Original paper

Which is the best choice for *Helicobacter pylori* eradication? Dual therapy or quadruple therapy?

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Abstract

Introduction: Standard triple therapy used to be the first-line treatment for *Helicobacter pylori* (Hp) infection, but today it is a treatment regimen with a low eradication rate due to increasing resistance to the antibiotics included in the triple therapy.

Aim: To compare the eradication rates of dual treatment regimens and quadruple treatment regimens.

Material and methods: Patients over 18 years of age, who were indicated to undergo upper gastrointestinal system (GIS) endoscopy for any reason, had their upper gastrointestinal endoscopy performed, were detected to have Hp as a result of the histopathological evaluation of the biopsy material, and in whom eradication control was also performed by histopathological evaluation, were included in the study. These patients were divided into 4 groups, each containing 50 people.

Results: Considering the eradication rates of Hp-positive patients according to different treatment options, 78% (n = 39) of the patients in Group 1 were eradicated after the treatment while 66% (n = 33) of the patients in Group 3, 58% of the patients in Group 2 (n = 29), and 58% (n = 29) of the patients in Group 4 had Hp negative results after treatment. When high-dose dual treatments were compared, the highest eradication rate was obtained with rabeprazole, but no statistically significant difference was detected (p = 0.11).

Conclusions: This is the first study to include dual therapies consisting of 3 different PPIs at the same time. The low eradication rates obtained in our study suggest that the determination of individualized treatment strategies in which CYP2C19 polymorphism is detected may result in higher eradication rates.

Introduction

Helicobacter pylori (Hp) infection is the most common chronic bacterial infection associated with peptic ulcer disease in the world [1]. According to estimates, more than 50% of the world's population is thought to be infected with Hp. This rate rises to 70–80% in developing countries [2].

There are endoscopic and non-endoscopic methods available to diagnose Hp infection. These methods can detect Hp directly (histology, bacterial antigen in stool, cultivation) or indirectly (urease detection or antibody response) [3].

Histology of the gastric mucosa is not essential for the diagnosis of Hp but it contributes to the information regarding the severity of inflammation in the mucosa and to the detection of pre-cancerous lesions. Therefore, histology is the gold standard method for the detection of bacteria. The sensitivity of histology is 95% while its specificity is around 98% [4]. Urea breath test, stool antigen test and endoscopic-based tests may be used to confirm a successful treatment. These tests should be performed 6–8 weeks after the end of treatment. The tests performed earlier may lead to false negative results.

Although many antibiotic regimens have been developed for the treatment of Hp, several of them have achieved high eradication rates. In the ideal personalized treatment regimen, the antibiotic resistance of the Hp strain in the infected individual should be determined. Information obtained regarding the local antibiotic resistance and previous antibiotic exposure of the patient is also significant for the determination of the treatment regimen [5]. Nowadays, we see that the standard triple therapy consisting of proton pump inhibitor (PPI), clarithromycin, and amoxicillin or metronidazole

usually provides recovery in only 70% of the patients [6]. Alternative treatment regimens should be considered in regions with high clarithromycin resistance.

Due to the increased resistance rates for clarithromycin and metronidazole observed in the treatment of Hp infection, increased side effects associated with long-term treatment regimens and multiple drug use, and decreased compliance with treatment, different treatment regimens with less medication and shorter duration have come into prominence [7].

Despite the widespread use of amoxicillin, its resistance rates in Hp eradication are quite low. The antibiotic effect of amoxicillin depends on pH and time [8]. An increase in intragastric pH also increases the efficacy of amoxicillin. Therefore, PPI are irreplaceable drugs in eradication treatment. In addition to their anti-secretory effects, PPIs show both indirect and direct antibacterial activity by preventing the deterioration of antibiotics in the gastric mucosa [9]. Patients' responses to PPIs are determined by their capacity to metabolize the drug depending on Cytochrome P450 2C19 (CYP2C19) and MDR 1 gene polymorphism. It was predicted that a significant eradication rate may be achieved even in extensive metabolizers by providing the desired gastric pH level with high PPI doses [10].

Aim

It was aimed to compare the efficacy of double antibiotic + double dose PPI + bismuth salt combination used for 14 days and high-dose PPI + amoxicillin combinations in different varieties on Hp eradication in our study.

