Clin. Lab. 2023;69:XXX-XXX

ORIGINAL ARTICLE

Helicobacter pylori Empirical and Tailored Eradication Therapy and Factors Influencing Eradication Rate: a 4-Year Single-Center Study

Seung Wan Kim [1], Ju Yup Lee [1], Myeongsoon Park [2], Jin Wook Lee [1], Yoo Jin Lee [1], Kwang Bum Cho [1], Hye Ra Jung [3]

[1] *Department of Internal Medicine, Keimyung University Dongsan Hospital, Keimyung University School of Medicine, Daegu, Republic of Korea*
[2] *Department of Internal Medicine, Keimyung University Daegu Dongsan Hospital, Keimyung University School of Medicine, Daegu, Republic of Korea*
[3] *Department of Pathology, Keimyung University Dongsan Hospital, Keimyung University School of Medicine, Daegu, Republic of Korea*

SUMMARY

Background: **The *Helicobacter pylori* eradication rate with standard triple therapy (STT) is continuously decreasing due to clarithromycin resistance. This study aimed to investigate the eradication rate of empirical and tailored therapy and explore various factors affecting this eradication rate using clarithromycin resistance test data for the last 4 years at a single institution in Daegu.**
Methods: **From August 2018 to July 2021, a total of 1,395 patients diagnosed with *H. pylori* infection based on rapid urea testing and histology at Keimyung University Dongsan Hospital were retrospectively examined. Participants were classified into the empirical and tailored therapy groups according to the results of the clarithromycin resistance test using the polymerase chain reaction.**
Results: **The overall eradication rate of empirical STT was 72.8%, and the eradication rate by year was 71.6% in 2018, 77.4% in 2019, 70.3% in 2020, and 70.6% in 2021; the differences were not statistically significant (p = 0.173). No significant difference was noted in the eradication rate according to gender, age, type of proton pump inhibitors, and use of probiotics. Significant differences were noted in the eradication rate according to the treatment period: 69.7% in the 7-day, 67.3% in the 10-day, and 81.4% in the 14-day group (p = 0.001). The eradication rate with STT was 87.4% in the non-resistant group. In the case of clarithromycin resistance, treatment was mainly with bismuth quadruple therapy (BQT), and the eradication rate was 86.1%. The eradication rate was higher with administration of BQT for 10 days or 14 days than for administration of BQT for 7 days, but with no statistical significance (p = 0.364).**
Conclusions: **Extending the treatment period of STT helped in improving the eradication rate, and tailored therapy through clarithromycin resistance testing showed superior results when compared to empirical therapy.**
(Clin. Lab. 2023;69:xx-xx. DOI: 10.7754/Clin.Lab.2023.230512)

Correspondence:
Ju Yup Lee, MD, PhD
Department of Internal Medicine
Keimyung University Dongsan Hospital
Keimyung University School of Medicine
1035, Dalgubeol-daero
Dalseo-gu, Daegu, 42601
Republic of Korea
Phone: + 82 53-258-4349
Email: leejygi@naver.com

Manuscript accepted May 23, 2023

KEYWORDS

Helicobacter pylori, clarithromycin, standard triple therapy, eradication

INTRODUCTION

Helicobacter pylori infection is closely associated with the development of peptic ulcers, gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphomas. If left untreated, the bacteria continue to reside in the stomach and cause chronic inflammation [1]. The

prevalence of *H. pylori* infection is declining; however, a 2015 - 2016 nationwide study conducted by the Korean College of Helicobacter and Upper Gastrointestinal Research showed a seroprevalence of 51.0% in Korea, with a prevalence of more than 50% in individuals aged 40 years and older [2]. *H. pylori* eradication therapy comprises an acid blocker and two or more antibiotics, with standard triple therapy (STT), including clarithromycin, which is the recommended first-line therapy in Korea [3]. However, the efficacy of STT is declining worldwide due to the increased antibiotic resistance of *H. pylori* [4,5], and the success rate with STT is consistently reported to be decreasing in Korea as well [6-8]. Various attempts have been made to increase the declining eradication rate, such as extension of the duration of therapy, use of powerful acid reducers such as potassium-competitive acid blockers (P-CABs), sequential therapy, concomitant therapy, and new combinations of antibiotics [3]. Probiotics have been known to have an inhibitory effect on *H. pylori* and have been co-administered with eradication therapy [9-11].

Given the above context, this study aimed to examine the annual trends of eradication rate in the past 4 years among patients who have been treated for *H. pylori* infection at a single healthcare facility in Korea and to investigate the effects of gender, age, duration of treatment, use of proton pump inhibitors (PPI) or P-CAB, and concurrent use of probiotics on the *H. pylori* eradication rate.

