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ORIGINAL ARTICLE

Retrospective Study

Fourteen- *vs* seven-day bismuth-based quadruple therapy for second-line *Helicobacter pylori* eradication

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Abstract

AIM: To compare the efficacy of 14- and 7-d bismuth-based quadruple therapies as second-line eradication treatment for *Helicobacter pylori* (*H. pylori*) infection.

METHODS: Between 2004 and 2014, the medical records of 790 patients who had experienced failure of first-line proton pump inhibitor (PPI)-based eradication therapy and were then treated with bismuth-based quadruple therapy were retrospectively reviewed. Those who received bismuth-based quadruple therapy [PPI, bismuth, metronidazole, and tetracycline (PBMT)] for either 7 d or 14 d were assigned to a PBMT-7 group (n = 543) or a PBMT-14 group (n = 247), respectively. The eradication rates for both groups were determined by intention-to-treat (ITT) and per-protocol (PP) analyses. ITT analysis compared the treatment groups as originally allocated while the PP analysis including only those patients who had completed the treatment as originally allocated. Successful eradication therapy for *H. pylori* infection was defined as a negative ^{13}C-urea breath test 4 wk after the end of eradication treatment.

RESULTS: The overall ITT eradication rate was 69.1% (546/790). Final ITT eradication rates were 67.4% (366/543; 95%CI: 63.1%-71.7%) in the PBMT-7 group and 72.8% (180/247; 95%CI: 67.4%-78.2%) in the PBMT-14 group (P = 0.028). The overall PP eradication rate was 80.0% (546/682), and the final PP eradication rates were 78.2% (366/468; 95%CI: 72.1%-84.0%) in the PBMT-7 group and 84.1% (180/214; 95%CI: 76.8%-90.8%) in the PBMT-14 group (P = 0.009). The *H. pylori* eradication rates in the PBMT-14 group were

significantly higher than in the PBMT-7 group according to both ITT (P = 0.028) and PP analysis (P = 0.009). Compliance was similar in both groups (PBMT-7 group: 97.9%; PBMT-14 group: 96.4%). Adverse event rates were 10.7% (51/478) and 17.1% (38/222) in the PBMT-7 and PBMT-14 groups, respectively (P = 0.487).

CONCLUSION: The 14-d bismuth-based quadruple therapy is a significantly more effective second-line eradication treatment for *H. pylori* infection than the 7-d alternative.

Key words: *Helicobacter pylori*; Treatment failure; Second-line treatment; Bismuth; Eradication rate

Core tip: This study evaluated the efficacy of 14-d bismuth-based quadruple therapy compared with a corresponding 7-d quadruple therapy as second-line eradication treatment of *Helicobacter pylori* (*H. pylori*) infection in South Korea. *H. pylori* eradication rates in the 14-d treatment group were significantly higher than in the 7-d treatment group for both the intent-to-treat and per-protocol analysis. The high eradication rate, excellent compliance, and safety of the 14-d regimen suggest its potential suitability as a second-line eradication treatment. The 14-d bismuth-based quadruple therapy is a significantly more effective second-line eradication treatment than the 7-d alternative for *H. pylori* infection in Korean patients.

Hwang JJ, Lee DH, Lee AR, Yoon H, Shin CM, Park YS, Kim N. Fourteen- *vs* seven-day bismuth-based quadruple therapy for second-line *Helicobacter pylori* eradication. *World J Gastroenterol* 2015; 21(26): 8132-8139 Available from: URL: http://www.wjgnet.com/1007-9327/full/v21/i26/8132.htm DOI: http://dx.doi.org/10.3748/wjg.v21.i26.8132

INTRODUCTION

Helicobacter pylori (*H. pylori*) infection is a primary risk factor for chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue lymphoma, and gastric cancer[1]. The most effective first-line eradication therapy known to date is a standard triple therapy consisting of a proton pump inhibitor (PPI), clarithromycin, and amoxicillin (or metronidazole)[2,3]. Although many clinical studies have shown standard triple therapy to be highly effective, a number of meta-analyses have found eradication rates for standard triple therapy to vary from 70% to 95%[4,5], and there have been reports of increased antibiotic resistance to clarithromycin and metronidazole[6,7]. Standard triple therapy is recommended in South Korea as first-line eradication therapy for *H. pylori*[8], but eradication rates for standard triple therapy range from 60% to 90%[9], with decreasing eradication rates of first-line eradication therapy due to increased antibiotic resistance rates among *H. pylori* strains in South Korea[10,11].