Material and methods

Patient selection

Patients over 18 years of age, who were admitted to the Hospital Gastroenterology Outpatient Clinic between 1 January 2011 and 1 June 2018, who were detected to have Hp as a result of the histopathological evaluation of the biopsy material taken from the stomach corpus or antrum during the upper gastrointestinal system (GIS) endoscopy performed for any reason, and whose eradication control was also performed by the histopathological evaluation of the same biopsy material taken during the endoscopy, were included in the study. Patients diagnosed with Hp via different methods and patients treated with different antibiotic combinations were not included in this study.

Method

The patients meeting the inclusion criteria were randomized into 4 groups of 50 people. The outpatient clinic admission complaints, endoscopy results, and findings of histopathological examinations performed on the biopsy materials of these patients were obtained from their medical charts and recorded.

Group 1 received quadruple treatment consisting of 2 antibiotics, bismuth salt and PPI (amoxicillin 1 gr 2 × 1 + clarithromycin 500 mg 2 × 1 + PPI 2 × 1 + bismuth subcitrate 300 mg 2 × 2); Group 2 received esomeprazole 40 mg 2 × 1 + amoxicillin 500 mg 4 × 1; Group 3 received rabeprazole 20 mg 2 × 1 + amoxicillin 500 mg 4 × 1, and Group 4 received pantoprazole 40 mg 2 × 1 + amoxicillin 500 mg 4 × 1. After the specified treatments were administered for 14 days, it was determined that the PPI 2 × 1 treatment should be continued to complete 8 weeks in all groups. Because some of our patients were diagnosed with ulcers, PPI treatments were extended to 8 weeks to ensure their treatment and homogenization among other patients. The eradication rates were compared by examining the eradication controls of the biopsy materials obtained during the upper GIS endoscopies performed after a 1-week off-treatment period following the treatment period of 8 weeks in total by histopathological examination.

The study was approved by the Ethics Committee of Tepecik Training and Research Hospital Application and Research Centre with decision number 2018/7-14 dated 28/06/2018.

Statistical analysis

Statistical Package for Social Sciences 23.0 (SPSS 23.0, Chicago, IL, USA) software was used for statistical analysis. The Kolmogorov-Smirnov, Kurtosis, and Skewness tests were used to evaluate the normality of the data distribution. The data collected as part of the study were summarized as mean ± standard deviation. In data analysis, "One-way analysis of variance: ANOVA" was used for the mean differences of four independent groups when the parametric test prerequisites are met; when these prerequisites were not met, the "Kruskal Wallis" test was used. The Fisher's Exact test or Pearson χ^2 test was used in the analysis of categorical data. $P < 0.05$ value was considered to be statistically significant.

Results

The mean age of the patients was 54 ±14.9 (min.–max.: 31–78) in Group 1, 50 ±12.57 (min.–max.: 25–83) in Group 2, 49.5 ±13.83 (min.–max.: 19–77) in Group 3 and 57 ±14.42 (min.–max.: 28–69) in Group 4 ($p > 0.05$). When the distribution of patients according to gender was examined, it was found out that 58% ($n = 29$) of Group 1, 56% ($n = 28$) of Group 2 and 3 and 36% ($n = 18$) of Group 4 was female ($p = 0.82$). There was no statistically significant difference between the groups in terms of age and gender distribution.

Patients' distribution into groups were examined according to their outpatient clinic admission complaints. According to this examination, 70% (n = 35) of Group 1, 52% (n = 26) of Group 2, 100% (n = 50) of Group 3, and 52% (n = 26) of Group 4 were suffering from dyspepsia (Table I). When the dyspepsia complaint was evaluated between the groups, statistical differences were detected (p = 0.001). When the complaint of abdominal pain was evaluated separately, it was found out that 42% (n = 21) of Group 1, 30% (n = 15) of Group 2, 56% (n = 28) of Group 3, and 30% (n = 15) of Group 4 suffered from abdominal pain. When the complaint of abdominal pain was evaluated between the groups, statistical differences were detected (p = 0.02). When the presence of bloating complaint in patients was evaluated, it was found out that 28% (n = 14) of Group 1, 10% (n = 5) of Group 2, 38% (n = 19) of Group 3, and 10% (n = 5) of Group 4 suffered from this complaint. When the bloating complaint was evaluated between the groups, statistical differences were detected (p = 0.001) (Table I). The complaints of dyspepsia, abdominal pain, and bloating were detected to be highest in the rabeprazole group (Table I).

The treatment groups were classified according to pre-treatment and post-treatment distribution based on the endoscopic findings. Endoscopic findings were screened from the endoscopy reports. Endoscopic complaints were classified as endoscopic antral gastritis, endoscopic erythematous pangastritis, endoscopic erythematous bulbitis, stomach ulcer, and bulbus ulcer. The changes in the pre-treatment and post-treatment endoscopic findings were evaluated (Tables II, III).