MATERIALS AND METHODS

Participants

In this retrospective study, we included adults aged 18 years or older who were diagnosed with *H. pylori* infection through rapid urease test (RUT) and gastric biopsy polymerase chain reaction (PCR) tests performed at the Department of Gastroenterology and Health Examination Center of Keimyung University Dongsan Hospital from August 11, 2018, to July 26, 2021. The patients' demographic and treatment-related data were obtained from medical records.

Methods

H. pylori diagnostic criteria and eradication strategy

H. pylori infection was diagnosed based on a positive finding with RUT (CLO test; BALLARD Medical Products, Draper, UT, USA) using tissue obtained from the body or antrum during endoscopy.

H. pylori PCR testing and clarithromycin susceptibility testing using gastric mucosal tissue samples

Genomic DNA from biopsied samples was extracted using the QIAamp DNA FFPE Tissue Kit (Qiagen; Maxwell® 16 FFPE Purification Kit for DNA, Promega), according to the manufacturer's instructions. The Nanodrop (Thermo) and subsequent gel electrophoresis were performed to evaluate the quality and quantity of genomic DNA samples. To analyze the presence and mutation status of *H. pylori*, we used the U-TOP TM HPy & ClaR Detection Kit (SeaSun Biomaterials). According to the manufacturer's instructions, we performed real-time PCR with the CFX96 Real-Time PCR Detection system (Bio-Rad, Hercules, CA, USA). Real-time PCR reactions were performed in 20-μL reaction mixtures containing 10 μL × 2 qPCR PreMix (SeaSun Biomaterials), 5 μL primer and detection PNA probe mixture, and 3 μL DNA template (15 ng/μL). Real-time PCR was performed for each wild-type (negative control) and *H. pylori*-infected sample (positive control). The reaction conditions for amplification and melting point analysis were 95°C for 10 minutes; 42 cycles of 95°C for 30 seconds, 58°C for 45 seconds, and 72°C for 45 seconds, followed by melting point analysis. Melting point analysis was performed using a denaturation step of 95°C for 5 minutes; 1-minute hybridization steps of 75°C, 55°C, and 45°C; and a stepwise temperature increase from 20°C to 85°C at 1°C per step, with a 5-second interval between each step. The data were analyzed using Bio-Rad CFX manager v1.6 software (Bio-Rad). Fluorescence was measured for 10 seconds at each cycle of touchdown PCR. The melting peaks obtained were analyzed to detect alterations in the two mutations and the wild type. *H. pylori* and its mutations were distinguished using the fluorescence signal of detection probes and corresponding melting temperatures (Tm). The Tm of the internal positive control (IPC) was 59 ± 3°C, Tm of wild-type *H. pylori* was 67 ± 3°C, Tm of *H. pylori* with A2142G mutation was 58 ± 3°C, and Tm of *H. pylori* with A2143G mutation was 77 ± 3°C. One sharp melting peak at 67 ± 3°C was interpreted as a perfect match (wild type), and a melting peak at 58 ± 3°C or 77 ± 3°C was interpreted as a mismatch (mutant type). The presence of two small peaks at 67 ± 3°C and 58 ± 3°C or 77 ± 3°C was interpreted as a mismatch (mutant type) with heterozygote type.

Eradication therapy

The first-line eradication therapy included a PPI, (PPI, lansoprazole 30 mg, rabeprazole 20 mg, esomeprazole 40 mg, pantoprazole 40 mg) or P-CAB with amoxicillin 1 g and clarithromycin 500 g administered twice a day for 7, 10, or 14 days. If the standard first-line therapy failed, the following were administered as rescue therapies: bismuth quadruple therapy (BQT) (PPI bid, bismuth 120 mg qid, tetracycline 500 mg qid, metronidazole 500 mg tid), metronidazole triple therapy (PPI bid, amoxicillin 1 g bid, metronidazole 500 mg bid), levofloxacin triple therapy (PPI, amoxicillin 1 g bid, levofloxacin 250 mg bid), levofloxacin quadruple therapy (PPI bid, levofloxacin 500 mg qd, bismuth 120 mg qd, amoxicillin 1 g bid), or moxifloxacin triple therapy (PPI bid, moxifloxacin 400 mg qd, amoxicillin 1 g bid). There were no specific restrictions on the selection of PPIs or the duration of eradication therapy, and these parameters were determined based on the physician's preference. In some cases, probiotics were added to

