

## Trends in the eradication rates of *Helicobacter pylori* infection for eleven years

Jai Hoon Yoon, Gwang Ho Baik, Kyoung Min Sohn, Dae Yong Kim, Yeon Soo Kim, Ki Tae Suk, Jin Bong Kim, Dong Joon Kim, Jin Bae Kim, Woon Geon Shin, Hak Yang Kim, Il Hyun Baik, Hyun Joo Jang

Jai Hoon Yoon, Gwang Ho Baik, Kyoung Min Sohn, Dae Yong Kim, Yeon Soo Kim, Ki Tae Suk, Jin Bong Kim, Dong Joon Kim, Department of Internal Medicine, Hallym University College of Medicine, Chuncheon Sacred Heart Hospital, 153, Gyo-dong, Chuncheon, Gangwon-do 200-704, South Korea

Jin Bae Kim, Department of Internal Medicine, Hallym University College of Medicine, Kangnam Sacred Heart Hospital, Seoul 150-950, South Korea

Woon Geon Shin, Hak Yang Kim, Department of Internal Medicine, Hallym University College of Medicine, Kangdong Sacred Heart Hospital, Seoul 134-814, South Korea

Il Hyun Baik, Department of Internal Medicine, Hallym University College of Medicine, Hallym University Sacred Heart Hospital, Anyang 431-070, South Korea

Hyun Joo Jang, Department of Internal Medicine, Hallym University College of Medicine, Hangang Sacred Heart Hospital, Seoul 150-719, South Korea

**Author contributions:** Yoon JH and Baik GH made substantial contributions to the conception and design of the study the acquisition of the data, and the analysis and interpretation of the data and wrote the paper; Sohn KM, Kim DY, Kim YS, Suk KT, Kim JB, Kim DJ, Kim JB, Shin WG, Kim HY, Baik IH and Jang HJ contributed to the statistical analysis of data and to the interpretation of data.

**Correspondence to:** Gwang Ho Baik, MD, Department of Internal Medicine, Hallym University College of Medicine, Chuncheon Sacred Heart Hospital, 153, Gyo-dong, Chuncheon, Gangwon-do 200-704, South Korea. [baikgh@hallym.or.kr](mailto:baikgh@hallym.or.kr)  
Telephone: +82-33-2405645 Fax: +82-33-2418064

Received: June 16, 2012 Revised: October 10, 2012

Accepted: October 22, 2012

Published online: December 7, 2012

### Abstract

**AIM:** To evaluate the trends in the eradication rate of *Helicobacter pylori* (*H. pylori*) over the past 11 years in a single center.

**METHODS:** This retrospective study covered the period from January 2000 to December 2010. We evalu-

ated 5746 patients diagnosed with gastric ulcers (GU), duodenal ulcers (DU), GU + DU, or nonpeptic ulcers associated with an *H. pylori* infection. We treated them annually with the 2 wk standard first-line triple regimen, proton pump inhibitor (PPI) + amoxicillin + clarithromycin (PAC; PPI, clarithromycin 500 mg, and amoxicillin 1 g, all twice a day). The follow-up test was performed at least 4 wk after the completion of the 2 wk standard *H. pylori* eradication using the PAC regimen. We also assessed the eradication rates of 1 wk second-line therapy with a quadruple standard regimen (PPI *b.i.d.*, tripotassium dicitrate bismuthate 300 mg *q.i.d.*, metronidazole 500 mg *t.i.d.*, and tetracycline 500 mg *q.i.d.*) after the failure of the first-line therapy. Statistical analysis was performed with 95%CI for the differences in the annual eradication rates.

**RESULTS:** A total of 5746 patients [2333 males (58.8%), 1636 females (41.2%); mean age of males *vs* females  $51.31 \pm 13.1$  years *vs*  $52.76 \pm 13.6$  years,  $P < 0.05$ , total mean age  $51.9 \pm 13.3$  years (mean  $\pm$  SD)] were investigated. Among these patients, 1674 patients were excluded: 35 patients refused treatment; 18 patients ceased *H. pylori* eradication due to side effects; 1211 patients had inappropriate indications for *H. pylori* eradication, having undergone stomach cancer operation or chemotherapy; and 410 patients did not undergo the follow-up. We also excluded 103 patients who wanted to stop eradication treatment after only 1 wk due to poor compliance or the side effects mentioned above. Finally, we evaluated the annual eradication success rates in a total of 3969 patients who received 2 wk first-line PAC therapy. The endoscopic and clinical findings in patients who received the 2 wk PAC were as follows: gastric ulcer in 855 (21.5%); duodenal ulcer in 878 (22.1%); gastric and duodenal ulcer in 124 (3.1%), erosive, atrophic gastritis and functional dyspepsia in 2055 (51.8%); and other findings (e.g., MALToma, patients who wanted to receive the therapy even though they had no abnormal endoscopic finding) in 57 (0.5%).

