

The Efficacy of Moxifloxacin-Containing Triple Therapy after Standard Triple, Sequential, or Concomitant Therapy Failure for *Helicobacter pylori* Eradication in Korea

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Background/Aims: Retreatment after initial treatment failure for *Helicobacter pylori* is very challenging. The purpose of this study was to evaluate the efficacies of moxifloxacin-containing triple and bismuth-containing quadruple therapy.

Methods: A total of 151 patients, who failed initial *H. pylori* treatment, were included in this retrospective cohort study. The initial regimens were standard triple, sequential, or concomitant therapy, and the efficacies of the two following second-line treatments were evaluated: 7-day moxifloxacin-containing triple therapy (rabeprazole 20 mg twice a day, amoxicillin 1,000 mg twice a day, and moxifloxacin 400 mg once daily) and 7-day bismuth-containing quadruple therapy (rabeprazole 20 mg twice a day, tetracycline 500 mg 4 times a day, metronidazole 500 mg 3 times a day, and tripotassium dicitrate bismuthate 300 mg 4 times a day). **Results:** The overall eradication rates after moxifloxacin-containing triple therapy and bismuth-containing quadruple therapy were 69/110 (62.7%) and 32/41 (78%), respectively. Comparison of the two regimens was performed in the patients who failed standard triple therapy, and the results revealed eradication rates of 14/28 (50%) and 32/41 (78%), respectively ($p=0.015$). The frequency of noncompliance was not different between the two groups, and there were fewer adverse effects in the moxifloxacin-containing triple therapy group (2.8% vs 7.3%, $p=0.204$ and 25.7% vs 43.9%, $p=0.031$, respectively). **Conclusions:** Moxifloxacin-containing triple therapy, a recommended second-line treatment for initial concomitant or sequential therapy failure, had insufficient efficacy. (*Gut Liver* 2014;8:605-611)

Key Words: Anti-bacterial agents; *Helicobacter pylori*; Moxi-

floxacin; Salvage therapy

INTRODUCTION

Helicobacter pylori is one of the most common pathogens, affecting over 50% of the global population, and is a well-known important cause of duodenal or gastric ulcers, gastric cancer, and gastric mucosa-associated lymphoid-tissue lymphoma.^{1,2} According to current guidelines, *H. pylori* eradication is recommended for several conditions including dyspepsia, peptic ulcer disease, gastric mucosa-associated lymphoid-tissue lymphoma, atrophic gastritis, and after the gastric cancer resection.³

During the last decade, standard first-line treatment regimen for *H. pylori* eradication was triple therapy with a proton pump inhibitor (PPI), clarithromycin and amoxicillin (or metronidazole) for 7 to 14 days.³ However, in recent years, the eradication rate of triple therapy has steadily decreased. Recently, sequential therapy, that is 5 days of PPI plus amoxicillin followed by 5 additional days of PPI, clarithromycin and metronidazole, or concomitant therapy, that is four drugs (PPI, clarithromycin, metronidazole, and amoxicillin) given concomitantly, has been proposed; these regimens produced higher eradication rates than standard triple therapy.⁴⁻⁷ However, eradication failure of first-line treatment is yet to be solved and retreatment regimens after initial treatment failure are very challenging.

The Maastricht IV consensus report recommended bismuth-containing quadruple therapy as the preferred option for second-line treatment.^{3,8} However, in a pooled analysis, which included 40 trials, the average eradication rate of second-line bismuth-containing quadruple therapy was 76%.⁹ Of note, this regimen requires that four drugs be administered with a com-

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Received on August 16, 2013. Revised on October 5, 2013. Accepted on October 6, 2013. Published online on April 23, 2014

pISSN 1976-2283 eISSN 2005-1212 <http://dx.doi.org/10.5009/gnl13303>

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plicated dosing schedule and is associated with a relatively high incidence of adverse effects.^{9,10} Furthermore, it remains unclear how to choose second-line treatment when *H. pylori* persists after newer first-line therapies, such as sequential therapy, concomitant therapy or hybrid therapy. Bismuth-containing quadruple therapy may not be a good choice for patients who failed after sequential therapy or concomitant therapy since such patients already received metronidazole as a first-line treatment and metronidazole resistance could be a reason for the treatment failure. Additionally, bismuth is not currently available in many countries.