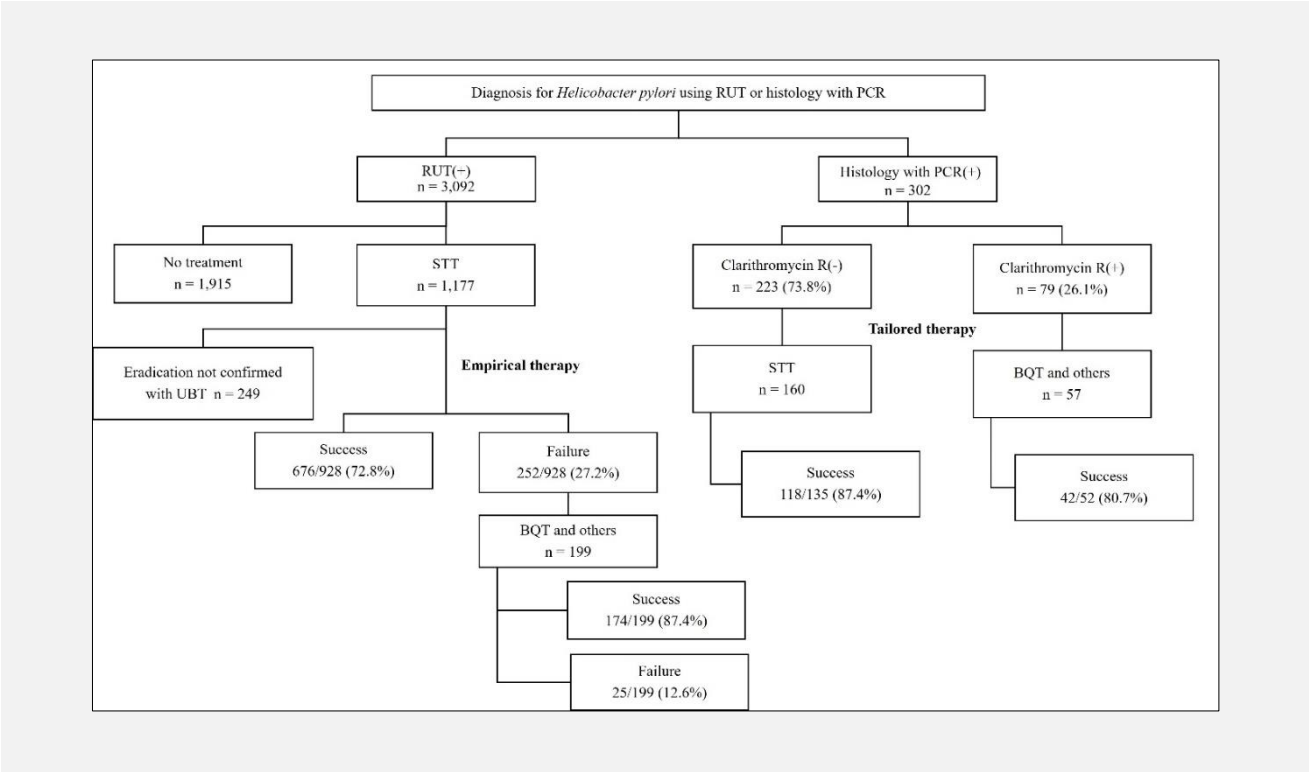

Figure 1. Schematic of the study design and treatment results of empirical and tailored therapy.

RUT - rapid urease test, PCR - polymerase chain reaction, STT - standard triple therapy, R - resistance, UBT - urea breath test, BQT - bismuth quadruple therapy.

Table 1. Baseline characteristics of the empirical therapy and tailored therapy groups.

Characteristics		Empirical therapy (n = 928)	Tailored therapy	
			Clari R (-) (n = 135)	Clari R (+) (n = 52)
Gender	Male	491 (52.9)	85 (63.0)	24 (46.1)
	Female	437 (47.0)	50 (37.8)	28 (53.8)
Age (years)		58.0 ± 11.36	60.8 ± 10.34	59.3 ± 12.15
PPI/P-CAB				
Lansoprazole		460 (49.5)	70 (51.9)	26 (50)
Rabeprazole		225 (24.2)	1 (0.7)	2 (3.8)
Esomeprazole		228 (24.6)	49 (36.3)	23 (44.2)
Pantoprazole		4 (0.4)	14 (10.3)	0 (0.0)
Tegoprazan		9 (0.9)	1 (0.7)	1 (1.9)
Probiotics				
Saccharomyces boulardii		251 (72.7)	52 (82.5)	19 (65.5)
Lactobacillus acidophilus		47 (13.6)	3 (4.7)	2 (6.8)
Lactobacillus casei		47 (13.6)	8 (12.6)	8 (27.5)
Treatment period				
7 days		552 (59.4)	81 (60.0)	18 (34.6)
10 days		107 (11.5)	25 (18.5)	10 (19.2)
14 days		269 (28.9)	29 (21.5)	24 (46.1)

Data are expressed as mean ± SD or n (%).
Clari R - clarithromycin resistance, PPI - proton pump inhibitor, P-CAB - potassium competitive acid blocker.

Table 2. Characteristics of patients with empirical first-line standard triple therapy.