The overall eradication rate of the 2 wk standard first-line triple regimen was 86.5%. The annual eradication rates from 2000 to 2010 were 86.7%, 85.4%, 86.5%, 83.3%, 89.9%, 90.5%, 88.4%, 84.5%, 89.1%, 85.8%, and 88.3%, sequentially ( $P = 0.06$ ). No definite evidence of a significant change in the eradication rate was seen during the past eleven years. The eradication rates of second-line therapy were 88.9%, 82.4%, 85%, 83.9%, 77.3%, 85.7%, 84.4%, 87.3%, 83.3%, 88.9%, and 84% ( $P = 0.77$ ). The overall eradication rate of 1 wk quadruple second-line therapy was 84.7%. There was no significant difference in the eradication rate according to the *H. pylori* associated diseases.

**CONCLUSION:** This study showed that there was no trend change in the *H. pylori* eradication rate over the most recent 11 years in our institution.

© 2012 Baishideng. All rights reserved.

**Key words:** *Helicobacter pylori*; Eradication; Proton pump inhibitor; Therapy; Clarithromycin

**Peer reviewers:** Dr. Shahab Abid, Associate Professor, Department of Medicine, Aga Khan University, Stadium Road, PO Box 3500, Karachi 74800, Pakistan; Francesco Luzzo, Professor, MD, Department of Clinical and Experimental Medicine, University of Catanzaro "Magna Graecia", Campus Universitario di Germaneto, Viale Europa, 88100 Catanzaro, Italy

Yoon JH, Baik GH, Sohn KM, Kim DY, Kim YS, Suk KT, Kim JB, Kim DJ, Kim JB, Shin WG, Kim HY, Baik IH, Jang HJ. Trends in the eradication rates of *Helicobacter pylori* infection for eleven years. *World J Gastroenterol* 2012; 18(45): 6628-6634 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v18/i45/6628.htm> DOI: <http://dx.doi.org/10.3748/wjg.v18.i45.6628>

## INTRODUCTION

*Helicobacter pylori* (*H. pylori*) has been one of the most common human infections worldwide and is associated with a number of gastrointestinal diseases, including chronic gastritis, peptic ulcer disease, and gastric malignancy<sup>[1]</sup>. In multicenter studies, it has been shown that triple therapy with a proton pump inhibitor (PPI), clarithromycin 500 mg and either amoxicillin 1000 mg or metronidazole 500 mg, all taken twice daily, is one of the most effective treatments for *H. pylori* eradication<sup>[2]</sup>. However, there is no consensus on the length of treatment among the various management guidelines, including the Asia-Pacific consensus guideline<sup>[3]</sup> and the consensus statements from North America<sup>[4]</sup> and Europe<sup>[5]</sup>. European guidelines recommend 1 wk of treatment, whereas in the United States, it is recommended that the triple standard regimen be given for 10-14 d. The second Asia-Pacific consensus guideline recommends a 7-14 d standard regimen; however, it mentions that 14 d triple therapy confers a limited advantage

over 7-d triple therapy in *H. pylori* eradication rates. In recent years, a decrease in the eradication success rate of 1 wk of triple therapy has been reported due to antibiotic resistance, especially to clarithromycin<sup>[6]</sup>. Although clarithromycin resistance is increasing year by year, the current recommended first-line therapy for *H. pylori* infection is PPI, amoxicillin, and clarithromycin for 7-14 d in Korea<sup>[7]</sup>. The aim of this retrospective observational study was to investigate the trend in the 2 wk PPI-based standard regimen, which included amoxicillin and clarithromycin, under the unfavorable conditions of increasing antibiotic resistance. In addition, we also studied the trend in the eradication success rate of 1 wk second-line therapy that consisted of bismuth-containing quadruple therapy including PPI, metronidazole, and tetracycline.