The improvement in the pre-treatment and post-treatment endoscopic findings of the patients was compared between the groups, and while a significant improvement was observed in the findings of endoscopic

Table I. The demographics of patient groups and distribution of patients according to their admission complaints

Parameter	Group 1 *n* (%)	Group 2 *n* (%)	Group 3 *n* (%)	Group 4 *n* (%)	*P*-value
Mean age	57 ±14.9	50 ±12.57	49.5 ±13,83	57 ±14.42	0.05
Gender Male/female (%)	21/29 (42/58)	22/28 (44/56)	22/28 (44/56)	32/18 (64/36)	0.82
Dyspepsia	35 (70)	26 (52)	50 (100)	26 (52)	0.001
Abdominal pain	21 (42)	15 (30)	28 (56)	15 (30)	0.02
Bloating	14 (28)	5 (10)	19 (38)	5 (10)	0.001

Table II. Distribution of the pre-treatment endoscopic findings

Variable	Group 1 *n* (%)	Group 2 *n* (%)	Group 3 *n* (%)	Group 4 *n* (%)	*P*-value
Endoscopic antral gastritis	47 (94)	49 (98)	49 (98)	49 (98)	0.56
Endoscopic erythematous pangastritis	12 (24)	14 (28)	13 (26)	14 (28)	0.96
Endoscopic erythematous bulbitis	19 (38)	11 (22)	11 (22)	11 (22)	0.17
Gastric ulcer	6 (12)	8 (16)	3 (6)	8 (16)	0.38
Bulbus ulcer	7 (14)	5 (10)	4 (8)	5 (10)	0.79

Table III. Distribution of the post-treatment endoscopic findings

Variable	Group 1 *n* (%)	Group 2 *n* (%)	Group 3 *n* (%)	Group 4 *n* (%)	*P*-value
Endoscopic antral gastritis	16 (32)	24 (48)	21 (42)	24 (48)	0.32
Endoscopic erythematous pangastritis	7 (14)	9 (18)	6 (12)	9 (18)	0.79
Endoscopic erythematous bulbitis	8 (16)	9 (18)	7 (14)	9 (18)	0.94
Gastric ulcer	3 (6)	8 (16)	2 (4)	8 (16)	0.08
Bulbus ulcer	4 (8)	2 (4)	1 (2)	2 (4)	0.27

erythematous antral gastritis, endoscopic erythematous pangastritis, and endoscopic erythematous bulbitis in all groups, no statistically significant difference was detected in the regression rates between the groups ($p = 0.32$, $p = 0.79$, $p = 0.94$) (Tables II, III).

In the comparison of pre-treatment and post-treatment gastric ulcers between patient groups, it was found that there was a regression in the rabeprazole and quadruple treatment groups while the pantoprazole and esomeprazole groups remained constant, but no difference was detected between the groups in the comparison of the regression rates ($p = 0.08$) (Tables II, III). A significant improvement was observed in the pre-treatment and post-treatment comparison of the bulbus ulcers in all treatment groups (Tables II, III). No statistical difference was detected in terms of endoscopic erythematous antral gastritis, endoscopic erythematous pangastritis, endoscopic erythematous bulbitis, gastric ulcer, and bulbus ulcer between the treatment groups in comparison of the regression rates in pre-treatment and post-treatment endoscopic findings (Table IV).

As a result of the histopathological examination of patients' biopsy materials taken before and after the treatment, the presence of intestinal metaplasia, atrophy, dysplasia, and *H. pylori* in pathology reports was recorded. It was observed that intestinal metaplasia, atrophy, and dysplasia rates regressed in all groups. However, no statistically significant difference was observed in the changes in intestinal metaplasia and dysplasia in the comparison between the groups. When atrophy was evaluated, a statistically significant difference was observed between groups 1–3, 2–3, and 3–4 (Tables V, VI).