Characteristics	Eradication success (n = 676)	Eradication failure (n = 252)	p-value
PPI/P-CAB			
Lansoprazole	325 (70.7)	135 (29.3)	0.179
Rabeprazole	168 (74.7)	57 (25.3)	
Esomeprazole	172 (75.1)	57 (24.9)	
Pantoprazole	2 (50.0)	2 (50.0)	
Tegoprazan	8 (88.9)	1 (11.1)	
Probiotics			
STT	417 (71.5)	166 (28.5)	0.240
STT + probiotics	238 (73.4)	86 (26.6)	
Treatment duration			
7 days	385 (69.7)	167 (30.3)	0.001
10 days	72 (67.3)	35 (32.7)	
14 days	219 (81.4)	50 (18.6)	
Year			
2018	53 (71.6)	21 (28.4)	0.173
2019	240 (77.4)	70 (22.6)	
2020	246 (70.3)	104 (29.7)	
2021	137 (70.6)	57 (29.4)	
Total	676 (72.8)	252 (27.2)	

Data are expressed as n (eradication rate %).
PPI - proton pump inhibitor, P-CAB - potassium competitive acid blocker, STT - stand triple therapy.

Table 3. Characteristics of non-clarithromycin-resistant patients for first-line therapy.

Characteristics	Eradication success (n = 118)	Eradication failure (n = 17)	p-value
PPI/P-CAB			
Lansoprazole	62 (88.6)	8 (11.4)	0.455
Rabeprazole	0 (0.0)	1 (100.0)	
Esomeprazole	44 (89.8)	5 (10.2)	
Pantoprazole	11 (78.6)	3 (21.4)	
Tegoprazan	1 (100.0)	0 (0.0)	
Probiotics			
STT	62 (87.3)	9 (12.7)	1.000
STT + probiotics	56 (87.5)	8 (12.5)	
Treatment duration			
7 days	71 (87.7)	10 (12.3)	0.364
10 days	20 (80.0)	5 (20.0)	
14 days	27 (93.1)	2 (6.9)	
Year			
2019	47 (90.4)	5 (9.6)	0.492
2020	21 (80.8)	5 (19.2)	
2021	50 (87.7)	7 (12.3)	
Total	118 (87.4)	17 (12.6)	

Data are expressed as n (eradication rate %).
PPI - proton pump inhibitor, P-CAB - potassium competitive acid blocker, STT - stand triple therapy.

Table 4. Characteristics of clarithromycin-resistant patients for first-line therapy.

Characteristics	Eradication success (n = 42)	Eradication failure (n = 10)	p-value
PPI/P-CAB			
Lansoprazole	**20 (76.9)**	**6 (23.1)**	**0.231**
Rabeprazole	**2 (100.0)**	**0 (0.0)**	
Esomeprazole	**20 (87.0)**	**3 (13.0)**	
Pantoprazole	**0 (0.0)**	**0 (0.0)**	
Tegoprazan	**0 (0.0)**	**1 (100.0)**	
Treatment Regimen			
A	**31 (86.1)**	**5 (13.9)**	**0.013**
B	**7 (100.0)**	**0 (0.0)**	
C	**3 (16.7)**	**4 (57.1)**	
D	**0 (0.0)**	**1 (100.0)**	
E	**1 (100.0)**	**0 (0.0)**	
Probiotics			
without probiotics	**24 (75.0)**	**8 (25.0)**	**0.283**
with probiotics	**18 (90.0)**	**2 (10.0)**	
Treatment duration			
7 days	**13 (68.4)**	**6 (31.6)**	**0.364**
10 days	**10 (100.0)**	**0 (0.0)**	
14 days	**18 (81.8)**	**4 (18.2)**	
Year			
2019	**12 (63.2)**	**7 (36.8)**	**0.047**
2021	**20 (87.0)**	**3 (13.0)**	
Total	**42 (80.7)**	**10 (19.3)**	

Data are expressed as n (eradication rate %).
PPI - proton pump inhibitor, P-CAB - potassium competitive acid blocker, STT - stand triple therapy, A - bismuth quadruple, B - levofloxacin quadruple, C - moxifloxacin triple, D - levofloxacin triple, E - bismuth + amoxicillin + metronidazole + PPI.

PPIs and antibiotics.

Determination of eradication

Eradication therapy was determined to be successful if the urea breath test (UBT) or RUT performed 4 weeks after the eradication therapy showed a negative finding.

Statistical analysis

Statistical analysis was performed using the IBM SPSS Statistics ver. 26 (IBM SPSS Statistics for Windows; IBM Corp., Armonk, NY, USA). Continuous variables are expressed as mean ± standard deviation and categorical variables are presented as numbers and percentages. The differences in the eradication rate according to the variables were analyzed using the chi-squared test. Differences in the eradication rates across years were analyzed based on linear-by-linear association. A p-value of < 0.05 was considered to be statistically significant.

RESULTS

Participants' characteristics

During the study period, 3,092 patients tested positive using RUT and 1,177 of them underwent eradication therapy. Among 302 patients diagnosed with *H. pylori* infection via PCR, 217 patients underwent eradication therapy. Hence, a total of 1,394 patients underwent eradication therapy during the study period. After excluding 280 patients lost to follow-up, 1,114 patients were included in the analysis.