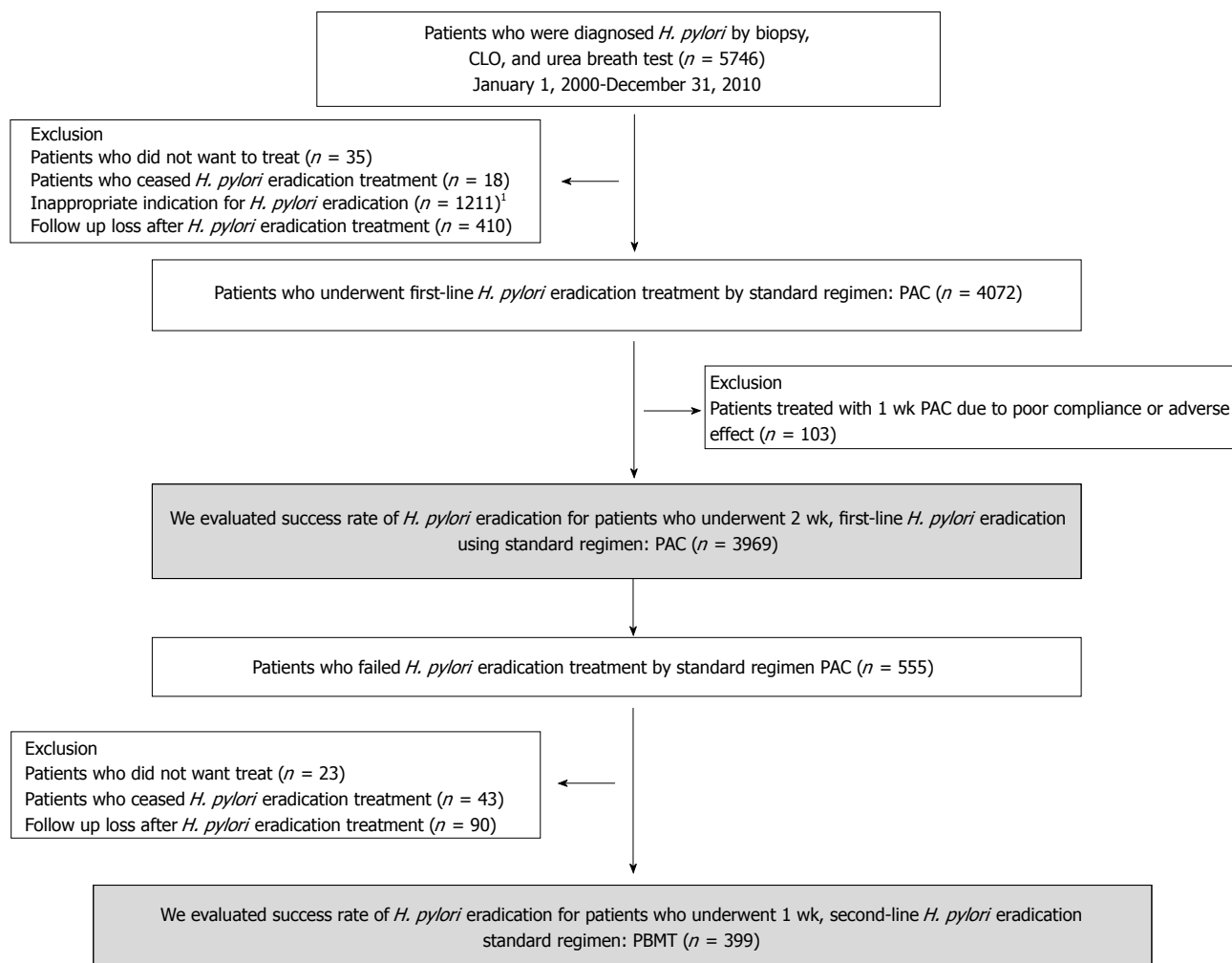
## MATERIALS AND METHODS

### Patients

We retrospectively investigated the annual *H. pylori* eradication success rate of patients who visited our hospital from January 2000 to December 2010 and who had been diagnosed as *H. pylori*-infected by at least one positive result from an *H. pylori* culture test, microscopy of a biopsy specimen, or <sup>13</sup>C-urea breath test. Patients were excluded due to the following reasons: patient refusal of treatment, abandonment of *H. pylori* eradication treatment, inappropriate indications for *H. pylori* eradication because of a stomach cancer operation or chemotherapy, or follow-up loss after *H. pylori* eradication treatment. We also excluded patients receiving 1 wk PPI + amoxicillin + clarithromycin treatment (PAC; PPI: omeprazole, lansoprazole, pantoprazole, rabeprazole, or esomeprazole, clarithromycin 500 mg, and amoxicillin 1 g, all twice a day) that exhibited poor compliance or adverse effects. We evaluated the success rate of *H. pylori* eradication for all patients who received the 2 wk, first-line standard *H. pylori* eradication PAC regimen. We also evaluated the success rate of eradication of 1 wk bismuth-containing quadruple therapy (PPI *b.i.d.*, tripotassium dicitrate bismuthate 300 mg *q.i.d.*, metronidazole 500 mg *t.i.d.*, and tetracycline 500 mg *q.i.d.*) of patients who failed *H. pylori* eradication treatment by the standard PAC regimen. Among these, patients who did not want treatment, patients who ceased *H. pylori* eradication treatment, and patients lost to follow-up after *H. pylori* eradication treatment were excluded. In the end, we evaluated the success rate of *H. pylori* eradication for a total of 399 patients who received a 1 wk, second-line bismuth-containing quadruple therapy *H. pylori* eradication regimen. This study was approved by the institutional review board of Hallym University Chuncheon Hospital.

