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Comparison of Tegoprazan- and Lansoprazole-Based Fourteen-Day Triple Therapies as First-Line Treatments for *Helicobacter pylori* Eradication

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Objectives: Tegoprazan, a novel potassium-competitive acid blocker with rapid and effective antisecretory activity, was approved for the treatment of *Helicobacter pylori* infections in Korea in March 2020. However, real-world data regarding tegoprazan-based therapies are scarce. We compared the efficacies of tegoprazan- and lansoprazole-based triple therapies (TTs). **Methods:** Between March 2020 and February 2023, this study enrolled patients diagnosed with *H. pylori* infections who were prescribed either 14-day tegoprazan- or lansoprazole-based TTs as first-line treatments. Their medical records were retrospectively reviewed to compare *H. pylori* eradication rates and the rates of patient adherence to the recommended therapy. **Results:** A total of 670 patients diagnosed with *H. pylori* infections were prescribed 14-day TT regimens between March 2020 and February 2023 at Ilsan Paik Hospital (Goyang, Korea). Of those enrolled in the study, 64 received tegoprazan-based TT and 295 received lansoprazole-based TT as their first-line treatment. The *H. pylori* eradication rates for tegoprazan- and lansoprazole-based TTs were 76.6% and 75.6%, respectively, in the intent-to-treat population; the rates were 88.9% and 88.4%, respectively, in the per-protocol population (non-inferiority test, p=0.03 and p=0.01 in the respective populations). No significant differences were observed between the two groups with regards to treatment adherence rates (84.4% vs. 85.1%, p=0.78). **Conclusions:** As a first-line treatment for *H. pylori* eradication, 14-day tegoprazan-based TT demonstrated non-inferior efficacy compared with 14-day lansoprazole-based TT.

Keywords *Helicobacter pylori*; Potassium-competitive acid blockers; Proton pump inhibitors; Tegoprazan.

INTRODUCTION

Helicobacter pylori is a flagellated, microaerophilic, gram-negative, spiral-shaped bacterium that colonizes the stomach. It is one of the most common human pathogens and is a significant risk factor for various gastrointestinal diseases, including gastritis, peptic ulcers, gastric cancer, and gastric mucosa-associated lymphoid tissue lymphoma, as well as extragastric diseases, such as idiopathic thrombocytopenic purpura and iron deficiency anemia.[1,2] Eradicating *H. pylori* infections could, therefore, potentially contribute to public health by reducing the incidence of these diseases.

Adequate acid suppression plays a crucial role in the treatment of *H. pylori* infections because the bacteria transition into a coccoid form at acidic pHs, rendering them resistant to antibiotics.[3-5] Moreover, maintaining a neutral intragastric pH enhances antibiotic concentrations in the gastric fluid by ensuring drug stability and reducing the minimum inhibitory

concentrations (MICs).[6,7] A 14-day triple therapy (TT) consisting of a proton pump inhibitor (PPI), clarithromycin, and amoxicillin is one of the most widely prescribed first-line treatment regimens, worldwide, including in Korea.[8]

Tegoprazan is a novel potassium-competitive acid blocker (P-CAB) that inhibits H^+/K^+-ATPase pumps in gastric parietal cells, similar to the action of PPIs. However, unlike PPIs, P-CABs do not require activation by gastric acid, can act on inactive H^+/K^+-ATPases, and remain stable at acidic pHs. Furthermore, P-CABs are less influenced by cytochrome P450 2C19 (CYP2C19). Thus, P-CABs are theoretically expected to be more rapid and effective acid blockers than PPIs.[9-11] The current Japanese guidelines recommend P-CAB-based TT as a first-line regimen.[12]

In March 2020, tegoprazan was approved for the treatment of *H. pylori* infections in Korea. Unfortunately, limited data are available regarding tegoprazan-based therapy regimens, particularly in real-world settings. We assessed the comparative efficacies tegoprazan- and lansoprazole-based TTs as well as patient adherence to the therapeutic regimens.