Various eradication regimens are being studied as possible alternative treatments to overcome decreasing eradication rates. The Maastricht IV/ Florence Consensus Report currently recommends a bismuth-based quadruple therapy consisting of PPI, bismuth, metronidazole, and tetracycline (PBMT) as the preferred second-line therapy following failure of first-line eradication therapy[2]. Metronidazole, one of the key antibiotics used in bismuth-based quadruple therapy, has been reported to have high antibiotic resistance rates of 34.4%-66% in South Korea[6,7,12]. Although metronidazole resistance is known to have little influence on successful eradication[13], eradication rates of 7-d bismuth-based quadruple therapy in per-protocol (PP) analysis have been reported to be 70% in South Korea[14].

There is much controversy about bismuth-based quadruple therapy treatment duration. Recommended treatment duration varies according to individual guidelines; for instance, a treatment duration of more than 1 wk is recommended in Europe, while 1-2 wk and 1 wk are recommended in the United States and South Korea, respectively[8,15,16]. One report indicated that in some metronidazole-resistant areas, extending the bismuth-based quadruple therapy treatment duration to 10-14 d was highly effective[17]; similarly, another study found that administering metronidazole for 14 d could overcome the negative influence of metronidazole resistance[18]. There is also much debate about the value and efficacy of 7- *vs* 14-d of bismuth-based quadruple therapy as a second-line eradication therapy in South Korea[14,19,20]. However, few studies have examined the efficacies of these treatments; most had relatively low samples sizes, making adequate efficacy comparisons between the two treatment regimens difficult. Accordingly, the aim of the present study was to investigate effective treatment duration for bismuth-base quadruple therapy by comparing eradication rate, compliance, and adverse event rate between 7- and 14-d bismuth-based quadruple therapies administered to patients after failure of first-line eradication therapy in South Korea.

MATERIALS AND METHODS

Patient selection

This study was conducted at Seoul National University Bundang Hospital between January 2004 and August 2014. The medical records of 790 patients who had experienced failure of first-line PPI-based eradication therapy for *H. pylori* infection were reviewed in this retrospective study. Eradication failure was defined by at least one of the following three tests: a positive ^{13}C-urea breath test (^{13}C-UBT); histologic evidence

of *H. pylori* by modified Giemsa staining in the lesser and greater curvature of the body and antrum; and/or a positive rapid urease test (CLOtest; Delta West, Bentley, Australia) by gastric mucosal biopsy from the lesser curvature of the body and antrum. None of the patients had previously received *H. pylori* eradication therapy before their first-line treatment. Patients were excluded if they had received PPIs, H_2 receptor antagonists, or antibiotics in the previous 4 wk, or if they had used non-steroidal anti-inflammatory drugs or steroids in the 2 wk prior to the ^{13}C-UBT. Other exclusion criteria were as follows: (1) age below 18 years; (2) previous gastric surgery or endoscopic mucosal dissection for gastric cancer; (3) advanced gastric cancer; (4) severe current disease (hepatic, renal, respiratory, or cardiovascular); (5) pregnancy; and (6) any condition likely to be associated with poor compliance (*e.g.*, alcoholism or drug addiction). The study protocol was approved by the Ethics Committee at Seoul National University Bundang Hospital (IRB number: B-1412/278-106).

Study design

Patients were classified into two groups. Those who received bismuth-based quadruple therapy [orally: 300 mg tripotassium dicitrato bismuthate 4 times/d, 500 mg tetracycline 4 times/d, 500 mg metronidazole 3 times/d, and 20 mg rabeprazole (or 40 mg esomeprazole)] for either 7 d or 14 d were assigned to PBMT-7 and PBMT-14 groups, respectively. Compliance was evaluated by counting remnant pills and asking direct questions during physician evaluation 1 wk after completion of treatment, and was defined as good when drug intake was at least 85%. All patients were asked about adverse events. Successful eradication therapy for *H. pylori* infection was defined as a negative ^{13}C-UBT test 4 wk after the cessation of eradication treatment. Data on demographics (age, gender distribution, smoking status, alcohol use, diabetes, and hypertension) and endoscopic diagnosis were recorded.