Alternatives suggested for second-line treatment are levofloxacin or rifabutin (combined with PPI and amoxicillin); these are two classes of antibiotics different from those employed in first-line therapies. However, rifabutin must be used cautiously because its use can select for resistance among Mycobacteria. Additionally, fluoroquinolone susceptibilities were rarely reported; however, recent data indicate that levofloxacin resistance reaches 20% in some areas and can result in eradication failure.^{3,11,12} Moxifloxacin, another option for the second-line treatment, is also a second-generation fluoroquinolone that is currently widely used for various infections.¹³ Several studies of second-line *H. pylori* treatment found higher efficacy and tolerance with moxifloxacin-containing triple therapy than with bismuth-containing quadruple therapy.¹⁴⁻¹⁷ However, those reports did not represent all the regions and populations. Moreover, there are limited data for patients who failed to eradicate *H. pylori* with newer first-line therapies.

Retreatment after initial failure of *H. pylori* eradication is still complicated issue and eradication rates vary depending on race, country, and previous treatment regimens because the antimicrobial resistance patterns differ. The purpose of this study was to compare the efficacy and safety of moxifloxacin-containing triple therapy with bismuth-containing quadruple therapy as a second-line *H. pylori* treatment.

MATERIALS AND METHODS

1. Patients

Between January 1, 2010 and January 30, 2013, 151 *H. pylori*-infected patients who failed first-line *H. pylori* eradication treatment with standard triple, sequential or concomitant regimen were included in this retrospective analysis. Exclusion criteria included: 1) age less than 18; 2) patients with previous gastric surgery; 3) patients with serious comorbidity (e.g., decompensated liver cirrhosis, disseminated malignancy, and uremia); 4) patients who were treated with second-line regimens different from moxifloxacin-containing triple therapy or bismuth-containing quadruple therapy, 5) allergy to any of the drugs used in the study, and 6) pregnancy. Initial diagnosis of *H. pylori* infection was defined as a positive rapid urease test or histology. Treatment failure of *H. pylori* after both first-line

and second-line therapy was defined as a positive urea breath test, performed 4 weeks or longer after completion of therapy. Completion of a urea breath test after the second-line therapy was an inclusion criterion.

2. Study design

In the study period, a total of 151 patients whose initial treatment failure was confirmed by urea breath test were included. Their initial treatment regimens were the following: standard triple therapy (rabeprazole 20 mg twice a day, clarithromycin 500 mg twice a day, and amoxicillin 1,000 mg twice a day for 7 days; n=69), sequential therapy (rabeprazole 20 mg twice a day and amoxicillin 1,000 mg twice a day for 5 days followed by rabeprazole 20 mg twice a day, clarithromycin 500 mg twice a day, and metronidazole 500 mg twice a day for 5 more days; n=42), concomitant therapy (rabeprazole 20 mg twice a day, clarithromycin 500 mg twice a day, amoxicillin 1,000 mg twice a day, and metronidazole 500 mg twice a day for 14 days; n=40). All the patients received the second-line regimen chosen nonrandomly by their physician, either moxifloxacin-containing triple therapy (rabeprazole 20 mg twice a day, amoxicillin 1,000 mg twice a day, and moxifloxacin 400 mg once daily for 7 days; n=110) or bismuth-containing quadruple therapy (rabeprazole 20 mg twice a day, tetracycline 500 mg 4 times a day, metronidazole 500 mg 3 times a day, and tripotassium dicitrate bismuthate 300 mg 4 times a day for 7 days; n=41). However, all the patients who received sequential therapy or concomitant therapy as first-line regimen were received bismuth-containing quadruple therapy as second-line regimen. All patients underwent a urea breath test 4 to 6 weeks after the completion of second-line eradication therapy. Then the patients visited an outpatient clinic where drug compliance and adverse events were assessed and recorded. Eradication was defined as a negative urea breath test. Medical records were reviewed to obtain initial endoscopic findings, histologic findings, complete medical history, history of smoking and alcohol consumption, and demographic data including age and sex. The study protocol was approved by the Institutional Review Board of Seoul National University Bundang Hospital (IRB number: B-1203/148-105) and confirmed to the ethical guidelines of the Declaration of Helsinki, 1964, as revised in 2004. The requirement for informed consent was waived.