Among patients who tested positive on RUT, 1,177 underwent the STT. Except for 249 patients who did not undergo the UBT, 928 patients were included in the empirical therapy group. Among patients who tested positive on PCR test, 223 (73.8%) patients tested negative on the clarithromycin resistance test, whereas 79 (26.1%) tested positive on the clarithromycin resistance test. Of these 79 patients, 73 had A2143G mutation, four had A2142G mutation, and two had A2143G and A2142G mutations. Depending on the resistance status, these patients underwent tailored therapies, such as STT or BQT (Figure 1).

In the empirical therapy group, 491 (52.9%) were men, and 437 (47.0%) were women. The patients' ages ranged from 18 to 87 years, and the mean age was 58.0 years. The most commonly used PPI for the eradication therapy was lansoprazole (n = 460, 49.5%), and P-CAB tegoprazan was used in 9 (0.9%) patients. Probiotics were used concurrently with eradication therapy in 345 patients. The types of probiotics used were *Saccharomyces boulardii* (Bioflor®) (n = 251, 72.7%), *Lactobacillus acidophilus* (Antibio®) (n = 47, 13.6%), or *Lactobacillus casei* (Ramnos®) (n = 47, 13.6%). The duration of STT was 7 days (n = 552, 59.4%), 10 days (n = 107, 11.5%), or 14 days (n = 269, 28.9%) (Table 1). Patients who were confirmed with *H. pylori* infection based on PCR test findings underwent tailored therapy depending on clarithromycin resistance. The patients' baseline characteristics are shown in Table 1.

Eradication rates of first-line, second-line, and third-line therapies in patients who tested positive on RUT

Of 3,092 patients who tested positive for *H. pylori* on RUT, 1,177 underwent STT, while 249 were lost to follow-up. Of 928 patients who were followed-up, 676 had successful eradication, with an eradication rate of 72.8% after first-line therapy. The eradication rates did not differ by gender, with 75.4% in men and 70.0% in women (p = 0.068). Among patients who achieved eradication after the first-line therapy, the mean age was 57.65 ± 11.09 years, and the eradication rate did not differ by age (p = 0.054). The eradication rate also did not differ by type of PPI (p = 0.455). The eradication rate was 71.5% in the STT-only group and 73.4% in the probiotics-added group, with no significant difference between the two groups (p = 0.240). The eradication rate differed significantly according to treatment duration, with 69.7% in the 7-day group, 67.3% in the 10-day group, and 81.4% in the 14-day group (p = 0.001). By year, the eradication rate with STT was 71.6% in 2018, 77.4% in 2019, 70.3% in 2020, and 70.6% in 2021, showing no marked changes over the years (p = 0.173) (Table 2).

Of 252 patients who failed to achieve eradication after the first-line therapy, 230 patients underwent second-line therapy. After excluding 31 patients lost to follow-up, 199 patients were examined. Of these 199 patients, 174 successfully achieved eradication, with an eradication rate of 87.4% after second-line therapy. BQT was the most common second-line therapy (n = 136), and other therapies included levofloxacin quadruple, moxifloxacin triple, and levofloxacin triple therapies. By gender, the eradication rate after second-line therapy was 80.6% in men (75/93) and 92.5% in women (98/106), showing a significant difference between genders (p = 0.014). The eradication rate decreased significantly with advancing age (p = 0.014). No significant differences were noted in the eradication rate according to type of PPI: lansoprazole 92.8% (77/83), rabeprazole 87.8% (36/41), esomeprazole 80.8% (59/73), and tegoprazan 50% (1/2) (p = 0.055). Moreover, the eradication rate did not differ significantly according to the duration of treatment, with 87.1% (81/93) in the 7-day group, 85.7% (18/21) in the 10-day group, and 87.1% (74/85) in the 14-day group (p = 1.000). In the probiotics-added group, the eradication rate was 85.0%, which was not significantly different from that in the group without probiotics (p = 0.497). By year, the eradication rate was 100% (17/17) in 2018, 85.5% (47/55) in 2019, 88.2% (75/85) in 2020, and 81.0% (34/42) in 2021, showing no significant differences across the years (p = 0.254). Of 25 patients who failed to achieve eradication after the second-line therapy, 12 underwent third-line therapy. Among these 12 patients, two were lost to follow-up and 10 completed follow-up. Nine of them successfully achieved eradication. The eradication rate after third-line therapy was 90.0%. If all first, second, and third-line therapies were performed, the overall eradication rate was 92.6% (860/928).