METHODS

Patients

Between March 2020 and February 2023, 670 patients were diagnosed with *H. pylori* infections and prescribed TT regimens for the treatment of *H. pylori* at Ilsan Paik Hospital (Goyang, Korea). Patients were excluded from the study if they had previous histories of *H. pylori* eradication (59 patients), received 7- or 10-day TT regimens (176 patients), or were prescribed acid suppressants other than tegoprazan or lansoprazole (76 patients). Finally, 359 patients who received either 14-day tegoprazan- (tegoprazan group, 64 patients) or lansoprazole-based TT (lansoprazole group, 295 patients) as the first-line treatment for *H. pylori* infections were included in the study (Fig. 1). The patients' baseline characteristics; main indications for *H. pylori* eradication; and treatment outcomes, including the results of *H. pylori* eradication therapy, treatment regimen adherence, and adverse events (AEs), were retrospectively investigated.

Diagnosis of *H. pylori* infection and confirmation of *H. pylori* eradication

H. pylori infections were diagnosed using one of the following tests (Supplementary Table 1 in the online-only Data Supplement): rapid urease test (Pyloplus®; ARJ Medical, Oldsmar, FL, USA), histological examination involving modified Giemsa staining, or ^{13}C-urea breath test (Otsuka Pharmaceutical, Tokyo, Japan).

Multiple national guidelines recommend the ^{13}C-urea breath test for confirming *H. pylori* eradication.[12-15] Thus, patients underwent this confirmatory test at least 4 weeks after completion of the medication regimen. Breath samples were collected after the patient had fasted for at least 4 h. A tablet containing 100 mg of ^{13}C-urea (UBIT®; Otsuka Pharmaceutical) was administered, per os, with 100 mL of water. Follow-up breath samples were collected 20 min after the tablet had been swallowed. The presence of *H. pylori* was determined using the collected breath samples (Analyzer POCone; Otsuka Electronics,

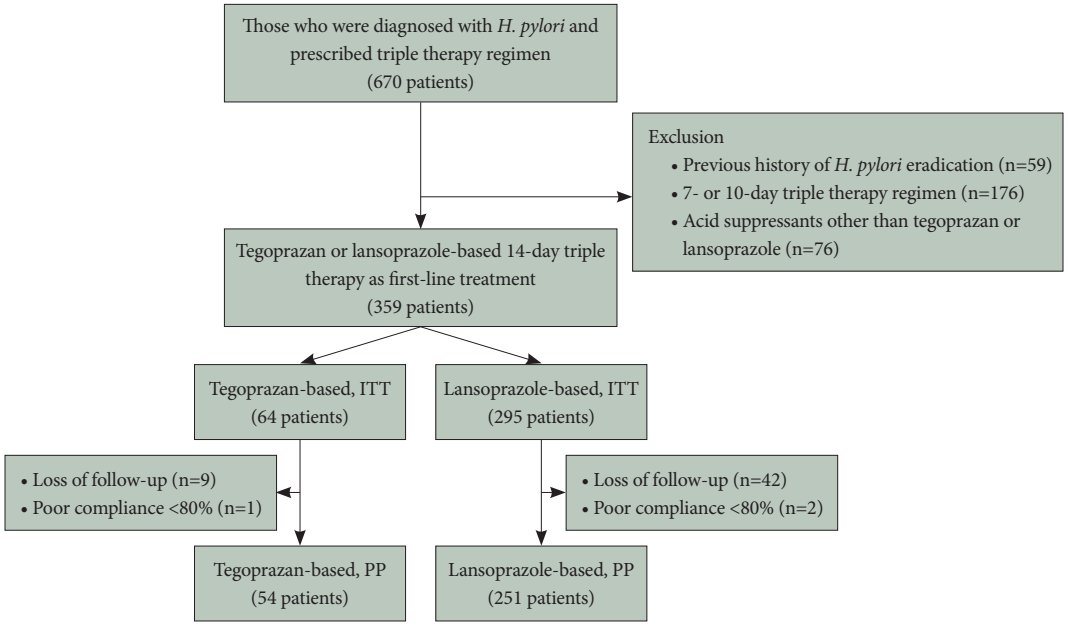

Fig. 1. Flowchart of study enrollment. ITT, intent-to-treat; PP, per-protocol.