3. Rapid urease test, histology, and urea breath test

To identify the presence of *H. pylori* infection, both histology (by modified Giemsa stain) and the campylobacter-like organism test (CLO test [rapid urease test]; Delta West Ltd., Bentley, WA, Australia) were performed. In addition, gastric biopsy specimens obtained from the corpus were evaluated for the degree of inflammatory cell infiltration, atrophy and intestinal metaplasia (all determined by hematoxylin and eosin staining). The histological features of the gastric mucosa were ranked us-

ing the updated Sydney scoring system (0, none; 1, slight; 2, moderate; and 3, marked).¹⁸ If either of the two tests (CLO test or histology) was positive, the specimen was classified as *H. pylori* positive. To identify the presence of *H. pylori* after the completion of therapy, the urea breath test was performed. During the urea breath test, an initial breath sample was obtained after a 4-hour fast. One hundred milligrams of ¹³C-urea powder (UBiT-kit; Otsuka Pharmaceutical, Tokyo, Japan) dissolved in 100 mL water was administered orally. The second breath sample was obtained 20 minutes later. The cutoff value was 2.5%. Collected samples were analyzed using an isotope ratio mass spectrometer (UBiT-IR300; Otsuka Pharmaceutical).

4. Statistical analysis

The primary outcome variables were eradication rates, presence of adverse events, and compliance with the second-line therapy. Eradication rate of two regimens were compared only with the patients who failed first-line standard triple therapy. Adverse events and compliance of the two regimens were compared with all study participants. Overall eradication rates and their 95% confidence intervals (CIs) were estimated in accordance with the definition of eradication. The chi-square test and Fisher exact test were used when appropriate to compare the frequencies of the major outcomes between groups using the SPSS program version 18.0.0 (SPSS Inc., Chicago, IL, USA). A p-value <0.05 was considered statistically significant. To determine the independent factors that affected treatment response, clinical and endoscopic parameters were analyzed by univariate analysis. These variables included the following: age (<60 or ≥60 years), sex, cigarette smoking, and alcohol consumption during the treatment period, baseline endoscopic appearance, histological features of the gastric mucosa and drug compliance (complete or incomplete). Those variables found to be significant by univariate analysis were subsequently assessed by stepwise logistic regression to identify factors that were independently associated with eradication of *H. pylori*.

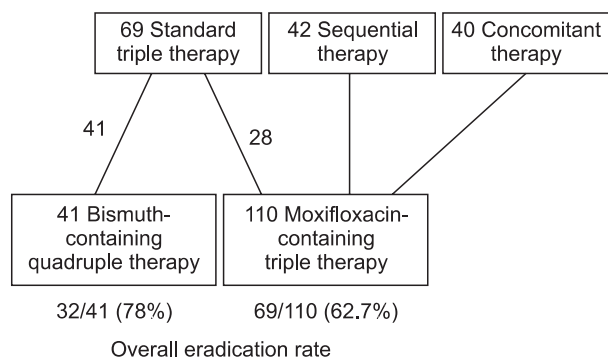


Fig. 1. The flow chart shows the numbers of patients treated with each first- and second-line regimen for *Helicobacter pylori* eradication.