Eradication rate after first-line therapy in the group of patients who tested positive on PCR and resistance testing

Of 302 patients who tested positive for *H. pylori* on PCR test, 223 did not have clarithromycin resistance (73.8%), whereas 79 patients had resistance (26.1%). Of 223 patients with the non-clarithromycin-resistant strain, 160 underwent eradication therapy. After excluding 135 patients lost to follow-up, 118 patients successfully achieved eradication with the STT at a success rate of 87.4%. Among 11 patients who underwent second-line therapy, three were lost to follow-up. Seven of the remaining eight patients successfully achieved eradication after second-line therapy at a success rate of 87.5%. No significant difference was noted in the eradication rate after the first-line therapy according to gender (p = 0.107), but the eradication rate differed significantly according to age (p = 0.033). The eradication rate did not differ according to the duration of therapy (p = 0.364), use of probiotics (p = 1.000), or year (p = 0.492) (Table 3).

Of 79 patients who had a clarithromycin-resistant strain, 57 underwent eradication therapy. There were 26 men and 31 women, with a mean age of 59.68 years. The most commonly prescribed eradication therapy was BQT (68.4%), and the most common treatment duration was 14 days (48.0%). The most commonly prescribed PPI was lansoprazole (55.7%). After excluding five patients who were lost to follow-up, 42 out of 52 patients successfully achieved eradication, at a success rate of 80.7%. The treatment outcomes of the clarithromycin-resistant group are shown in Table 4.

DISCUSSION

This study retrospectively analyzed the *H. pylori* eradication rate at a single center in Daegu, Korea and examined the differences in the eradication rates according to gender, age, type of PPI or P-CAB, duration of treat-

ment, use and type of probiotics, and year. The results indicated that the eradication rate with STT did not significantly differ according to gender and age in patients with unknown clarithromycin resistance status. No significant differences were noted in the eradication rate according to the type of PPI or P-CAB and the use of probiotics. The success rates did not significantly differ from 2018 to 2021, but the eradication rate was significantly higher in the 14-day treatment group than in the 7-day or 10-day treatment groups.

The eradication rate with STT in this study (72.8%) fell short of the 80% eradication expected with first-line therapies. Although STT has been the most commonly used first-line therapy for *H. pylori* infection, a recent study recommends STT as the first-line therapy owing to the increasing clarithromycin resistance in recent years [12]. Clarithromycin resistance has been reported to increase in Korea as well [13], but a recently updated guideline (2020) still recommends 1-week or 2-week STT as the first-line therapy depending on the clarithromycin resistance status [3]. The eradication rates investigated in a multicenter study in Daegu and Gyeongbuk regions did not significantly differ across a 13-year period, with 78.0% in 1999 and 79.3% in 2011 [14], but our study showed that the eradication rates of STT from 2018 to 2021 (72.8%) were lower than those reported previously in the same regions. However, the eradication rates did not differ significantly over the 4-year period (71.6%, 77.4%, 70.3%, and 70.4% from 2018 to 2021, respectively).

The most important factor in the decreased eradication rate is speculated to be antibiotic resistance [15], and clarithromycin resistance is closely associated with the reduction in eradication rate with STT [12,16,17]. Although the prevalence of clarithromycin resistance differs across studies, one common result is that it is gradually increasing. A previous study reported that the prevalence of clarithromycin resistance increased from 22.9% in 2003 - 2005 to 37% in 2009 - 2012 [13]. The mean prevalence of clarithromycin resistance observed in the present study was 26.1% in 2019 - 2021. Based on an eradication rate of 78.0% - 95.7% in 1999 - 2011 in Daegu and Gyeongbuk regions [14], clarithromycin resistance is suspected to have become more prevalent. A recent clinical practice guidelines mentions the need for new triple therapy regimens with varying drug combinations and durations, given the decreased eradication rate with STT due to increased clarithromycin resistance in Korea. In order to use STT as a first-line therapy, clarithromycin susceptibility results should be incorporated or other eradication therapies should be selected. Further, if STT is used as a first-line therapy without performing a clarithromycin susceptibility test, a 14-day therapy is recommended. In the present study, the eradication rate with STT differed significantly between 7-day (69.7%) therapy and 14-day (81.4%) therapy if clarithromycin resistance was not tested. However, even when the bacterial strain was confirmed to be susceptible to clarithromycin, a significant difference was noted in the eradication rate with STT between the 7-day (87.7%) therapy and 14-day therapy (93.1%), although not to a statistically significant extent.

In addition, a new treatment strategy involves choosing the drugs using PCR or sequencing of 23S ribosome RNA, which is known to be associated with clarithromycin resistance. According to a recent case-control study, the eradication rate was higher with BQT and PPI + amoxicillin + metronidazole (PAM) therapy (chosen based on clarithromycin susceptibility testing results) than with STT [18-20]. In the present study, the overall eradication rate in cases of clarithromycin resistance was 87.4%; however, the rates differed slightly depending on the specific regimen, showing that this eradication rate was higher than the eradication rate with STT administered randomly. Therefore, antibiotic susceptibility testing should be performed before the eradication therapy to improve the eradication rate. Several guidelines recommend BQT or non-BQT as the first-line therapy in regions with high clarithromycin resistance (≥ 15%) [3,21]. However, a recently updated clinical practice guideline showed that BQT was not significantly superior to STT or 10-day sequential therapy and had higher adverse reactions than other eradication therapies in a meta-analysis. Thus, the guideline recommends the use of BQT as the first-line therapy only when other therapy regimens cannot be used.