Osaka, Japan). The cutoff value was 2.5%.

H. pylori eradication therapy

Current Korean guidelines recommend the empirical treatment of *H. pylori* infections[8] with TT regimens consisting of acid suppression and two antibiotics. The tegoprazan group received tegoprazan (50 mg), amoxicillin (1000 mg), and clarithromycin (500 mg) twice daily for 14 days. The lansoprazole group received lansoprazole (30 mg), amoxicillin (1000 mg), and clarithromycin (500 mg) twice daily for 14 days. Treatment adherence was defined as the administration of at least 80% of the prescribed medications. AEs were classified into three categories: mild (symptoms subsided spontaneously), moderate (symptoms requiring management), and severe (symptoms necessitating emergency room visits).

Statistical analysis

All statistical analyses were conducted using R (Version 4.1.1; The R Foundation for Statistical Computing, Vienna, Austria). Categorical variables were analyzed using chi-square or Fisher's exact tests, as indicated; continuous variables were analyzed using Student's t-test or the Mann–Whitney U test. *p*-values <0.05 were considered statistically significant. A non-inferiority test was conducted in both the intent-to-treat (ITT) and per-protocol (PP) populations; non-inferiority was declared if the lower limit of the one-sided 95% confidence interval for the difference in eradication rates was above the non-inferiority margin value of -0.1.

Ethics statement

Ethics approval for this study was obtained from the Ilsan Paik Hospital Institutional Review Board (approval number 2022-10-007-001). The requirement for informed consent was waived due to the retrospective nature of the study.

RESULTS

Baseline characteristics

Table 1 presents the baseline characteristics of the 359 patients in the tegoprazan (64 patients) and lansoprazole (295 patients) groups. There were no significant differences in ages or sex distributions between the two groups. The most common indication for treatment in both groups was *H. pylori*-associated gastritis, followed by peptic ulcers.

Adherence and AEs

In the tegoprazan group, nine patients were lost to follow-up and one received insufficient medication (<80% of the prescribed medications). In the lansoprazole group, 42 patients were lost to follow-up, and two received insufficient medication (Fig. 1). Consequently, the adherence rates of the patients in the tegoprazan and lansoprazole groups were 84.4% (54/64) and 85.1% (251/295), respectively (Fig. 2); no significant difference was observed (p=0.78).

The AEs associated with tegoprazan-based TT are shown in Table 2. The overall AE rate was 23.4% (15/64). The most common AE was diarrhea (7.8%), followed by dysgeusia (6.3%). Of

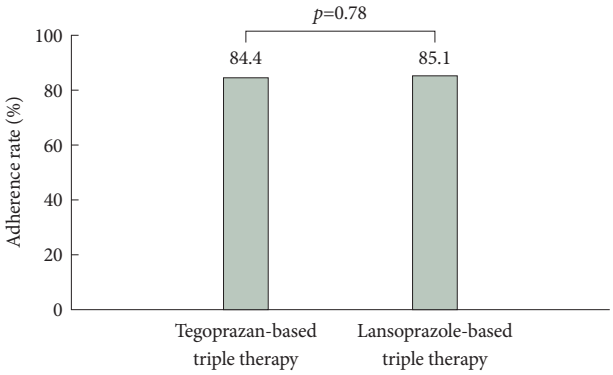

Fig. 2. The adherence rates for tegoprazan- and lansoprazole-based triple therapies.