Considering the eradication rates of Hp-positive patients according to different treatment options, 78% ($n = 39$) of the patient group receiving quadruple therapy were eradicated after the treatment while 66% ($n = 33$) of the rabeprazole group, 58% ($n = 29$) of the esomeprazole group, and 58% ($n = 29$) of the pantoprazole group had Hp-negative results after treatment. According to these findings, the quadruple treatment regimen was found to be superior to dual treatments. When the high-dose dual therapies were compared, the highest eradication rate was achieved with rabeprazole,

Table IV. Comparison of the regression rates in the pre-treatment and post-treatment endoscopic findings between the patient groups

Variable	Group 1 – 2	Group 1 – 3	Group 1 – 4	Group 2 – 3	Group 2 – 4	Group 3 – 4
Endoscopic antral gastritis	0.15	0.4	0.15	0.68	1	0.68
Endoscopic erythematous pangastritis	0.78	1	0.78	0.57	1	0.57
Endoscopic erythematous bulbitis	1	1	1	0.78	1	0.78
Gastric ulcer	0.2	0.64	0.2	0.09	1	0.09
Bulbus ulcer	0.17	0.16	0.17	0.98	1	0.98

Table V. Distribution of the pre-treatment histopathological findings

Variable	Group 1 *n* (%)	Group 2 *n* (%)	Group 3 *n* (%)	Group 4 *n* (%)	*P*-value
H. pylori	50 (100)	50 (100)	50 (100)	50 (100)	
Intestinal metaplasia	3 (6)	5 (10)	8 (16)	5 (10)	0.44
Atrophy	6 (12)	3 (6)	10 (20)	3 (6)	0.09
Dysplasia	0 (0)	0 (0)	1 (2)	0 (0)	0.39

Table VI. Distribution of the post-treatment histopathological findings

Variable	Group 1 *n* (%)	Group 2 *n* (%)	Group 3 *n* (%)	Group 4 *n* (%)	*P*-value
H. pylori	11 (22)	21 (42)	17 (34)	21 (42)	0.11
Intestinal metaplasia	5 (10)	2 (4)	7 (14)	2 (4)	0.18
Atrophy	3 (6)	2 (4)	4 (8)	2 (4)	0.001
Dysplasia	0	0	1 (2)	0	0.38

Table VII. Comparison of the regression rates in the pre-treatment and post-treatment histopathological findings between the patient groups

Variable	Group 1 – 2	Group 1 – 3	Group 1 – 4	Group 2 – 3	Group 2 – 4	Group 3 – 4
H. pylori	0.05	0.26	0.05	0.53	1	0.53
Intestinal metaplasia	0.24	0.76	0.24	0.08	1	0.08
Atrophy	0.64	0.006	0.64	0.002	1	0.002
Dysplasia	Not calculated	0.31	Not calculated	0.31	Not calculated	0.31

and the eradication rate was equal in the esomeprazole and pantoprazole groups. However, there was no statistically significant difference in the evaluation between the groups (p = 0.11) (Table VII).

Discussion

Many treatment regimens have been developed for Hp eradication. Nevertheless, several treatment regimens have high eradication rates. Increasing Hp resistance against previously effective antibiotic regimens is concerning and requires these therapeutic strategies to be modified [11].

Triple therapy consisting of PPI-clarithromycin and amoxicillin or metronidazole, which was first recommended for the treatment of Hp infection at the Maastricht conference held in 1997, has become a universal phenomenon as it was proposed by all consensus conferences worldwide [12]. In the Maastricht V consensus, which is the last of the periodically renewed Maastricht conference proposals, treatment regimens were re-determined according to treatment durations, antibiotic resistance, and previous results (Maastricht V).

Although no new drugs have been developed to provide *H. pylori* eradication, there has been an effort to determine effective treatment regimens as a result of the studies performed with different antibiotic combinations.

Recent studies show that the standard therapy has lost its efficacy, and in most cases only 70% of the patients achieve recovery [13]. The reasons for this decrease in the efficacy of standard triple therapy include high stomach acidity, high bacterial burden, a variety of bacteria strains, and most importantly the increasing rates of resistance against clarithromycin.

When the eradication rates of standard treatment from 2003 to 2012 were examined in a study conducted with 1413 patients, it was observed that the eradication rates decreased from 93.5% to 78.8% from 2003 to 2012. Smoking and female gender were shown to be associated with treatment failure in the same study [14]. In our study, there was no statistically significant difference in terms of age and gender distribution (p = 0.065, p = 0.524).

In the Maastricht V consensus, bismuth-containing quadruple therapy was recommended as the first-line treatment in regions where the clarithromycin resistance rate exceeded 15–20%. Several recent studies have confirmed that the addition of bismuth into treatment regimens containing clarithromycin or levofloxacin increased the efficacy even in regions with high resistance [15]. Bismuth salts exert their activity topically, and less than 1% is absorbed. Their activity is pH dependent, and they do not dissolve in acidic pH. They contribute to the improvement of ulcers. Bismuth citrates inhibit Hp's motility and various enzymes, disrupt its morphological structure, suppress the growth of Hp, and show an antibacterial effect. It has long been proven that bismuth has a strong anti-Hp effect and does not show *in vitro* resistance. Therefore, it can be used as a component of dual, triple, and quadruple eradication regimens [16].