^{13}C-urea breath test

Before ^{13}C-UBT testing, patients were instructed to stop taking medications (*i.e.,* bismuth and antibiotics for 4 wk prior; PPIs for 2 wk prior) that could affect the result, and fast for a minimum of 4 h. After the patient's oral cavity was cleaned by gargling, a pre-dose breath sample was obtained. Then, 100 mg of ^{13}C-urea powder (UBiTkit™; Otsuka Pharmaceutical Co. Ltd., Tokyo, Japan) was dissolved in 100 mL of water and administered orally. Breath samplings were performed with special breath collection bags while patients were in the sitting position, both before drug administration (baseline) and 20 min after the powder medication. The samples were analyzed using an isotope-selective, non-dispersive infrared spectrometer (UBiT-IR 300®; Otsuka Pharmaceutical Co. Ltd, Tokyo, Japan).

Statistical analysis

The primary and secondary outcomes of the present study were *H. pylori* eradication rates and treatment-related adverse events, respectively. Eradication rates were determined by ITT and PP analyses. Treatment groups were compared by ITT analysis, which included all patients as originally allocated, and PP analysis, which included only those patients who had completed the treatment as originally allocated. Mean ± SD was calculated for all quantitative variables. Student's *t* test was used to evaluate continuous variables, and chi-square and Fisher's exact tests were used to assess non-continuous variables. All statistical analyses were performed using the Predictive Analytics Software (PASW) 20.0 version for Windows (SPSS Inc., IBM, Chicago, IL, United States). A *P*-value of less than 0.05 was defined as carrying clinical significance.

RESULTS

Characteristics of patients

A schematic diagram of the study is provided in Figure 1. A total of 790 patients who had experienced failure of first-line eradication therapy for *H. pylori* were enrolled (mean age, 54 years; range: 25-89 years). Of the 790 patients, 682 (86.3%) were considered to have completed their allocated regimens. The remaining 108 patients (13.7%) were excluded from the study: 75 (9.4%) from the PBMT-7 group and 33 (4.3%) from the PBMT-14 group. In the PBMT-7 group, the 75 patients were excluded from the study for loss to follow-up (65 patients), medication non-compliance (taking < 85% of the assigned tablets; 2 patients), and treatment discontinuation due to adverse events (8 patients). In the PBMT-14 group, 33 patients were excluded from the study for loss to follow-up (25 patients), non-compliance (taking < 85% of the assigned tablets; 2 patients), and treatment discontinuation due to adverse events (6 patients). Finally, 468 PBMT-7 patients and 214 PBMT-14 patients were included in the PP analysis. The enrolled patients' baseline demographic and clinical data are provided in Table 1. There were no statistical differences in age, gender distribution, smoking status, alcohol use, diabetes, hypertension, or endoscopic diagnosis between the two groups ($P > 0.05$).

H. pylori eradication rates

Table 2 shows the eradication rates for *H. pylori* infection according to ITT and PP analyses. Overall ITT eradication rate was 69.1% (546/790). Final ITT eradication rates were 67.4% (366/543; 95%CI: 63.1%-71.7%) in the PBMT-7 group and 72.8% (180/247; 95%CI: 67.4%-78.2%) in the PBMT-14 group ($P = 0.028$, Table 2). The overall PP eradication rate was 80.0% (546/682), and final PP eradication rates were 78.2% (366/468; 95%CI: 72.1%-84.0%) in the PBMT-7 group and 84.1% (180/214; 95%CI:

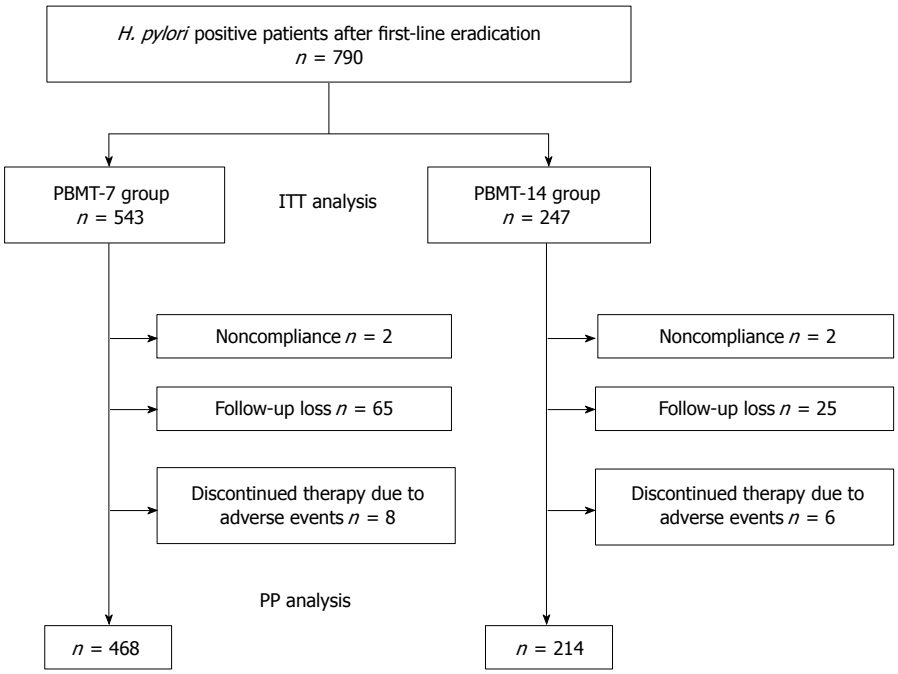

Figure 1 Flow schematic of the study included in intention-to-treat and per-protocol analyses. ITT: Intention-to-treat; PP: Per-protocol; PBMT-7: 7-d bismuth-based quadruple therapy; PBMT-14: 14-d bismuth-based quadruple therapy; ITT: Intention-to-treat; PP: Per-protocol.

Table 1 Demographic and clinical data at baseline (intention-to-treat population) *n* (%)

	PBMT-7	PBMT-14	*P* value
Included in ITT analysis	543	247	ns
Age (mean ± SD, yr)	54.83 ± 11.97	54.69 ± 11.86	0.779
Gender (male)	277 (51.0)	129 (52.2)	0.648
Current smoker	81 (14.9)	47 (19.0)	0.175
Alcohol drinking	118 (21.7)	50 (20.2)	0.641
Diabetes	54 (9.9)	31 (12.6)	0.322
Hypertension	128 (23.6)	53 (21.5)	0.524
Endoscopic diagnosis			0.598
Gastritis	257 (47.4)	146 (59.1)	
Gastric ulcer	93 (17.1)	18 (7.3)	
Duodenal ulcer	170 (31.3)	73 (29.6)	
Gastric and duodenal ulcer	23 (4.2)	10 (4.0)	

PBMT-7: 7-d bismuth-based quadruple therapy; PBMT-14: 14-d bismuth-based quadruple therapy; ITT: Intention-to-treat.

Table 2 *Helicobacter pylori* eradication rates

	PBMT-7	PBMT-14	*P* value
ITT analysis			
Eradication rate	366 (67.4)	180 (72.8)	0.028
95%CI	63.1%-71.7%	67.4%-78.2%	
PP analysis			
Eradication rate	366 (78.2)	18 (84.1)	0.009
95%CI	72.1%-84.0%	76.8%-90.8%	

ITT: Intention-to-treat; PP: Per-protocol; PBMT-7: 7-d bismuth-based quadruple therapy; PBMT-14: 14-d bismuth-based quadruple therapy.

76.8%-90.8%) in the PBMT-14 group (P = 0.009). *H. pylori* eradication rates in the PBMT-14 group were significantly higher than in the PBMT-7 group according to both ITT (P = 0.028) and PP analyses (P = 0.009). Figure 2 shows the eradication rates during 2004-2009 and 2010-2014. The eradication rates during 2004-2009 and 2010-2014 were significantly higher in the PBMT-14 group than those in the PBMT-7 according to both ITT and PP analyses (P < 0.05).

Adverse events and compliance

Table 3 lists the compliance and adverse events for both the PBMT-7 and PBMT-14 groups. Adverse events occurred for 51 of 478 patients (10.7%) in the PBMT-7 group and for 38 of 222 patients (17.1%) in the PBMT-14 group, without statistically significant differences (P = 0.487). The most common adverse events were nausea (16/478, 3.3%) and epigastric discomfort (15/478, 3.1%) in the PBMT-7 group and nausea (13/222, 5.9%) and diarrhea (8/222, 3.7%) in the PBMT-14 group. There were 14 patients with adverse events serious enough to warrant discontinuation of treatment: 8 from the PBMT-7 group and 6 from the PBMT-14 group. Of the 8 patients in the PBMT-7 group who discontinued treatment, 6 did so for nausea and 2 for epigastric discomfort. Of the 6 patients in the PBMT-14 group who discontinued the treatment, 5 did so for nausea, and 1 for diarrhea. Treatment compliance was 97.9% (468/478) in the PBMT-7 group and 96.4% (214/222) in the PBMT-14 group, without statistically significant differences (P = 0.304, Table 3).