In general, the eradication rate increases with increasing potency of gastric acid suppression; therefore, the PPI dose in triple therapy regimens is two-fold higher than the general dose [22]. Previous studies have reported that esomeprazole, a second-generation PPI, is more effective than first-generation PPIs in eradication [23-25], but meta-analyses analyzing the eradication rates with varying types of PPIs did not find marked differences. In the present study, no significant difference was noted in the eradication rate according to the type of PPI. This is speculated to be due to the minimal variations in the potency of PPIs in gastric acid suppression; in other words, antibiotic resistance has a greater impact on the eradication rate than does the type of PPI used. In a previous study, the eradication rate with a triple therapy including lansoprazole was 75.9%, which is significantly different from the 92.7% with a triple therapy including vonoprazan [26]. In the present study, the eradication rate was higher when a P-CAB (tegoprazan) was used (88.9%) than when a PPI was used in STT in patients with unknown clarithromycin resistance status, indicating the need for further research.

As a means to increase the eradication rate, the use of probiotics has been studied [27]. Probiotics are known to not only suppress the adverse effects of antibiotics but also directly inhibit *H. pylori* [27]. However, a previous study reported that probiotics did not significantly increase the eradication rate [28]. In the present study, the effects of probiotics on increasing the eradication rate were unclear, and no significant differences were found between the types of probiotics. However, additional research is needed to examine factors that con-

tribute to the effects of probiotics on the eradication rate.

This study has some limitations, including the single-center retrospective nature. First, we only used data from patients of a single center in one region; therefore, the findings have limited generalizability. Second, medication adherence, smoking, and drinking are known to be important factors that affect the success of eradication therapy, but we could not fully investigate these factors. Third, we could not obtain information about patients' antibiotic use history.

In conclusion, we found that the eradication rate with STT at a single center in Daegu region falls short (72.8%) of the expected rate and is lower than the eradication rate reported previously. Extending the duration of STT to 2 weeks can help increase the eradication rate. Tailored therapy based on the results of clarithromycin susceptibility testing produces superior outcomes than empirical therapy. Therefore, susceptibility testing should be actively utilized to enhance the efficacy of eradication therapies.

Declaration of Interest:

The authors declare no conflict of interest.

References:

1. McColl KE. Clinical practice. *Helicobacter pylori* infection. N Engl J Med 2010 Apr 29;362(17):1597-604. (PMID: 20427808)

2. Lee JH, Choi KD, Jung HY, et al. Seroprevalence of *Helicobacter pylori* in Korea: A multicenter, nationwide study conducted in 2015 and 2016. Helicobacter 2018 Apr;23(2):e12463. (PMID: 29345022)

3. Jung HK, Kang SJ, Lee YC, et al. Evidence-based guidelines for the treatment of Helicobacter pylori infection in Korea 2020. Gut Liver 2021 Mar 3;15(2):168-95. (PMID: 33468712)

4. Thung I, Aramin H, Vavinskaya V, et al. Review article: the global emergence of Helicobacter pylori antibiotic resistance. Aliment Pharmacol Ther 2016 Feb;43(4):514-33. (PMID: 26694080)

5. Rokkas T, Gisbert JP, Malfertheiner P, et al. Comparative effectiveness of multiple different first-line treatment regimens for Helicobacter pylori infection: a network meta-analysis. Gastroenterology 2021 Aug 1;161(2):495-507. (PMID: 33839101)

6. Gong EJ, Yun SC, Jung HY, et al. Meta-analysis of first-line triple therapy for helicobacter pylori eradication in Korea: is it time to change? J Korean Med Sci 2014 May 1;29(5):704-13. (PMID: 24851029)

7. Kim SE, Park MI, Park SJ, et al. Trends in Helicobacter pylori eradication rates by first-line triple therapy and related factors in eradication therapy. Korean J Intern Med 2015 Nov;30(6):801-7. (PMID: 26552455)

8. Shin WG, Lee SW, Baik GH, et al. Eradication rates of Helicobacter pylori in Korea over the past 10 years and correlation of the amount of antibiotics use: nationwide survey. Helicobacter 2016 Aug;21(4):266-78. (PMID: 26470999)

9. Lee JH, Ahn JY, Choi KD, et al. Nationwide antibiotic resistance mapping of Helicobacter pylori in Korea: A prospective multicenter study. Helicobacter 2019 Aug;24(4):e12592. (PMID: 31111572)