When the standard triple therapy and bismuth-containing quadruple therapy were compared in the first-line treatment as part of the study conducted by Venerito *et al.*, the eradication rate with the standard triple therapy was 68.9% while this rate was 77.6% with the bismuth-containing quadruple therapy [17]. It was predicted in a study performed in Turkey that compared consecutive therapy and bismuth-added consecutive therapy that the addition of bismuth into consecutive therapy increased the eradication rates. The eradication rates of both groups were determined to be 74.6% and 73.7%, respectively, and the anticipated increase with the addition of bismuth could not be achieved [18].

In our study, the eradication rate obtained after a total of 14 days of treatment was 78% with the standard triple therapy + regimen containing bismuth. In 2006, 10-year eradication rates of the standard triple therapy in Turkey were observed to decrease to 60%. The eradication rate of 78% obtained in our study could not achieve the eradication success rate anticipated in the Maastricht consensus. However, the increase from 60% to 78% in the eradication rate showed that the addition of bismuth salt increased the eradication success.

Different treatment protocols were tried due to the low eradication rates achieved with the standard treat-

ment regimen. The use of dual therapies combining high-dose PPI and amoxicillin in first-line therapy or as rescue therapy has become the main agenda.

Amoxicillin belongs to a group of beta lactamase antibiotics. As a result of its strong interaction with penicillin binding proteins (PBPs), it inhibits the cell wall synthesis, resulting in bacterial cell-wall dissolution. Amoxicillin resistance is generally low in *H. pylori* eradication. While the resistance rate varies between 1% and 5% in China, this rate is even lower in developed countries [19]. Intragastric pH increase improves the effectiveness of amoxicillin. Therefore, PPI are irreplaceable drugs in eradication treatment. In addition to their anti-secretory effects, PPIs show both indirect and direct antibacterial activity by preventing the deterioration of antibiotics in the gastric mucosa [20]. Patients' responses to PPIs are determined by their capacity to metabolize the drug depending on CYP2C19 and MDR polymorphism. This polymorphism greatly affects the eradication rates. It was predicted that a significant eradication rate may be achieved even in extensive metabolizers by providing the desired gastric pH level with high PPI doses. Some meta-analyses showed that success rates of triple therapies containing omeprazole and lansoprazole were affected by CYP2C19 polymorphism whereas regimens containing rabeprazole and esomeprazole did not have a similar effect. Because rabeprazole is mainly metabolized by non-enzymatic means, it is predicted to be the PPI least affected by CYP2C19 polymorphism [21]. A meta-analysis showed that high-dose PPIs increased eradication rates by 6–10% compared to standard doses. Increasing esomeprazole and rabeprazole doses from 20 mg to 40 mg can increase cure rates by 8–12% [22]. An intragastric pH of 5 or above is very important for the success of the treatment. The PPI dose frequency is controlled by several factors including the CYP2C19 polymorphism and IL-1β genotype.

The dual therapy containing a combination of PPI and amoxicillin was first investigated in 1989 and resulted in a better eradication rate (62.5%) compared to the treatments with PPI or amoxicillin alone [23].

In a study conducted by Shirai *et al*., the eradication rates of rabeprazole/amoxicillin dual therapy were compared according to the CYP2C19 genotype status of the patients. The eradication rate in poor metabolizers was quite high (93.8%), but this rate was shown to be quite low (60.6%) in homozygous patients [24]. It was demonstrated that the success of dual therapies was highly influenced by CYP2C19 polymorphism.

In a study comparing the triple therapy containing metronidazole with a dual therapy containing high-dose rabeprazole + amoxicillin used as a second-line rescue regimen after a treatment failure with standard regimen, which was conducted by Shirai *et al*. in 2007, a high eradication rate of 90.9% was obtained with dual therapy [25]. In a previous study conducted with rabeprazole in CYP2C19-positive patients by Shirai *et al*., it was observed that the administration of PPI at a dose of 10 mg four times a day provides a much higher rate of gastric acid suppression compared to the administration at a dose of 20 mg twice a day. In this study, increasing the frequency of administration of PPI doses and the use of dual therapy as a rescue regimen provided a high eradication rate. The eradication rates were detected to be 71.8% with the dual therapy containing rabeprazole performed by Goh *et al*. [26]. In this study conducted in Malaysia, clarithromycin resistance in that region was stated to be below 15%. PPI was administered 3 times a day, and post-treatment control was performed with a urea breath test. The eradication rate obtained with the dual treatment regimen containing rabeprazole was detected to be 66% in our study. Lower eradication rate may be attributed to the fact that performing eradication control by histopathological method with higher sensitivity and specificity might have increased the bacterial identification rate. It was also considered to be a significant factor that the administration of the PPI dose twice a day might have led to a lower rate or short-term acid suppression.