DISCUSSION

Single-drug therapeutic effects are considered

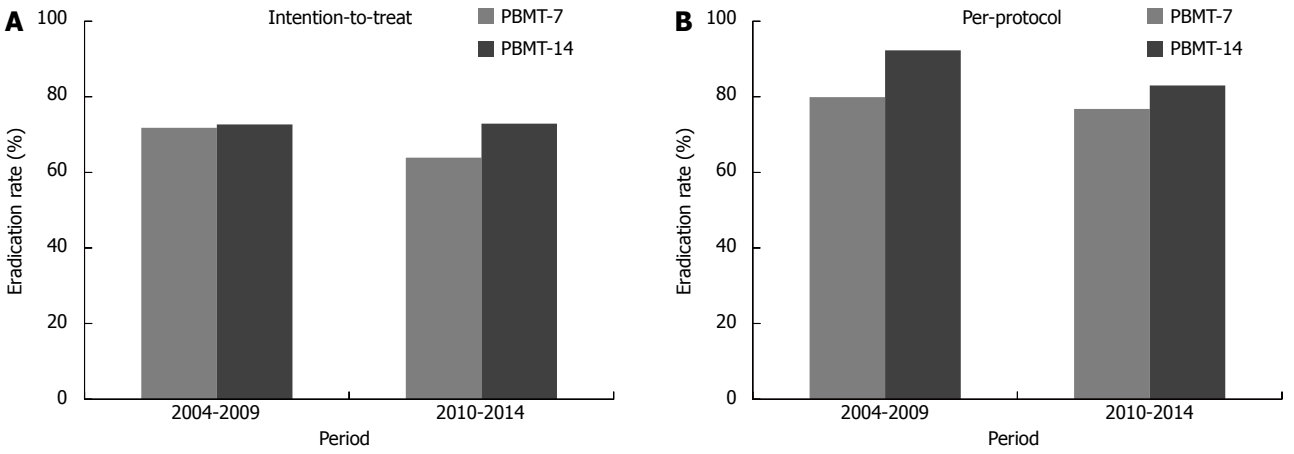

Figure 2 Comparison of the eradication rate between 2004-2009 and 2010-2014 periods in the 7-d bismuth-based quadruple therapy and 14-d bismuth-based quadruple therapy group according to the intention-to-treat (A) and per-protocol analyses (B) ($P < 0.05$). PBMT-7: 7-d bismuth-based quadruple therapy; PBMT-14: 14-d bismuth-based quadruple therapy.

Table 3 Adverse events and compliance *n* (%)

Adverse events	PBMT-7 (*n* = 478)	PBMT-14 (*n* = 222)	*P*-value
Bloating/dyspepsia	3 (0.6)	7 (3.2)	
Dry mouth	4 (0.8)	0 (0.0)	
Taste distortion	2 (0.4)	1 (0.5)	
Epigastric discomfort	15 (3.1)	5 (2.3)	
Nausea	16 (3.3)	13 (5.9)	
Diarrhea	8 (1.7)	7 (3.2)	
Urticaria	3 (0.6)	3 (1.4)	
Headache	0 (0.0)	1 (0.5)	
Chest discomfort	0 (0.0)	1 (0.5)	
Total	51 (10.7)	38 (17.1)	0.487
Compliance	468 (97.9)	214 (96.4)	0.304

PBMT-7: 7-d bismuth-based quadruple therapy; PBMT-14: 14-d bismuth-based quadruple therapy.

weak and likely to lead to increased *H. pylori* drug resistance. Hence, multidrug combination therapies using various antibiotics with bismuth preparations and PPI are recommended. However, because antibiotics used for *H. pylori* eradication are increasingly prescribed for treatment of other diseases, eradication therapy failures due to antibiotic resistance are increasing, resulting in 10%-20% failure rates for first-line eradication therapy even with effective eradication regimens[21,22]. Consequently, a significant number of patients require second-line eradication therapy, which has led to increased interest in related eradication rates. In response to decreasing eradication rates in first-line *H. pylori* eradication therapy, the present study examined effective treatment duration for bismuth-based quadruple therapy consisting of PPI, bismuth, tetracycline, and metronidazole, which is currently recommended as the preferred second-line eradication therapy following failure of first-line eradication therapy. Eradication rates, compliance, and adverse event rates were compared between 7- and 14-d bismuth-based quadruple therapies.