### Diagnosis of *H. pylori* infection and assessment of *H. pylori* eradication

*H. pylori* infection was defined according to at least one of the following three tests: (1) a positive rapid urease test (CLO test, Delta West, Bentley, Australia) by gastric mucosal biopsy from the lesser curvature of the mid-antrum or



**Figure 1 Flow of the study.** <sup>1</sup>Inappropriate indications for *Helicobacter pylori* (*H. pylori*) eradication: Stomach cancer operation or chemotherapy. PAC: Proton pump inhibitor *b.i.d.* + amoxicillin 1 g *b.i.d.* + clarithromycin 500 mg; PBMT: Proton pump inhibitor *b.i.d.* + tripotassium dicitrate bismuthate 300 mg *q.i.d.* + metronidazole 500 mg *t.i.d.* + tetracycline 500 mg *q.i.d.*

mid-body; (2) histological evidence of *H. pylori* by modified Giemsa staining in the lesser and greater curvature of the mid-antrum or mid-body, respectively; or (3) a positive C-urea breath test. *H. pylori* eradication was defined as a negative <sup>13</sup>C-urea breath test or a combination of the rapid urease test, Giemsa staining, and culture when follow-up endoscopy was necessary. The follow-up test was performed at least 4 wk after the completion of the 2 wk standard *H. pylori* eradication using the PAC regimen.

### Statistical analysis

Statistical analysis was performed with 95%CI for the differences in the annual eradication rates from January 2000 to December 2010. Continuous variables were analyzed by Student's *t* test, and categorical variables, by the  $\chi^2$  test or Fisher's exact test. A *P* value of < 0.05 was considered to be statistically significant.

## RESULTS

A total of 5746 patients [2333 males (58.8%), 1636 fe-

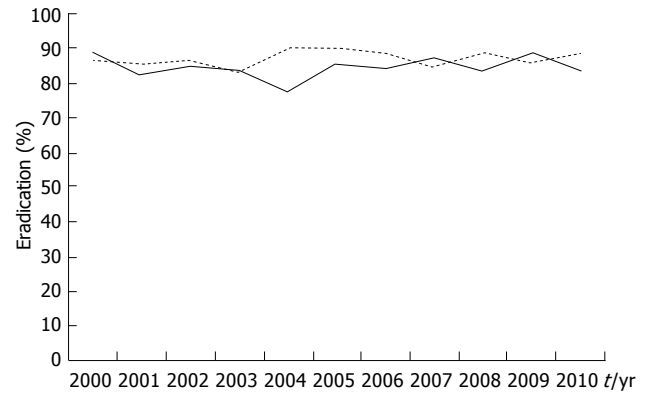
males (41.2%); mean age of males *vs* females  $51.31 \pm 13.1$  years *vs*  $52.76 \pm 13.6$  years, *P* < 0.05, total mean age  $51.9 \pm 13.3$  years (mean  $\pm$  SD)] were retrospectively investigated for the period of January 2000 to December 2010 in this study. The retrospective assessment flow is summarized in Figure 1. Among these patients, 1674 patients were excluded: 35 patients refused treatment; 18 patients ceased *H. pylori* eradication treatment due to side effects, such as abdominal discomfort, diarrhea, taste disturbance, or nausea; 1211 patients had inappropriate indications for *H. pylori* eradication therapy, having undergone a stomach cancer operation or chemotherapy; and 410 patients did not undergo the follow-up assessment for *H. pylori* eradication after the 2 wk PAC treatment. We also excluded 103 patients who wanted to stop the eradication treatment after only 1 wk due to poor compliance or the side effects mentioned above. Finally, we evaluated the annual eradication success rates in a total of 3969 patients who received 2 wk PAC therapy. Demographic characteristics are summarized in Table 1. Of the patients included in the study, 735 (18.5%) were current smokers, and 28.7%

**Table 1** Baseline characteristics of the *Helicobacter pylori* eradication population

Baseline characteristics	Data n (%)
Sex	
Male	2333 (58.8)
Female	1636 (41.2)
Age (yr, mean $\pm$ SD)	51.9 $\pm$ 13.3
Current smoker	735 (18.5)
Alcohol intake	1140 (28.7)
Endoscopic and clinical diagnosis	
GU	855 (21.5)
DU	878 (22.1)
GU + DU	124 (3.1)
Non-ulcer dyspepsia <sup>1</sup>	2055 (51.8)
Other <sup>2</sup>	57 (1.4)

<sup>1</sup>Functional dyspepsia, erosive gastritis, atrophic gastritis; <sup>2</sup>Gastric cancer, MALToma. GU: Gastric ulcers; DU: Duodenal ulcers.