In a study performed with 36 patients by Graham *et al*., an insufficient eradication rate of 72.2% was obtained with the treatment regimen containing high-dose esomeprazole + amoxicillin [27]. Although an eradication rate of 90% or above was anticipated with poor PPI metabolizers in this study, the desired success could not be achieved with 40 mg esomeprazole administered 3 times a day. More studies were recommended to be performed with higher doses and frequencies of PPIs or by using longer acting PPIs. In another study conducted by Tai *et al*., the 2-week treatment, in which esomeprazole 40 mg 3 × 1 + amoxicillin 70 mg 4 × 1 were administered, was compared with non-bismuth-based quadruple therapy. The eradication rate was detected to be 86.7% with non-bismuth-based therapy and 91.7% with dual therapy. The amoxicillin resistance rate was 0%, the clarithromycin resistance rate was 14.6%, and the metronidazole resistance rate was 33.7% in the same study [28]. The key factor for the treatment success was explained as the lack of resistance to amoxicillin and the achievement of intragastric pH 6 and above with esomeprazole administered at a dose of 40 mg three times a day. In our study, we achieved a low eradication rate of 58% with the esomeprazole + amoxicillin regimen administered to 50 patients. Therefore, it was considered that higher dose and frequency of PPI may be required to increase

eradication rates, or this regimen may be preferred after the CYP2C19 polymorphism of the patients is determined.

The eradication rate of the pantoprazole group (58%) was found to be comparable with the esomeprazole group. There was no study performed with a dual treatment regimen containing high-dose pantoprazole in the literature. Therefore, our study is the first to investigate pantoprazole among all dual treatments.

Considering that *H. pylori* is an important factor in gastric carcinogenesis, it has been hypothesized that its eradication may play an important role in the prevention of gastric cancer. In recent years (2007, 2011, and 2016) 3 meta-analyses systematically reviewed the long-term effects of *H. pylori* eradication on gastric histology (i.e. effects on gastric atrophy and intestinal metaplasia for both antrum and corpus) by meta-analysing all relevant studies [29–31]. In all 3 meta-analyses the results were consistent, showing significant improvement of gastric atrophy, whereas improvement was not shown for intestinal metaplasia. The results we obtained regarding atrophy and intestinal metaplasia in our study were similar to the results in meta-analyses.

Studies have shown that *H. pylori* eradication improves chronic active gastritis. This can be associated with a certain regeneration of glands with specialized cells, and therefore with a decrease in atrophic gastritis.

In addition, studies have shown that eradication of Hp reduces the level of p53 expression and mutations in this gene, which are important steps in gastric carcinogenesis. These changes may also be associated with improvements in gastric atrophy and intestinal metaplasia, and may be associated with the prevention of gastric cancer.

Despite the advantage of amoxicillin provided by its low resistance rate, different studies showed that the eradication rates of high-dose dual therapies were quite variable. This variability in the eradication rates may be attributed to the intragastric pH differences due to variation in the doses and frequencies administered. Limitations of our study include the inability to determine PPI metabolizer status, administration of treatment without determining the CYP2C19 polymorphism, inability to measure whether the dose frequency is sufficient, and the fact that the study was performed retrospectively. When our patients were questioned, it was seen that very few of them smoked, and there was no equal questioning within each group. Therefore, the smoking status among the patients could not be evaluated.

Conclusions

Our study is significant because it is the first to include dual therapies consisting of 3 different PPIs at the same time and pantoprazole, which has not previously been included in the literature. It was considered that the desired eradication rates might be achieved with the administration of higher doses and frequency of PPI. However, this method may cause a disadvantage such as reducing patient compliance. Therefore, it was thought that individualized treatment strategies, which were prominent in many diseases, might also be applied for *H. pylori* eradication. It was concluded that individualized treatment strategies in which CYP2C19 polymorphism was detected will be required to achieve a high eradication rate.

Conflict of interest

The authors declare no conflict of interest.

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