Table 1. Demographic and baseline characteristics of the study population

Characteristics	Tegoprazan (n=64)	Lansoprazole (n=295)	Total (n=359)	*p*-value
Age (yr)	56.0 (32–78)	58.0 (15–89)	57.0 (15–89)	0.45
Male	42 (65.6)	177 (60.0)	219 (61.0)	0.49
Main indication for *H. pylori* eradication				
Peptic ulcer	14 (21.9)	79 (26.8)	93 (25.9)	
EGC resected endoscopically	0 (0)	3 (1.0)	3 (0.8)	
Gastric adenoma resected endoscopically	7 (10.9)	10 (3.4)	17 (4.7)	
Hyperplastic polyp	4 (6.2)	3 (1.0)	7 (1.9)	
Atrophic gastritis	10 (15.6)	9 (3.1)	19 (5.3)	
H. pylori-associated gastritis	28 (43.8)	190 (64.4)	218 (60.7)	
Others	1 (1.6)	1 (0.3)	2 (0.6)	

Data are presented as median (range) or n (%).
EGC, early gastric cancer.

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Table 2. Adverse events of 14-day tegoprazan-based triple therapy

Adverse events	Value (n=64)
Any adverse events	15 (23.4)
Diarrhea	5 (7.8)
Dysgeusia	4 (6.3)
Nausea	2 (3.1)
Urticaria	1 (1.6)
Constipation	1 (1.6)
Abdominal discomfort	1 (1.6)
Headache	1 (1.6)

Data are presented as n (%).

the 15 AEs, 14 were mild and one (patient experienced nausea and was prescribed prokinetics at a local clinic) was classified as moderate. The AEs in the lansoprazole group were unavailable due to the lack of medical records.

Outcomes

The overall *H. pylori* eradication rates were 75.8% (272/359) in the ITT population and 88.5% (270/305) in the PP population. In the ITT population, the *H. pylori* eradication rates for patients in the tegoprazan- and lansoprazole groups were 76.6% (49/64) and 75.6% (223/295), respectively (Fig. 3). The lower limit of the one-sided 95% confidence interval for the difference in eradication rates was -0.087, which was above the non-inferiority margin of -10% (p=0.03). In the PP population, the eradication rates for patients in the tegoprazan- and lansoprazole groups were 88.9% (48/54) and 88.4% (222/251), respectively (Fig. 3); the lower limit of the one-sided 95% confidence interval (-0.074) was also above the non-inferiority margin of -10% (p=0.01).

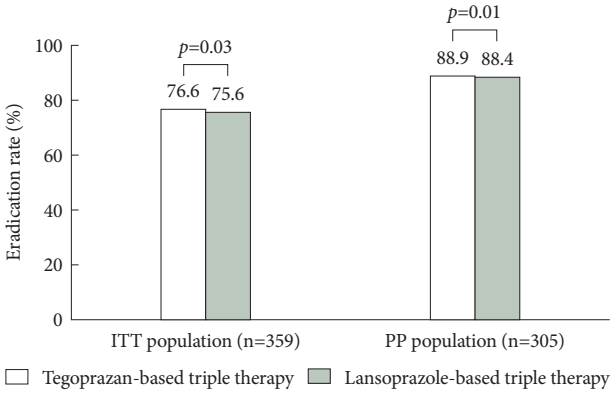

Fig. 3. The eradication rates for tegoprazan- and lansoprazole-based triple therapies. The *p*-values for non-inferiority tests are indicated. ITT, intent-to-treat; PP, per-protocol.

DISCUSSION

P-CABs are known for their more rapid and potent acid-suppressing properties compared with PPIs. P-CABs have demonstrated superior or comparable efficacies in the treatment of various acid-related diseases, such as gastroesophageal reflux disease and peptic ulcers, for which PPIs are commonly used. In the context of *H. pylori* treatment, the stronger antisecretory potency of P-CABs is expected to increase antibiotic stability in the gastric fluid and reduce antibiotic MICs, thereby elevating the eradication rate.[6,7,16]