RESULTS

1. Patients

Among the 151 patients who failed with first-line *H. pylori* eradication, 110 patients received moxifloxacin-containing triple therapy, and 41 patients received bismuth-containing quadruple therapy. The 110 patients who were treated with moxifloxacin-containing triple therapy as a second-line treatment had received the following first-line treatment regimens: 1)

Table 1. Baseline Characteristics of Patients in the Second-Line Treatment Group

Characteristic	Moxifloxacin-containing triple therapy (n=110)	Bismuth-containing quadruple therapy (n=41)	p-value
Male sex	50 (45.5)	14 (34.1)	0.211
Age, yr	56.7±11.57	57.7±11.73	0.650
Alcohol	24 (22.0)	1 (2.4)	0.003
Smoking	7 (6.4)	1 (2.4)	0.447
Histology			
HP colonization			0.324
Absent	8 (7.3)	0	
Mild	33 (30.3)	12 (29.3)	
Moderate	41 (37.6)	20 (48.8)	
Marked	17 (15.6)	7 (17.1)	
NA	10 (9.2)	2 (4.9)	
Neutrophil			0.056
Absent	12 (11.0)	1 (2.4)	
Mild	9 (8.3)	0	
Moderate	65 (59.6)	29 (70.7)	
Marked	13 (11.9)	9 (22.0)	
NA	10 (9.2)	2 (4.9)	
Atrophic change			0.696
Present	9 (8.3)	4 (9.8)	
Absent	41 (37.6)	18 (43.9)	
NA	59 (54.1)	19 (46.3)	
Intestinal metaplasia			0.885
Present	19 (17.4)	7 (17.1)	
Absent	80 (73.4)	32 (78.0)	
NA	10 (9.2)	2 (4.9)	
EGD feature			
GERD	32 (29.4)	14 (34.1)	0.571
DU	17 (15.6)	4 (9.8)	0.358
GU	7 (6.4)	3 (7.3)	1.000
Gastric polyp	17 (15.6)	6 (14.6)	0.884

Data are presented as mean±SD or number (%).

HP, *Helicobacter pylori*; NA, not available; EGD, esophagogastroduodenoscopy; GERD, gastroesophageal reflux disease; DU, duodenal ulcer; GU, gastric ulcer.

Table 2. Adverse Events by Study Group

	Moxifloxacin-containing triple therapy (n=109)	Bismuth-containing quadruple therapy (n=41)	p-value
Bitter taste	0	4 (9.8)	0.005
General body ache	1 (0.9)	2 (4.9)	0.181
Dyspepsia	6 (5.5)	5 (12.2)	0.161
Diarrhea	8 (7.3)	3 (7.3)	1
Epigastric fullness	3 (2.8)	3 (7.3)	0.346
Epigastric soreness	1 (0.9)	1 (2.4)	0.473
Nausea/vomiting	8 (7.3)	6 (14.6)	0.209
Urticaria	0	1 (2.4)	0.273
Dizziness	1 (0.9)	2 (4.9)	0.181
Constipation	1 (0.9)	1 (2.4)	0.473
Headache	1 (0.9)	1 (2.4)	0.473

Data are presented as number (%).

standard triple therapy (n=28); 2) concomitant therapy (n=29); and 3) sequential therapy (n=21). All of the patients who received bismuth-containing quadruple therapy as a second-line therapy were received standard triple therapy as first-line treatment (Fig. 1). The baseline clinical characteristics of patients (before first-line treatment) are summarized in Table 1. The two second-line treatment groups had comparable age, sex, and history of cigarette smoking. However, the moxifloxacin-containing triple therapy group had a higher frequency of alcohol consumption (p=0.003) than the bismuth-containing quadruple therapy group. Additionally, the frequency of gastroesophageal reflux disease, gastric ulcer, duodenal ulcer, and gastric polyp at endoscopy were similar between two groups. There were no differences in histologic features (*H. pylori* colonization, mucosal atrophy, and intestinal metaplasia) between the two groups.

2. Eradication of *H. pylori*

The overall eradication rates after second-line treatment with moxifloxacin-containing triple therapy and bismuth-containing quadruple therapy were 69/110 (62.7%) and 32/41 (78%). However, when comparing the two regimen only with patients who failed standard triple therapy, the eradication rate was 14/28 (50%) in moxifloxacin-containing triple therapy group and 32/41 (78%) in bismuth-containing quadruple therapy group (p=0.015).

