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Editorial

Role of Tegoprazan in *Helicobacter pylori* Eradication Therapy

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See "Triple Therapy-Based on Tegoprazan, a New Potassium-Competitive Acid Blocker, for First-Line Treatment of *Helicobacter pylori* Infection: A Randomized, Double-Blind, Phase III, Clinical Trial" by Yoon Jin Choi, et al. on page 535, Vol. 16, No. 4, 2022

Potassium-competitive acid blockers (P-CABs) have a stronger acid-suppressing effect than proton pump inhibitors (PPI), showing comparable or superior effects in various diseases in which PPIs were used. Many studies have reported the role of P-CAB in *Helicobacter pylori* eradication. Vonoprazan is a novel P-CAB approved and used for *H. pylori* eradication in Japan. In recent years, several studies have compared the eradication rates of vonoprazan- and PPI-containing triple therapies across centers in Japan. The superior efficacy of vonoprazan-containing eradication treatment has been demonstrated in recent meta-analyses[1-3] and is mainly explained by the rapid and potent suppression of gastric acid secretion. Tegoprazan is a P-CAB developed in Korea, and, similar to vonoprazan, it showed a stronger and faster effect than PPIs. Therefore, the rapid and potent anti-acid efficacy of tegoprazan is considered optimal for *H. pylori* eradication therapy.

In this issue of *Gut and Liver*, Choi *et al.*[4] report the efficacy of tegoprazan as a part of first-line triple therapy for *H. pylori* eradication. A randomized, double-blind, controlled, multicenter study was performed to evaluate whether a 50-mg tegoprazan-based triple therapy was non-inferior to a 30-mg lansoprazole-based triple therapy. A total of 350 *H. pylori*-positive patients were randomly allocated to either the tegoprazan or lansoprazole groups. The *H. pylori* eradication rates in the tegoprazan and lansoprazole groups were 62.86% (110/175) and 60.57% (106/175) in an intention-to-treat analysis, and 69.33% (104/150) and 67.33% (101/150) in a per-protocol analysis (non-inferiority test, p=0.0090 and p=0.0127). Although the results showed that tegoprazan was non-inferior to lansoprazole, the overall eradication rate was less than 70% in both groups. This is consistent with the recent trend of the lowering success rate of PPI-based triple therapy due to antibiotic resistance. The first-line therapy for *H. pylori* infection comprises triple therapy with the combination of a PPI, amoxicillin, and clarithromycin. However, the *H. pylori* eradication rate upon PPI-based triple therapy has fallen below 80% in many countries and has even reached 70% in Korea.[5] The main cause of eradication failure has been attributed to the increased antibiotic resistance of *H. pylori*, particularly to clarithromycin.[6]

Acid inhibition of PPI is known to play an important role in eradication treatment, and based on this, it was expected that P-CAB, which has a strong acid inhibitory effect, could exhibit a better eradication rate for patients with clarithromycin-resistant strains. Murakami *et al.*[7] reported that the eradication rate was significantly higher with vonoprazan than with lansoprazole in patients with clarithromycin-resistant strains (82% vs 40%, p=0.0001). Moreover, a recent meta-analysis showed that vonoprazan is superior to conventional PPIs in eradicating clarithromycin-resistant strains, while vonoprazan-based and conventional PPI-based therapies are similarly effective in patients with clarithromycin-susceptible strains.[2] Additionally, the gastric acid inhibitory effect of PPI differs according to an individual's CYP2C19 genotype, and vonoprazan is known to have a higher gastric acid inhibitory effect than other PPIs in extensive metabolizers. In fact, vonoprazan showed a superior effect compared to conventional PPIs in CYP2C19 extensive metabolizers during eradication treatment.[7]

Based on previous studies, tegoprazan, like vonoprazan, was expected to be superior to conventional PPIs in the

clarithromycin-resistant group and CYP2C19 extensive metabolizers. In their study, however, Choi *et al.*[4] did not show the superiority of tegoprazan in eradication rate. Subgroup analyses according to minimum inhibitory concentrations (MICs) or CYP2C19 genotype did not show any remarkable differences in eradication rates. As the authors mentioned in the discussion, there are several hypotheses as to why it is not superior to PPI in *H. pylori* eradication. The hypotheses are as follows: (1) insufficient dose of tegoprazan; (2) differences in the MIC distributions for clarithromycin-resistant *H. pylori* strains compared with those reported in the Japanese study; (3) pharmacological differences between tegoprazan and vonoprazan; and (4) insufficient eradication treatment period compared to 14 days of treatment. Additionally, all studies on vonoprazan-based *H. pylori* eradication were conducted in Japan; thus, it may be difficult to apply these findings to the general population because of the difference in the holding time ratio at pH >4 and the resistance pattern of *H. pylori* to antibiotics.

In summary, the authors provided evidence that tegoprazan-based 7-day triple therapy can be used as first-line *H. pylori* therapy, although tegoprazan doses do not overcome the clarithromycin resistance of *H. pylori*. Further studies on high-dose tegoprazan-based regimens, or 10- or 14-day triple therapy and analyses according to the MIC value, are needed to clarify whether tegoprazan-based therapy is more effective than PPI-based therapy for *H. pylori* eradication.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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