were alcohol drinkers. Endoscopic and clinical findings in patients who received the 2 wk PAC were as follows: gastric ulcer in 855 (21.5%); duodenal ulcer in 878 (22.1%); gastric and duodenal ulcer in 124 (3.1%), erosive, atrophic gastritis and functional dyspepsia in 2055 (51.8%), and other findings (e.g., MALToma, patients who wanted to receive the therapy even though they had no abnormal endoscopic finding) in 57 (1.4%). When endoscopy is not indicated, C<sup>13</sup> urea breath tests (3030, 76.3%), biopsies (22, 0.6%), and CLO test (503, 12.7%) are accepted to determine the outcome of *H. pylori* eradication therapy. In some cases, biopsy + CLO test (329, 8.2%) or CLO test + C<sup>13</sup> urea breath test was used for the diagnosis of *H. pylori* eradication therapy. Successful eradication rates for each year were follows: 2000, 86.7%; 2001, 85.4%; 2002, 86.5%; 2003, 83.3%; 2004, 89.9%; 2005, 90.5%; 2006, 88.4%; 2007, 84.5%; 2008, 89.1%; 2009, 85.8%; and 2010, 88.3% ( $P = 0.06$ ). Figure 2 summarizes the annual eradication rates year by year from 2000 to 2010. The overall eradication rate was 86.5%, that is, 3435 of 3969 patients who received the 2 wk PAC (95%CI: 85.4% to 87.6%). The  $P$  value was 0.09. The annual eradication rates of the 2 wk PAC regimen revealed a relatively constant rate over the years. According to endoscopic and clinical findings, the eradication rates were not significantly different by year. We also investigated the eradication rates of 1 wk bismuth-containing quadruple therapy for 555 patients who failed the *H. pylori* eradication treatment using the 2 wk PAC therapy. Among the 555 patients, 156 patients were excluded for the following reasons: 23 patients declined treatment, 43 patients ceased *H. pylori* eradication treatment due to poor compliance or side effects such as diarrhea, nausea, vomiting, or stool color change, and 90 patients were lost to follow-up after *H. pylori* eradication treatment. Finally, we found the rates of successful eradication in 399 patients who received 1 wk bismuth-containing quadruple second-line therapy for each year to be as follows: 2000, 88.9%; 2001, 82.4%; 2002, 85.0%; 2003, 83.9%; 2004, 77.3%; 2005, 85.7%; 2006, 84.4%; 2007, 87.3%; 2008, 83.3%; 2009, 88.9%; and 2010, 84.0% ( $P =$



**Figure 2** Efficacy of 2 wk first-line (a dotted line) proton pump inhibitor b.i.d. + amoxicillin 1 g b.i.d. + clarithromycin 500 mg and 1 wk second-line (a solid line) bismuth-containing quadruple therapy for the eradication of *Helicobacter pylori* by year.

0.77). Figure 2 summarizes the annual eradication rates year by year from 2000 to 2010. The overall eradication rate was 84.7%, and the rate among those who received 1 wk second-line therapy was 338 of 399 patients (95%CI: 80.9% to 87.9%). The  $P$  value was 0.07. The annual eradication rates of the 1 wk second-line therapy revealed a relatively constant rate over the years.

## DISCUSSION

The PAC regimen is one of the most widely used therapies for the first-line treatment of *H. pylori* infection. A recent study reported the eradication rate of *H. pylori* with one wk standard triple therapy to be 75% in Korea<sup>[8]</sup>. There is still no general consensus regarding the optimal duration of triple therapy for *H. pylori* eradication, as mentioned above. A recent large, multicenter, double-blind, randomized study concluded that the 1 wk and 2 wk standard triple regimens for *H. pylori* eradication are similar in terms of efficacy, safety, and patient compliance<sup>[9]</sup>. Two meta-analyses have reported that 2 wk triple therapy achieves considerably better results than 1 wk therapy<sup>[10,11]</sup>. Recently, many studies have reported that the efficacy of the standard triple regimen has decreased<sup>[12-14]</sup> because of the increased antibiotic resistance rate; that is, the standard triple regimen of PPI, amoxicillin, and clarithromycin administered to patients infected with the clarithromycin-resistant strain was not successful<sup>[15]</sup>. Although the general consensus is that a 1 wk PAC is preferable, we have treated patients infected by *H. pylori* with the 2 wk PAC to overcome increasing antibiotic resistance. Our data on the 2 wk PAC regimen shows a relatively constant rate over the year from 2000 to 2010. A recent chronological analysis of the results of meta-analyses performed between 1998 and 2010 showed that first-line standard triple regimens achieved eradication rates of around only 80% (intention-to-treat)<sup>[16]</sup>. Given that the overall eradication rate in this study was 86.5% (3435 of 3969 patients who received the 2 wk PAC), we concluded that the 2 wk PAC regimen had an accept-