10. Kwon YH, Jeon SW, Nam SY, Lee HS, Park JH. Efficacy of tailored therapy for Helicobacter pylori eradication based on clarithromycin resistance and survey of previous antibiotic exposure: A single-center prospective pilot study. Helicobacter 2019 Aug;24(4):e12585. (PMID: 30969459)

11. Godavarthy PK, Puli C. From antibiotic resistance to antibiotic renaissance: a new era in *Helicobacter pylori* treatment. Cureus 2023 Mar 12;15(3):e36041. (PMID: 36919111)

12. Chang YW, Ko WJ, Oh CH, et al. Clarithromycin resistance and female gender affect Helicobacter pylori eradication failure in chronic gastritis. Korean J Intern Med 2019 Sep;34(5):1022-9. (PMID: 29898576)

13. Lee JW, Kim N, Kim JM, et al. Prevalence of primary and secondary antimicrobial resistance of *Helicobacter pylori* in Korea from 2003 through 2012. Helicobacter 2013 Jun;18(3):206-14. (PMID: 23241101)

14. Jung YS, Lee SH, Park CS, et al. [Trends in the eradication rates of Helicobacter pylori infection in Daegu and Gyeongsangbuk-do, Korea: multicenter study over 13 years]. Korean J Gastroenterol 2014 Feb 1;63(2):82-9. (PMID: 24561694)

15. Mégraud F. *H. pylori* antibiotic resistance: prevalence, importance, and advances in testing. Gut 2004 Sep 1;53(9):1374-84. (PMID: 15306603)

16. Lee JY, Kim N, Kim MS, et al. Factors affecting first-line triple therapy of Helicobacter pylori including CYP2C19 genotype and antibiotic resistance. Dig Dis Sci 2014 Jun;59:1235-43. (PMID: 24599773)

17. Lee JH, Shin JH, Roe IH, et al. Impact of clarithromycin resistance on eradication of Helicobacter pylori in infected adults. Antimicrob Agents Chemother 2005 Apr;49(4):1600-3. (PMID: 15793150)

18. Cho JH, Jeon SR, Kim HG, Jin SY, Park S. Cost-effectiveness of a tailored Helicobacter pylori eradication strategy based on the presence of a 23S ribosomal RNA point mutation that causes clarithromycin resistance in Korean patients. J Gastroenterol Hepatol 2019;34:700-6. (PMID: 30011083)

19. Gweon TG, Kim JS, Kim BW. An economic modeling study of Helicobacter pylori eradication: comparison of dual priming oligonucleotide-based multiplex polymerase chain reaction and empirical treatment. Gut Liver 2018 Nov;12(6):648-54. (PMID: 30037167)

20. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG clinical guideline: treatment of Helicobacter pylori infection. Am J Gastroenterol 2017 Feb 1;112(2):212-39. (PMID: 28071659)

21. Malfertheiner P, Megraud F, Rokkas T, et al. Management of *Helicobacter pylori infection*: the Maastricht VI/Florence consensus report. Gut 2022 Aug 8:gutjnl-2022-327745. (PMID: 35944925)

22. Vallve M, Vergara M, Gisbert JP, Calvet X. Single vs. double dose of a proton pump inhibitor in triple therapy for Helicobacter pylori eradication: a meta-analysis. Aliment Pharmacol Ther 2002 Jun;16(6):1149-56. (PMID: 12030958)

23. Anagnostopoulos GK, Tsiakos S, Margantinis G, Kostopoulos P, Arvanitidis D. Esomeprazole versus omeprazole for the eradication of Helicobacter pylori infection: results of a randomized controlled study. J Clin Gastroenterol 2004 Jul 1;38(6):503-6. (PMID: 15220685)

24. Villoria A, Garcia P, Calvet X, Gisbert JP, Vergara M. Meta-analysis: high-dose proton pump inhibitors vs. standard dose in triple therapy for *Helicobacter pylori* eradication. Aliment Pharmacol Ther 2008 Oct;28(7):868-77. (PMID: 18644011)

25. Keum B, Lee SW, Kim SY, et al. Comparison of *Helicobacter pylori* eradication rate according to different PPI-based triple therapy-omeprazole, rabeprazole, esomeprazole and lansoprazole. Korean J Gastroenterol 2005 Dec 1;46(6):433-9. (PMID: 16371717)

26. 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 Sep 1;65(9):1439-46. (PMID: 26935876)

27. Kim MN, Kim N, Lee SH, et al. The effects of probiotics on PPI-triple therapy for Helicobacter pylori eradication. Helicobacter 2008 Aug;13(4):261-8. (PMID: 18665934)

28. Lu C, Sang J, He H, et al. Probiotic supplementation does not improve eradication rate of Helicobacter pylori infection compared to placebo based on standard therapy: a meta-analysis. Sci Rep 2016 Mar 21;6:23522. (PMID: 26997149)