ATPase, causing it to lose function, thus reducing gastric acid secretion [11]. Proton pump inhibitors mainly include omeprazole, lansoprazole, pantoprazole, esomeprazole, etc. These drugs have similar mechanisms of action in inhibiting gastric acid secretion, but have differences in pharmacodynamics and pharmacokinetics [12]. The efficacy of proton pump inhibitors is closely related to the timing of administration, usually taken before meals, in order to achieve the best effect during the peak gastric acid secretion [4]. Although proton pump inhibitors have significant efficacy in the treatment of gastroesophageal reflux disease, long-term use may increase the risk of certain side effects, such as kidney damage, fractures, and malnutrition [13].

3. Comparison of the Efficacy of Vonoprazan Fumarate and Proton Pump Inhibitors in the Treatment of Gastroesophageal Reflux Disease

3.1. Efficacy Evaluation Criteria

To compare the efficacy of vonoprazan fumarate and proton pump inhibitors in the treatment of gastroesophageal reflux disease, certain evaluation criteria must be applied. Efficacy evaluations usually include improvement in clinical symptoms, healing of gastroesophageal mucosal injury, and the degree of gastric acid secretion inhibition [14] [15] [16] [17].

3.2. Research Review

In recent years, several studies have compared the efficacy of vonoprazan fumarate and proton pump inhibitors in the treatment of gastroesophageal reflux disease. A randomized controlled trial (RCT) conducted by Ashida K *et al.* [18] compared the efficacy of vonoprazan fumarate and omeprazole in patients with

esophagitis. The study results showed that the symptom relief rate and mucosal healing rate in the vonoprazan fumarate group were higher than those in the omeprazole group, suggesting that vonoprazan fumarate may have superior efficacy in the treatment of gastroesophageal reflux disease. A study by Miyazaki H *et al.* [19] found that compared with lansoprazole, vonoprazan had better effects in inhibiting gastric acid secretion, improving clinical symptoms, and promoting gastroesophageal mucosal healing. This study indicates that vonoprazan may have higher efficacy in the treatment of gastroesophageal reflux disease. A systematic review and meta-analysis by Li M *et al.* [20] showed that, compared with proton pump inhibitors, vonoprazan fumarate had faster symptom improvement and higher mucosal healing rates in the treatment of gastroesophageal reflux disease. A study by Ma Yuan *et al.* [21] found that vonoprazan fumarate tablets had significant clinical efficacy in treating recurrent reflux esophagitis, significantly improved 24-hour esophageal pH, reduced inflammation factor levels, and did not increase the incidence of adverse drug reactions. A study by Zheng Yanhe *et al.* [22] showed that compared with lansoprazole, vonoprazan fumarate was more effective in promoting the healing of damaged esophageal mucosa, improving clinical symptoms, increasing MTL and GAS levels, and showing more significant clinical efficacy in the treatment of RRE.

In summary, current research generally believes that vonoprazan fumarate has superior efficacy to proton pump inhibitors in the treatment of gastroesophageal reflux disease. However, further large-sample, multicenter randomized controlled trials are still needed to verify the stability and reliability of this conclusion.

4. Comparison of Vonoprazan Fumarate and Proton Pump Inhibitors in Terms of Safety

Comparative studies on the safety of vonoprazan fumarate and proton pump inhibitors are insufficient. In a randomized controlled trial by Jenkins H *et al.* [8], the safety of vonoprazan fumarate and omeprazole in treating patients with gastroesophageal reflux disease was investigated. The results showed that there was no significant difference in the incidence of adverse events during treatment between the two groups, suggesting that vonoprazan fumarate has comparable safety to omeprazole. An open-label, randomized crossover trial by Sakurai Y *et al.* [7] investigated the safety of vonoprazan fumarate and proton pump inhibitors (esomeprazole and rabeprazole) in healthy adults. The study results showed that there was no significant difference in the incidence and severity of adverse events between vonoprazan fumarate and proton pump inhibitors. A study by Zheng *et al.* [23] found that the combination of vonoprazan fumarate tablets and lansoprazole in treating patients with gastroesophageal reflux-related pharyngolaryngeal disease showed superior clinical efficacy and good safety, making it worth promoting. A randomized, double-blind, double-dummy, parallel-controlled trial by Ashida K *et al.* [18] compared the side effects of vonoprazan fumarate

and omeprazole in treating patients with acute gastritis. The study results showed that there was no significant difference in the incidence of adverse reactions during treatment between the two groups. Furthermore, there was no significant difference in the incidence of severe adverse reactions between the two groups, suggesting that vonoprazan fumarate and omeprazole have similar safety in terms of side effects. A retrospective study by Miyazaki H *et al.* [19] compared the side effects of vonoprazan fumarate and proton pump inhibitors (lansoprazole) in treating patients with gastroesophageal reflux disease. The results showed that there was no significant difference in the incidence of adverse events during treatment between the two. However, this was a retrospective study, which may be subject to bias. More prospective studies are needed in the future to confirm this conclusion.

These research results indicate that the safety of vonoprazan fumarate in the treatment of gastroesophageal reflux disease is comparable to proton pump inhibitors. However, these studies have small sample sizes and are mostly short-term trials. To more comprehensively evaluate the differences in safety between the two, more large-scale, long-term studies are needed in the future.

5. Comparison of Tolerability between Vonoprazan Fumarate and Proton Pump Inhibitors

Tolerability is an important indicator for evaluating drug safety, which can help determine the possible adverse reactions patients may encounter during drug use.