able efficacy for *H. pylori* eradication. Many investigators have commented that the decreasing eradication rate using standard triple therapy is due to increasing antibiotic resistance. However, a number of factors, including resistance, which varies widely, influence the success of antibiotic regimens. The resistance rates of antibiotics that are widely used in eradication therapy, including amoxicillin and tetracyclines, are relatively lower than clarithromycin and metronidazole<sup>[15]</sup>. Therefore, the true challenge for clinical practice lies mainly in resistance to metronidazole or clarithromycin. In Korea, the rates of resistance to clarithromycin and metronidazole were reported from 1.6% up to 29.7% and from 35.7% up to 49.6 % from 1996 to 2006, respectively<sup>[17]</sup>. This is a major factor in the reduced effectiveness of triple regimens containing clarithromycin<sup>[18]</sup>. Clarithromycin must bind to ribosomes to kill *H. pylori*. Resistance is associated with failure to bind to ribosomes, such that resistance cannot be overcome by increasing the dose or duration<sup>[15]</sup>. However, patients do not always have perfect compliance. Because *H. pylori* treatment failures may also occur independently of resistance, that is, treatment may fail but the organism remains susceptible to the antibiotic<sup>[19]</sup>, we concluded that the 2 wk standard PAC regimen may be fit for use in eradicating *H. pylori*. Bacteria oscillate between a phenotypically resistant and a phenotypically susceptible state, during which they can be eradicated. To extend the duration of treatment such that the antibiotic will be present during at least one period of susceptibility may be an alternative option to overcome antibiotic resistance<sup>[20]</sup>. Consistent with the results from Korea in this study, several authors have reported an increasing trend in clarithromycin resistance rates in other areas, such as the United States<sup>[21]</sup>, Turkey<sup>[22]</sup>, *etc.* Nevertheless, exceptional cases where clarithromycin resistance rates have remained stable have also been reported<sup>[23]</sup>. These results strongly suggest that there is an institutional and geographical difference in the antibiotic resistance of *H. pylori*. This fact and our results in this study suggest that the 2 wk PAC regimen may be effective in eradicating *H. pylori* in some countries or limited geographical areas. In a recent review, the eradication rates of quadruple therapy were 75%-95%<sup>[24]</sup>. In Korea, where the resistance to metronidazole is high, the eradication rates of second line quadruple therapy have been reported to be 54.5%-76.7% and 70.4%-83.9% in intention to treat and per protocol analysis<sup>[25,26]</sup>, respectively, based on studies in which the therapeutic durations varied from 7 to 14 d. Metronidazole is a prodrug that is activated by *H. pylori* enzymes to become active within the cell. There are a number of different enzyme pathways that can accomplish this task, and clinically, by increasing the dose and duration, it is possible to overcome, at least partially, metronidazole resistance<sup>[2,27]</sup>. Thus, there is the possibility that quadruple therapy might be more effective with after a treatment duration of longer than 1 wk. However, some studies have shown the benefit of eradication with prolonged treatment durations<sup>[28]</sup>, while

others have not<sup>[29,30]</sup>. We previously reported that 1 wk bismuth-containing quadruple therapy can be as an effective as 2 wk therapy after the failure of the first-line eradication therapy. In this study, the eradication rates of 1 wk bismuth-containing quadruple therapy have no significant differences from the consecutive, annual eradication rates, in spite of increasing metronidazole resistance in Korea. Therefore, although 1 wk bismuth-containing quadruple therapy is not effective up to more than 90% yet, we concluded that 1 wk bismuth-containing quadruple therapy can be used to treat patients who failed the first *H. pylori* eradication. To raise the eradication rate of *H. pylori*, when the clarithromycin resistance rate is higher than 20%, it is recommended that drug sensitivity tests be carried out prior to eradication<sup>[5]</sup>. However, there are several limitations to performing a culture before the first-line treatment for *H. pylori* infection. Cultures are expensive, owing to the costs of the endoscopic procedures, and they are time-consuming. Therefore, cultures are not always available on a routine basis. Until now, cultures for *H. pylori* have mainly been used to perform epidemiological and pharmacologic research. Because extending the duration of the first line PAC regimen from 1 wk to 2 wk may improve the efficacy of the *H. pylori* eradication rate, the 2 wk PAC regimen is preferable for treating *H. pylori*. However, this study does have limitations. One is that it is a retrospective, observational study. Therefore, there was some bias, such as an uneven diagnostic method for the determination of the outcome of *H. pylori* eradication therapy in each year. The other endoscopic findings were not even taken in each year. Additionally, we could not obtain the data on antibiotic resistance including amoxicillin, clarithromycin, metronidazole, and tetracyclin in accordance with the eradication rate.

In conclusion, we show the efficacy of a 2 wk PAC regimen and 1 wk bismuth-containing quadruple therapy has not changed across the 2000 to 2010 period in South Korea. The efficacy of 2 wk PAC and 1 wk quadruple second line therapy is by no means acceptable and satisfactory.

## COMMENTS

### Background

In recent years, a decrease in the eradication success rate of 1 wk of triple therapy has been reported due to antibiotic resistance, especially to clarithromycin. Although clarithromycin resistance is increasing year by year, the currently recommended first-line therapy for *Helicobacter pylori* (*H. pylori*) infection is proton pump inhibitor (PPI), amoxicillin, and clarithromycin for 7-14 d in South Korea. This retrospective, observational study intended to investigate the trend in the 2 wk PPI-based standard regimen including amoxicillin and clarithromycin under the unfavorable conditions of increasing antibiotic resistance.

### Research frontiers

The overall eradication rate of the 2 wk standard first-line triple regimen from 2000 to 2010 was 86.5%. No definite evidence of a significant change in the eradication rate was seen during the past eleven years. The overall eradication rate of 1 wk bismuth-containing quadruple, second-line therapy from 2000 to 2010 was 84.7%. The annual eradication rates of the 1 wk second-line therapy revealed a relatively constant rate over the year.