Although bismuth-based quadruple therapy is currently recommended as second-line eradication therapy for *H. pylori* infections, there is some debate over treatment duration. Comparison of eradication rates based on second-line bismuth-based quadruple therapy treatment durations outside South Korea showed eradication rates of 68%-82% and 76%-90% for 7 and 14 d of treatment administration, respectively; however, these differences are not statistically significant[23]. In South Korea, eradication rates for 7- and 14-d administration groups were 70%-81% and 81%-96%, respectively, suggesting a higher eradication rate in the 14-d group, but this is also not statistically significant[14,20]. The present study, using ITT and PP analyses of 790 patients, found eradication rates with 7-d bismuth-based quadruple therapy to be 67.4% and 78.2%, respectively, and with 14-d therapy to be 72.8% and 84.1%, respectively. Eradication rates during 2004-2009 and 2010-2014 were also significantly higher in the group treated for 14 d with bismuth-based quadruple therapy than those in the group treated for 7 d. These results indicate that the group treated with 14-d bismuth-based quadruple therapy demonstrated statistically significantly higher eradication rates in both ITT and PP analyses, consistent with another recent study from South Korea that reported 70%-80% eradication rates[14,19,24].

Many factors can influence the effectiveness of *H. pylori* eradication therapy, including age, smoking status, compliance, and underlying diseases[25]. However, the most important factor in eradication failure is antibiotic resistance[26]. Resistance has a large influence on selection of both first- and second-line eradication therapy regimens. When possible, use of a second-line regimen that differs from that of the first-line eradication therapy is recommended[27]. Resistance to metronidazole, a component of bismuth-based quadruple therapy, occurs because of functional changes in *H. pylori* nitroreductase-encoding genes[13]. Metronidazole antibiotic resistance rate is reportedly

20%-40% in the United States and Europe, and higher rates of 50%-80% have been reported in developing countries[13]. Reported metronidazole antibiotic resistance rates in South Korea vary from 27.1% to 66.2%[7,12,28,29]. A comparative study based on treatment duration and metronidazole resistance reported no differences in eradication rates based on metronidazole resistance[30]; however, another report indicated that 14 d of metronidazole use can overcome the negative influence of metronidazole resistance[18], suggesting that an extended treatment duration may be helpful to overcome antibiotic resistance and improve eradication rates. Tetracycline, another antibiotic component of bismuth-based quadruple therapy, was reported as not playing an important role in *H. pylori* eradication therapy[31]. However, the role of tetracycline in *H. pylori* eradication requires further study. Furthermore, due to its role in protecting and healing the gastric mucosa, bismuth preparations have been used for some time as therapeutic agents for chronic gastritis and peptic ulcer diseases[32,33]. In *H. pylori* eradication therapy, it directly causes bacterial lysis and reduces bacterial density, which in turn increases the therapeutic effects of the antibiotics[34]. Bismuth is also known to reduce bacterial tolerance to eradication therapy by not inducing development of antibiotic resistance[35-37].

While the adverse event rate in the 14-d bismuth-based quadruple therapy group in the present study was higher than that of the 7-d therapy group, the difference was not statistically significant. Adverse events are known to be dosage and duration-dependent[38]; thus, the most serious adverse events were expected to occur during the second week of treatment. Contrary to previous studies[38], most adverse events in the present study, both mild-to-moderate, as well as serious adverse events leading to discontinuation of treatment, appeared during the early treatment stages. These findings may explain the statistically insignificant differences in adverse event rates between the two groups, suggesting that if no serious adverse events appear within the first 7 d of 14-d bismuth-based quadruple therapy, then the probability of any serious adverse events occurring is relatively low. Even when mild-to-moderate adverse events did occur, encouragement and appropriate assistance from medical staff enabled successful completion of 14-d bismuth-based quadruple therapy.