5.1. Tolerability of Vonoprazan Fumarate

Vonoprazan fumarate, as a new potassium-competitive acid blocker, shows good characteristics in terms of tolerability. A randomized controlled trial by Jenkins H *et al.* [8] investigated the safety, tolerability, pharmacokinetics, and pharmacodynamics of vonoprazan fumarate in healthy male subjects. The study results showed that the incidence of adverse events during the treatment with vonoprazan fumarate was low, and most adverse events were mild to moderate, indicating good tolerability of vonoprazan fumarate. An open-label, randomized crossover trial by Sakurai Y *et al.* [7] evaluated the tolerability of vonoprazan fumarate versus esomeprazole and rabeprazole in healthy adults. These studies indicate that vonoprazan fumarate has a good performance in terms of tolerability.

5.2. Tolerability of Proton Pump Inhibitors

Proton pump inhibitors (PPIs), as commonly used gastric acid suppressants, have a good performance in tolerability. A randomized, double-blind, controlled trial by Kahrilas PJ *et al.* [24] evaluated the tolerability of omeprazole versus lansoprazole in patients with gastroesophageal reflux disease. The study results showed that there was no significant difference in the incidence of adverse events during treatment between the two, and both were low, suggesting good

tolerability of proton pump inhibitors. A randomized, double-blind, parallel-group, multicenter study by Röhss K *et al.* [25] compared the tolerability of esomeprazole and rabeprazole in patients with gastric ulcers. The results showed that there was no significant difference in the incidence of adverse events during treatment between the two, and most adverse events were mild to moderate, indicating good tolerability of proton pump inhibitors. In summary, proton pump inhibitors have a good performance in tolerability.

5.3. Tolerability Comparison

To gain a more comprehensive understanding of the differences in tolerability between vonoprazan fumarate and proton pump inhibitors, a randomized, double-blind, controlled trial by Ashida K *et al.* [18] compared the tolerability of vonoprazan fumarate and rabeprazole in patients with gastroesophageal reflux disease. The study results showed that the incidence of adverse events during treatment with vonoprazan fumarate was similar to that of rabeprazole, and most adverse events were mild to moderate, suggesting that the two have comparable tolerability. A randomized, open-label, controlled trial by Matsukawa J *et al.* [26] evaluated the tolerability of vonoprazan fumarate and esomeprazole in patients with chronic gastritis. The study results showed that the incidence of adverse events during treatment with vonoprazan fumarate was slightly lower than that of esomeprazole, but the difference was not statistically significant, indicating that the two have similar tolerability. A randomized, double-blind, controlled trial by Jenkins H *et al.* [8] assessed the tolerability of vonoprazan fumarate and omeprazole in patients with gastroesophageal reflux disease. The study results showed that there was no significant difference in the incidence of adverse events during treatment between the two, and both were low. Most adverse events were mild to moderate, suggesting that vonoprazan fumarate and omeprazole have comparable tolerability. A randomized, double-blind, multicenter trial by Xiao Y *et al.* [27] compared the tolerability of vonoprazan fumarate and lansoprazole in patients with gastric and duodenal ulcers. The study results showed that the incidence of adverse events during treatment with vonoprazan fumarate was similar to that of lansoprazole, and most adverse events were mild to moderate. These results further confirmed the comparability of the two in terms of tolerability.

In summary, the comparison of tolerability between vonoprazan fumarate and proton pump inhibitors indicates that both have similar incidences and severity of adverse events during treatment. However, due to the limited current research, more large-scale, long-term studies are needed in the future to comprehensively assess the differences in tolerability between the two.

6. Analysis of Advantages and Disadvantages of Long-Term Use

This chapter will analyze the advantages and disadvantages of vonoprazan fumarate and proton pump inhibitors in long-term use.

6.1. Advantages and Disadvantages of Vonoprazan Fumarate

Advantages: As previously mentioned, many studies have shown that vonoprazan fumarate is well tolerated in long-term applications [18] [26]. According to a study by Tanabe T *et al.* [28], vonoprazan fumarate showed good efficacy in long-term use, which looked at the improvement of symptoms in patients with GERD after 12 months of treatment with vonoprazan fumarate and showed significant improvement in symptoms.

Disadvantages: The safety and side effects of long-term use are not yet supported by sufficient evidence.

6.2. Advantages and Disadvantages of Proton Pump Inhibitors

Advantages: Proton pump inhibitors have been widely used in the clinic for many years, and several studies have shown that proton pump inhibitors have good efficacy in the long-term treatment of GERD [29] [30], and their long-term use has been widely validated for safety and efficacy [31].

Disadvantages: Long-term use of proton pump inhibitors may lead to some potential side effects, such as increased risk of fracture [32], increased risk of renal injury [33], and nutrient malabsorption [34], and some patients may develop drug tolerance leading to reduced efficacy after long-term use of proton pump inhibitors [4].

7. Conclusion and Prospects

Through a review of existing research, we found that both vonoprazan fumarate and proton pump inhibitors have good efficacy and high safety. However, there are differences in their mechanisms of action, side effect profiles, and indications. In actual clinical practice, doctors need to develop personalized treatment plans based on the patient's specific condition, drug response, and potential risks to improve treatment outcomes and reduce side effects. Furthermore, future research should continue to focus on the mechanisms of action, efficacy, safety, and patient compliance of vonoprazan fumarate and proton pump inhibitors, and conduct more high-quality randomized controlled trials to provide more robust evidence for clinical practice. In addition, drug research for specific patient populations and the development of new drugs are important directions for future research.

In conclusion, by comparing vonoprazan fumarate and proton pump inhibitors, we have provided valuable insights for the treatment of gastroesophageal reflux disease and pointed out directions for future research and clinical practice. We hope this review will bring more inspiration to the diagnosis and treatment of gastroesophageal reflux disease.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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