3. Adverse events, compliances, and symptom improvement

At least one adverse event was reported by 18 patients (43.9%) who received bismuth-containing quadruple therapy and by 28 patients (25.7%) who received moxifloxacin-containing triple therapy (p=0.031). The frequency of adverse effects was significantly higher with bismuth-containing quadruple therapy. The

reported side effects are shown in Table 2. Three patients in the bismuth-containing quadruple therapy group stopped treatment because of generalized body ache (n=1), constipation (n=1) and dyspepsia and epigastric fullness (n=1). In the moxifloxacin-containing triple therapy group, one patient stopped treatment due to nausea and vomiting and one patient due to diarrhea. However, patients complied well with the eradication therapies; they took more than 70% of the assigned tablets. The groups had similar compliance rates (moxifloxacin-containing triple therapy 92.6% vs bismuth-containing quadruple therapy 92.7%; p=0.666). In addition, symptom improvement was reported in 55/109 (50.5%) of patients in moxifloxacin-containing triple therapy group and 24/41 (58.5%) of patients in bismuth-containing quadruple therapy group (p=0.377).

4. Factors associated with the efficacy of anti-*H. pylori* therapy

Efficacy analysis was performed only with the patients who failed standard triple therapy and the clinical and endoscopic factors that were assessed by univariate analysis for an association with the efficacy of second-line therapy are shown in Table 3. The eradication rates were significantly related to the eradication regimen (p=0.015). Other factors (sex, age, smoking, alcohol consumption, compliance, *H. pylori* colonization, atrophy, intestinal metaplasia, peptic ulcer, and gastroesophageal reflux disease) did not affect the eradication response. Multivariate analysis revealed that bismuth-containing quadruple therapy was independently and positively related to treatment success (odds ratio, 4.071; 95% CI, 1.025 to 16.177; p=0.046).

DISCUSSION

In previous studies, moxifloxacin-containing triple therapy was evaluated for three different stages of anti-*H. pylori* treatment and found to improve efficacy. Moreover, moxifloxacin-containing triple therapy has several advantages in terms of safety and simplicity of dosing schedules. In a previous study, moxifloxacin-containing triple therapy was evaluated as a third-line treatment after failed initial standard triple therapy and second-line bismuth-containing quadruple therapy; the eradication rates were 80.0% (8/10) and 88.9% (8/9) by intention-to-treat (ITT) and per protocol (PP) analysis, respectively.¹⁹ Furthermore, several studies evaluated moxifloxacin-containing triple therapy for first-line treatment. Their eradication rates were varied: 88% (70/80), 89% (70/79),²⁰ 86.4% (57/66); 90.5% (57/63),²¹ 42.2% (30/71), 47.6% (30/63),²² and 53.3% (16/30)²³ by ITT and PP analysis, respectively.

There are also studies of moxifloxacin-containing triple therapy for second-line treatment. In one such trial conducted in Korea, which investigated moxifloxacin-containing triple therapy of different durations (7, 10, and 14 days) found eradication rates from 68.0% to 75.6% (ITT) and from 79.9% to 83.8% (PP).

Table 3. The Clinical and Endoscopic Factors Associated with the Efficacy of Eradication Therapy according to Univariate Analysis

Clinical factor	Eradication rate	p-value
Age, yr		0.307
<60	20/33 (60.6)	
≥60	26/36 (72.2)	
Sex		0.592
Male	15/24 (62.5)	
Female	31/45 (68.9)	
Smoking		0.243
Absent	45/65 (69.2)	
Present	1/3 (33.3)	
Alcohol		0.156
Absent	41/57 (71.9)	
Present	5/11 (45.5)	
Compliance		0.656
Complete	43/63 (68.3)	
Incomplete	3/5 (60.0)	
HP colonization		0.372
Absent	2/2 (100.0)	
Mild	12/22 (54.5)	
Moderate	22/31 (71.0)	
Marked	7/11 (63.6)	
GERD		0.245
Absent	30/42 (71.4)	
Present	15/26 (57.7)	
Duodenal ulcer		0.250
Absent	38/60 (63.3)	
Present	7/8 (87.5)	
Gastric ulcer		1.000
Absent	42/63 (66.7)	
Present	3/5 (60.0)	
Gastric polyp		0.255
Absent	41/59 (69.5)	
Present	4/9 (44.4)	
Atrophy		0.950
Absent	29/44 (65.9)	
Present	16/24 (66.7)	
Intestinal metaplasia		1.000
Absent	40/61 (89.7)	
Present	5/7 (71.4)	
Eradication regimen		0.015
Moxifloxacin-containing triple therapy	14/28 (50.0)	
Bismuth-containing quadruple therapy	32/41 (78.0)	

Data are presented as number/total number (%).