Vonoprazan is a P-CAB approved and prescribed for first-line treatment of *H. pylori* infections in Japan.[12] Recently, a number of studies have been published regarding vonoprazan-based *H. pylori* eradication therapy. Even in cases involving clarithromycin-resistant *H. pylori* strains, vonoprazan-based TT showed an eradication rate of 82.0%, whereas the eradication rate of the comparator lansoprazole-based TT was 40.0%.[17] The strong acid suppression provided by vonoprazan appears to help TT regimens overcome the challenge of clarithromycin-resistant *H. pylori* strains. Furthermore, recent meta-analyses have indicated the superiority of vonoprazan-based therapy over PPI-based therapy.[18-22]

In our study, the 14-day tegoprazan-based TT demonstrated *H. pylori* eradication rates of 76.6% and 88.9% in the ITT and PP populations, respectively. The eradication rates for the 14-day lansoprazole-based TT were 75.6% and 88.4% in the ITT and PP populations, respectively. In contrast to the reported superiority of vonoprazan for *H. pylori* eradication, our study failed to demonstrate the superiority of tegoprazan over lansoprazole; rather, the tegoprazan-based TT was deemed non-inferior to the lansoprazole-based TT. There are several possible reasons for this finding. First, the clarithromycin MIC distribution for *H. pylori* may vary according to geographic region. Such differences in antibiotic resistance between the Korean and Japanese population could contribute to different efficacies. Second, the pharmacological differences between tegoprazan and vonoprazan, such as half-lives or maximum plasma concentrations, may limit the efficacy of tegoprazan. Moreover, twice daily 50-mg tegoprazan doses may be insufficient to achieve the necessary acid suppression and overcome clarithromycin resistance. A previous randomized clinical trial demonstrated that tegoprazan increases intragastric pH in a dose-dependent manner; the mean values of the 15-minute median intragastric pH over 24 h on day 7 was 5.2 with a 100-mg daily dose of tegoprazan and 6.4 with a 200-mg daily dose.[23] Therefore, increasing the tegoprazan dose to 100 mg twice daily may improve *H. pylori* eradication rates.

Poor therapeutic compliance is one reason for eradication failure. In our study, 1.6% and 0.7% of the patients in the tegoprazan and lansoprazole groups, respectively, received insuf-

ficient medication (<80% of the prescribed medications). Additionally, 14.1% and 14.2% of patients in the tegoprazan and lansoprazole groups, respectively, were lost to follow-up. Consequently, the adherence rates were similar for the tegoprazan (84.4%) and lansoprazole (85.1%) groups (p=0.78). Unfortunately, we were unable to investigate the AEs or other factors potentially contributing to patients being lost to follow-up due to the absence of relevant medical records.

AEs are among the most common factors leading to poor compliance. Hepatoxicity concerns were associated with the earlier P-CABs, leading to their discontinued clinical development.[24] However, vonoprazan showed similar rates of liver function abnormalities compared with lansoprazole during an 8-week treatment for erosive esophagitis, with no reported increase in hepatotoxicity during 52 weeks of maintenance therapy.[25] Furthermore, the safety profile of vonoprazan during long-term use was similar to that of lansoprazole.[26] Similarly, tegoprazan exhibited no significant difference in liver toxicity rates compared with lansoprazole, and its safety profile was similar to that of lansoprazole over a 24-week period.[27] Multiple randomized controlled trials have reported gastrointestinal disorders, including diarrhea and nausea, as the most common AEs associated with tegoprazan use, with the majority having mild intensity.[27-30] Likewise, previous studies investigating tegoprazan-based TT regimens have shown most AEs to be mild, requiring no medical management, with the most frequent ones being gastrointestinal disorders.[31-34] Our study found a 23.4% rate of AEs associated with tegoprazan-based TT, consistent with prior studies. Owing to the lack of relevant medical records, AE rates for lansoprazole-based TT could not be determined.