### Innovations and breakthroughs

Authors show that the efficacy of 2 wk PPI + amoxicillin + clarithromycin (PAC)

regimen and 1 wk bismuth-containing quadruple therapy did not change over the period from 2000 to 2010 in South Korea. The efficacy of the 2 wk PAC and 1 wk quadruple second line therapy is by no means acceptable and satisfactory.

### Applications

Authors conclude that the 2 wk standard PAC regimen may be fit for use in eradicating *H. pylori*. Bacteria oscillate between a phenotypically resistant and a phenotypically susceptible state, during which they can be eradicated. To extend the duration of treatment such that the antibiotic will be present during at least one period of susceptibility may be an alternative option to overcome antibiotic resistance.

### Peer review

In this study, the authors retrospectively evaluated the eradication rate of *H. pylori* in a single center in the Republic of Korea for the period of January 2000 to December 2010. In 3969 patients who received a two weeks standard first-line triple therapy, an overall eradication rate of 86.5% has been found, with no significant ( $P = 0.09$ ) difference in the annual eradication rate during the eleven years. Furthermore, in the 399 patients who failed *H. pylori* eradication and received a 1-wk second-line therapy, an overall eradication rate of 84.7% has been found, with a relatively constant rate over the years. The authors conclude that there was no trend of change in the *H. pylori* eradication rate over the last 11 years in their institution and that a 2-wk first-line and a 1-wk second-line therapy can still be used in Korea.