HP, *Helicobacter pylori*; GERD, gastroesophageal reflux disease.

Interestingly, in this trial, the eradication rate had a decreasing trend from 2004 to 2008.²⁴ Another study, which compared 10 days and 7 days of moxifloxacin-containing triple therapy found eradication rates in the 7-day-group, 84% (57/68); 76% (57/75), comparable to those of the 10-day-group, 90% (63/70); 84% (63/75), by PP and ITT analysis, respectively; the differences were not significant.²⁵ Trials also compared moxifloxacin-containing triple therapy with bismuth-containing quadruple therapy. One trial, conducted in Korea, found a higher eradication rate after 7 days of moxifloxacin-containing triple therapy than after 7 days of bismuth-containing quadruple therapy (75.6%/83.8% vs 54.5%/72.7%, $p=0.042/0.260$ by ITT/PP, respectively).¹⁵ Another trial, also conducted in Korea, found that 10 days of moxifloxacin-containing triple therapy had a comparable eradication rate, with fewer side-effects and better drug compliance, to that of 14 days of bismuth-containing quadruple therapy (71.9%/82.6% vs 71.7%/90.5%, $p=0.973/0.321$ by ITT/PP, respectively).¹⁴ Another trial, conducted in Austria, that compared 7 days of moxifloxacin-containing triple therapy with 7 of days bismuth-containing quadruple therapy found moxifloxacin-containing triple therapy more advantageous (eradication rates: 73.2%/78.9% vs 53.8%/64.6%, $p=0.018/0.088$ by ITT/PP).¹⁶ A recent meta-analysis, which included seven randomized controlled trials, also found superior efficacy and safety for moxifloxacin-containing triple therapy compared with bismuth-containing quadruple therapy.¹⁷ However, all of the abovementioned trials were conducted with patients who initially failed standard triple therapy; patients who failed initial sequential therapy or concomitant therapy were not included these trials. In contrast, our study included patients who initially failed sequential therapy or concomitant therapy. This is relevant because there are no reports of whether antibiotic resistance is acquired in patients who initially failed with sequential therapy or concomitant therapy and it is difficult to choose second-line treatment regimens in these patients.

Moxifloxacin is considered a promising candidate for second-line treatment of patients who initially fail to eradicate *H. pylori* with sequential therapy or concomitant therapy. However, in this study, the eradication rate of second-line moxifloxacin-containing triple therapy was only 64.3% and 70.0% with the patients who failed first-line sequential therapy and concomitant therapy. Moreover, the eradication rate of second-line moxifloxacin-containing triple therapy after failed with standard triple therapy was only 50.0%. This rate was lower than the eradication rate of bismuth-containing quadruple therapy (78.0%); it was unacceptably low. We speculate that the failure of moxifloxacin-containing triple therapy in this study was primarily due to moxifloxacin resistance. A previous study, in the same region, found a decreasing trend of the eradication rate after moxifloxacin-containing triple therapy from 2004 to 2008 (75.6% to 68.0% [ITT] and 83.8% to 79.9% [PP], p =not significant) and a parallel increase in the resistance rate of