In addition to eradication rate, follow-up loss and medication compliance are also important factors for successful *H. pylori* eradication. High eradication rates and compliance, along with low follow-up loss rates, make successful eradication therapy possible. In the present study, follow-up loss rates for the 7- and 14-d therapy groups were 11.9% (65/543) and 10.1% (25/247), respectively, whereas the compliance for these group were 97.9% (468/478) and 96.4% (214/222), respectively. The results were similar between groups, and the differences were not statistically significant. Although reducing the number of drugs or shortening the treatment duration are important for decreasing follow-up loss rates and increasing compliance, second-line eradication therapy has a high probability of antimicrobial resistance after failure of first-line eradication therapy. Even with a long treatment duration, it is especially important to minimize follow-up loss rates and increase treatment compliance through patient education.

This study has limitations. First, since this retrospective study used medical records, selection errors were possible. Second, since *H. pylori* strain identification and pre- and post-eradication therapy antibiotic susceptibility tests were not performed, the increase in the antibiotic resistance rate in participating patients were not verified. Ideally, it would be possible to utilize a mixture of drugs shown to be effective in antibiotic susceptibility tests in order to overcome reduced eradication rates caused by increasing antibiotic resistance. However, because it is difficult to culture *H. pylori*, the success rates of antibiotic susceptibility tests are low, and there are no established criteria for determining antibiotic resistance. Additional studies on the cost-effectiveness of and appropriate time for conducting antibiotic susceptibility tests are necessary.

The present study examined effective treatment duration for bismuth-based quadruple therapy by comparing eradication rates, compliance, and adverse event rates after administration of 7 and 14 d of bismuth-based quadruple therapies as a second-line eradication therapy following first-line therapy failure in South Korea. The results showed that the eradication rate of the 14-d bismuth-based quadruple therapy group was higher than that of the 7-d bismuth-based quadruple therapy group, while there were no differences in adverse event rates and compliance. The 14-d bismuth-based quadruple therapy is therefore believed to be the more effective second-line eradication therapy in South Korea. Moreover, encouragement and appropriate assistance from medical staff are necessary to address serious adverse events that can occur in the early stages of treatment, and efforts should be made to provide sufficient patient education to increase treatment success rates. In addition, further studies are necessary to develop more effective and safer second-line eradication therapies and evaluate new treatment regimens for second-line eradication therapies based on first-line eradication therapy failures.

COMMENTS

Background

A recent meta-analysis reported a decreased eradication rate using standard triple therapy for *Helicobacter pylori* (*H. pylori*) infection due to increasing antibiotic resistance. For patients whose first-line eradication therapy has failed, second-line eradication therapy for persistent *H. pylori* infection is required.

Research frontiers

There is controversy about the duration of bismuth-based quadruple therapy treatment. There has also been a great deal of debate about bismuth-based quadruple therapy as a second-line eradication therapy in South Korea.

Innovations and breakthroughs

This retrospective study was conducted to evaluate the efficacy of 14-d bismuth-based quadruple therapy as compared with 7-d bismuth-based quadruple therapy as a second-line eradication treatment of *H. pylori* infection. The high eradication rate, excellent compliance, and safety of the 14-d regimen suggest its potential suitability as a second-line eradication treatment of *H. pylori* infection.

Applications

This retrospective study's design and findings could be used to determine adequate sample sizes for a larger, prospective study designed to test the efficacy of 14-d bismuth-based quadruple therapy as a second-line eradication treatment for *H. pylori* eradication.

Terminology

H. pylori, found in the stomach, is associated with the development of gastritis, peptic ulcers, and stomach cancer. To prevent recurrence in patients with these diseases, it is necessary to eradicate *H. pylori* infection.

Peer-review

The study, conducted with 790 patients who failed proton pump inhibitor-based *H. pylori* eradication treatment, reports on the efficacy of 14-d bismuth-based quadruple therapy over that of 7-d therapy as a second-line treatment for *H. pylori* eradication. The results indicate that 14-d quadruple therapy had a significantly higher rate of *H. pylori* eradication, and no adverse effects. This study deals with apparent increased resistance to *H. pylori* eradication by a standard triple therapy among the Korean population, and provides only limited new insights into approaches to *H. pylori* eradication regimens.

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