To date, four studies have compared tegoprazan and PPIs for the treatment of *H. pylori* infections.[32,35-37] Kim et al.[35] compared the efficacy of a 7-day tegoprazan-based TT regimen (tegoprazan [50 mg], clarithromycin [500 mg], amoxicillin [1000 mg]) combined with twice daily bismuth (bismuth potassium citrate [300 mg]) against a lansoprazole-based TT regimen that replaced tegoprazan with lansoprazole (30 mg). In both the ITT and PP analyses, the *H. pylori* eradication rates were not significantly different, consistent with our findings (78.8% vs. 74.5% with p=0.323 in the ITT analysis and 88.3% vs. 82.8% with p=0.151 in the PP analysis).[35] However, the regimen employed by Kim et al.[35] (standard TT regimen plus bismuth) is not commonly prescribed in clinical practice and is not a recommended first-line treatment.[8,12-14] Choi et al.[32] conducted a randomized controlled trial comparing 7-day tegoprazan- and lansoprazole-based TTs. They demonstrating that tegoprazan is as effective as lansoprazole for eradicating *H. pylori* treatment, with eradication rates of 62.86% and 60.57%, respectively, in the ITT populations and 69.33% and 67.33%, respectively, in the PP populations. Their observed eradication rates were lower than those observed in our study. We believe that the extended 14-day treatment duration in our study contributed to the observed higher eradication rates. To improve eradication rates, the current Korean guidelines recommends 14-day TT regimens as first-line treatments.[8] In a retrospective study, Jung et al.[36] reported similar efficacies for 14-day tegoprazan- and rabeprazole-based TTs. The eradication rates of the tegoprazan- and rabeprazole-based regimens were 76.7% and 75.4%, respectively, in the ITT population and 83.4% and 83.5%, respectively, in the PP population, similar to our findings. Kim et al.[37] showed the non-inferiority of tegoprazan-based bismuth quadruple therapy to lansoprazole-based quadruple therapy as first-line *H. pylori* eradication treatments in a randomized controlled trial (80.0% vs. 77.4%, respectively, in the ITT analysis; 90.2% vs. 82.4%, respectively in the PP analysis). In addition, a recent retrospective study comparing tegoprazan with the combination of a PPI and an antacid for *H. pylori* eradication was published in 2023.[33] It showed no significant difference in the eradication rates between 14-day tegoprazan- and esomeprazole/sodium bicarbonate-based TTs (ITT population: 78.6% vs. 81.4%, respectively, p=0.313; PP population: 85.5% vs. 87.8%, respectively, p=0.339). Our study provides additional support for the non-inferior efficacy of the tegoprazan-based regimen as a first-line treatment for *H. pylori* eradication.

Our study had several limitations. First, this was a single-center retrospective observational study, which limits the generalizability of our findings. Second, the tegoprazan group had a relatively small sample size, which may have lowered the statistical power for assessing treatment efficacy. Third, adverse reactions and reasons for non-adherence were not examined due to the lack of medical records. Instead, we evaluated medication adherence and found no significant difference between tegoprazan and lansoprazole. Finally, antibiotic susceptibility tests were not performed, preventing an assessment of the efficacy of tegoprazan-based TT against clarithromycin-resistant *H. pylori* strains. However, we believe that the lack of antibiotic susceptibility data does not limit the clinical significance of our study as empirical therapy is commonly employed in real-world settings and continues to be recommended by guidelines.[8]

In conclusion, 14-day tegoprazan-based TT was non-inferior to 14-day lansoprazole-based TT as a first-line treatment for *H. pylori* eradication. Thus, tegoprazan may serve as an alternative to PPIs for eradicating *H. pylori*.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.7704/kjhugr.2024.0012.

Authors' Contribution

Conceptualization: Seokin Kang, Nam-Hoon Kim. Data curation: all authors. Formal analysis: Seokin Kang, Nam-Hoon Kim. Methodology: Seokin Kang, Nam-Hoon Kim. Supervision: Nam-Hoon Kim, Jong Wook Kim. Writing—original draft: Seokin Kang. Writing—review & editing: Seokin Kang, Nam-Hoon Kim. Approval of final manuscript: all authors.

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