moxifloxacin (7.4% to 28.2%, $p < 0.001$). In contrast, amoxicillin resistance decreased during this time period (7.4% to 2.0%, $p = 0.180$).²⁴ Moreover, in Korea, a recent study of primary antibiotic resistance of *H. pylori* reported a moxifloxacin resistance rate of 25.7% and an amoxicillin resistance rate of 13.8%.²⁶ Another study reported an upward trend in moxifloxacin resistance, from 8.3% to 33.6% during the time interval, from 2003 to 2010.²⁷ These recent reports of high resistance rates against moxifloxacin of *H. pylori* contrast markedly with an earlier study that reported a 5.6% resistance rate of *H. pylori* against moxifloxacin in 2006 from the same region.¹⁵ Additionally, a recent study conducted in China, reported that the primary antibiotic resistance rate against moxifloxacin was 15.1% in *H. pylori* isolates from Beijing children.²⁸ Moxifloxacin is a widely used antibiotic with broad indications that has great potency against gram-negative bacteria and a low frequency of side effects. Prior use of other quinolones might have caused primary resistance to moxifloxacin; resistance has rapidly increased in areas where fluoroquinolones are widely used. This may have influenced the persistence of *H. pylori* we observed after moxifloxacin-containing triple therapy. In previous study conducted in the same region of our study, moxifloxacin resistance rate of *H. pylori* was 5.6% in 2004, 12% in 2005 to 2006, and 28.2% in 2007 to 2008.²⁴ Considering our study period (2010 to 2013), moxifloxacin resistance rate in study period can be roughly estimated 50% by extrapolation which correspond with the eradication failure rate of our study. Unfortunately, in our study, details regarding previous antibiotics use were not adequately collected in the medical records; therefore, the relationship between prior use of moxifloxacin and eradication rate was not assessed. Additionally, this study did not evaluate the relationship between antibiotic resistance and treatment outcomes since we could not investigate the antibiotic resistance of *H. pylori* isolates.

Previous studies consistently reported that the frequencies of side effects and stopping therapy due to side effects were lower with moxifloxacin-containing triple therapy than with bismuth-containing quadruple therapy.¹⁴⁻¹⁷ This tendency was also reported with levofloxacin, another second-generation fluoroquinolones.²⁹ In our study, the frequency of side effects were significantly lower in moxifloxacin-containing triple therapy than bismuth-containing quadruple therapy which is similar with previous studies; however, the frequency of noncompliance were not significantly different between moxifloxacin-containing triple therapy and bismuth-containing quadruple therapy. In the context of previous reports, our study results may reflect its relatively small study population.

Notably, bismuth-containing triple therapy was superior to moxifloxacin-containing triple therapy and achieved an eradication rate of 78.0%. This result was similar to a pooled analysis of 40 trials of quadruple therapy as second-line therapy that reported an average eradication rate of 76%.⁹ There was a con-

sensus that anti-*H. pylori* treatment regimens should be simple, well tolerated and achieve an eradication rate over 80% on an ITT basis.³⁰ In that sense, bismuth-containing triple therapy also did not meet our expectations.

The limitations of our study are that this study was conducted in single center and the data was collected retrospectively and as previously mentioned, antibiotics resistance was not evaluated. We evaluated the efficacy of moxifloxacin-containing triple therapy and bismuth-containing quadruple therapy; however, comparison of the efficacy of two regimens were confined to the patients who failed first-line standard triple regimen and it is impossible to compare the efficacy of two regimen with patients who failed sequential regimen or concomitant regimen because none of this patients were received bismuth-containing quadruple regimen. In addition, we cannot collect sufficient sample within 2 year-period and the number of patients included was relatively small. This reduces the power of our result. Finally, baseline characteristics of two group was mostly similar but, there was significant difference in proportion of patients who drinking alcohol (37% in moxifloxacin-containing triple therapy group and 2.4% in bismuth-containing quadruple therapy group, $p < 0.001$). Although alcohol consumption is not significantly associated with eradication rate, this could affect the effect of the antibiotics and also the eradication rate.

In conclusion, moxifloxacin-containing triple therapy, which was recommended as an alternative therapeutic regimen, especially in patients who were initially treated with sequential therapy or concomitant therapy showed insufficient eradication rate and even lower than bismuth-containing quadruple therapy with patients who failed first-line standard triple regimen. It is presumed that high frequency of primary moxifloxacin resistance may have allowed *H. pylori* to persist after moxifloxacin-containing triple therapy. However, bismuth-containing quadruple therapy was also followed by an unsatisfactory eradication rate. Further studies are needed to find more effective alternatives for second-line therapy.

CONFLICTS OF INTEREST

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

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