## REFERENCES

- 1 Suerbaum S, Michetti P. Helicobacter pylori infection. *N Engl J Med* 2002; **347**: 1175-1186
- 2 Lind T, Mégraud F, Unge P, Bayerdörffer E, O'morain C, Spiller R, Veldhuyzen Van Zanten S, Bardhan KD, Hellblom M, Wrangstadh M, Zeijlon L, Cederberg C. The MACH2 study: role of omeprazole in eradication of Helicobacter pylori with 1-week triple therapies. *Gastroenterology* 1999; **116**: 248-253
- 3 Fock KM, Katelaris P, Sugano K, Ang TL, Hunt R, Talley NJ, Lam SK, Xiao SD, Tan HJ, Wu CY, Jung HC, Hoang BH, Kachintorn U, Goh KL, Chiba T, Rani AA. Second Asia-Pacific Consensus Guidelines for Helicobacter pylori infection. *J Gastroenterol Hepatol* 2009; **24**: 1587-1600
- 4 Chey WD, Wong BC. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. *Am J Gastroenterol* 2007; **102**: 1808-1825
- 5 Malfertheiner P, Megraud F, O'Morain C, Bazzoli F, El-Omar E, Graham D, Hunt R, Rokkas T, Vakil N, Kuipers EJ. Current concepts in the management of Helicobacter pylori infection: the Maastricht III Consensus Report. *Gut* 2007; **56**: 772-781
- 6 Hwang TJ, Kim N, Kim HB, Lee BH, Nam RH, Park JH, Lee MK, Park YS, Lee DH, Jung HC, Song IS. Change in antibiotic resistance of Helicobacter pylori strains and the effect of A2143G point mutation of 23S rRNA on the eradication of *H. pylori* in a single center of Korea. *J Clin Gastroenterol* 2010; **44**: 536-543
- 7 Kim N, Kim JJ, Choe YH, Kim HS, Kim JI, Chung IS. Diagnosis and treatment guidelines for Helicobacter pylori infection in Korea. *Korean J Gastroenterol* 2009; **54**: 269-278
- 8 Kim JJ, Reddy R, Lee M, Kim JG, El-Zaatari FA, Osato MS, Graham DY, Kwon DH. Analysis of metronidazole, clarithromycin and tetracycline resistance of Helicobacter pylori isolates from Korea. *J Antimicrob Chemother* 2001; **47**: 459-461
- 9 Zagari RM, Bianchi-Porro G, Fiocca R, Gasbarrini G, Roda E, Bazzoli F. Comparison of 1 and 2 weeks of omeprazole, amoxicillin and clarithromycin treatment for Helicobacter pylori eradication: the HYPER Study. *Gut* 2007; **56**: 475-479
- 10 Calvet X, García N, López T, Gisbert JP, Gené E, Roque M. A meta-analysis of short versus long therapy with a proton pump inhibitor, clarithromycin and either metronidazole or amoxycillin for treating Helicobacter pylori infection. *Aliment Pharmacol Ther* 2000; **14**: 603-609
- 11 Ford A, Moayyedi P. How can the current strategies for Helicobacter pylori eradication therapy be improved? *Can J Gastroenterol* 2003; **17** Suppl B: 36B-40B
- 12 Katelaris PH, Forbes GM, Talley NJ, Crotty B. A randomized comparison of quadruple and triple therapies for Helicobacter pylori eradication: The QUADRATE Study. *Gastroenterology* 2002; **123**: 1763-1769
- 13 Maconi G, Parente F, Russo A, Vago L, Imbesi V, Bianchi Porro G. Do some patients with Helicobacter pylori infection benefit from an extension to 2 weeks of a proton pump inhibitor-based triple eradication therapy? *Am J Gastroenterol* 2001; **96**: 359-366
- 14 Vakil N, Lanza F, Schwartz H, Barth J. Seven-day therapy for Helicobacter pylori in the United States. *Aliment Pharmacol Ther* 2004; **20**: 99-107
- 15 Mégraud F. H pylori antibiotic resistance: prevalence, importance, and advances in testing. *Gut* 2004; **53**: 1374-1384
- 16 Buzás GM. First-line eradication of Helicobacter pylori: are the standard triple therapies obsolete? A different perspective. *World J Gastroenterol* 2010; **16**: 3865-3870
- 17 Kim N, Kim JM, Kim CH, Park YS, Lee DH, Kim JS, Jung HC, Song IS. Institutional difference of antibiotic resistance of Helicobacter pylori strains in Korea. *J Clin Gastroenterol* 2006; **40**: 683-687
- 18 Fischbach LA, Goodman KJ, Feldman M, Aragaki C. Sources of variation of Helicobacter pylori treatment success in adults worldwide: a meta-analysis. *Int J Epidemiol* 2002; **31**: 128-139
- 19 Graham DY, Fischbach L. Helicobacter pylori treatment in the era of increasing antibiotic resistance. *Gut* 2010; **59**: 1143-1153
- 20 Tanimura H, Kawano S, Kubo M, Abe T, Goto M, Tanabe J, Asai A, Ito T. Does Helicobacter pylori eradication depend on the period of amoxicillin treatment? A retrospective study. *J Gastroenterol* 1998; **33**: 23-26
- 21 Meyer JM, Silliman NP, Wang W, Siepmann NY, Sugg JE, Morris D, Zhang J, Bhattacharyya H, King EC, Hopkins RJ. Risk factors for Helicobacter pylori resistance in the United States: the surveillance of *H. pylori* antimicrobial resistance partnership (SHARP) study, 1993-1999. *Ann Intern Med* 2002; **136**: 13-24
- 22 Simsek H, Balaban YH, Gunes DD, Hascelik G, Ozarlan E, Tatar G. Alarming clarithromycin resistance of Helicobacter pylori in Turkish population. *Helicobacter* 2005; **10**: 360-361
- 23 Kalach N, Serhal L, Asmar E, Campeotto F, Bergeret M, Dehecq E, Spyckerelle C, Charkaluk ML, Decoster A, Dupont C, Raymond J. Helicobacter pylori primary resistant strains over 11 years in French children. *Diagn Microbiol Infect Dis* 2007; **59**: 217-222
- 24 Di Mario F, Cavallaro LG, Scarpignato C. 'Rescue' therapies for the management of Helicobacter pylori infection. *Dig Dis* 2006; **24**: 113-130
- 25 Chung SJ, Lee DH, Kim N, Jung SH, Kim JW, Hwang JH, Park YS, Lee KH, Jung HC, Song IS. Eradication rates of helicobacter pylori infection with second-line treatment: non-ulcer dyspepsia compared to peptic ulcer disease. *Hepato-gastroenterology* 2007; **54**: 1293-1296
- 26 Lee JH, Cheon JH, Park MJ, Kim N, Lee DH, Kim JM, Kim JS, Jung HC, Song IS. The trend of eradication rates of second-line quadruple therapy containing metronidazole for Helicobacter pylori infection: an analysis of recent eight years. *Korean J Gastroenterol* 2005; **46**: 94-98
- 27 Lind T, Veldhuyzen van Zanten S, Unge P, Spiller R, Bayerdörffer E, O'Morain C, Bardhan KD, Bradette M, Chiba N, Wrangstadh M, Cederberg C, Idström JP. Eradication of Helicobacter pylori using one-week triple therapies combining omeprazole with two antimicrobials: the MACH I Study. *Helicobacter* 1996; **1**: 138-144
- 28 Baena Díez JM, López Mompó C, Rams Rams F, García

- Lareo M, Rosario Hernández Ibáñez M, Teruel Gila J. Efficacy of a multistep strategy for *Helicobacter pylori* eradication: quadruple therapy with omeprazole, metronidazole, tetracycline and bismuth after failure of a combination of omeprazole, clarithromycin and amoxycillin. *Med Clin (Barc)* 2000; **115**: 617-619
- 29 **Michopoulos S**, Tsibouris P, Bouzakis H, Balta A, Vouga-diotis J, Broutet N, Kralios N. Randomized study comparing omeprazole with ranitidine as anti-secretory agents combined in quadruple second-line *Helicobacter pylori* eradication regimens. *Aliment Pharmacol Ther* 2000; **14**: 737-744
- 30 **Rokkas T**, Sechopoulos P, Robotis I, Margantinis G, Pistiolas D. Cumulative *H. pylori* eradication rates in clinical practice by adopting first and second-line regimens proposed by the Maastricht III consensus and a third-line empirical regimen. *Am J Gastroenterol* 2009; **104**: 21-25

S- Editor Gou SX L- Editor A E- Editor Li JY