Comparison of Five-Day *Helicobacter pylori* Eradication Regimens: Rabeprazole-Based and Omeprazole-Based Regimens With and Without Omeprazole Pretreatment

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ABSTRACT

Background: The onset of antisecretory activity of rabeprazole is faster than that of omeprazole.

Objective: This study was performed to compare the efficacy of short-term rabeprazole-based triple therapy with that of omeprazole-based triple therapy and to determine the influence of omeprazole pretreatment in omeprazole-based short-term triple therapy.

Methods: This was a 2-center, open-label, prospective, randomized study. Patients who tested positive for *Helicobacter* (formerly *Campylobacter*) *pylori* were randomized to one of three 5-day regimens: (1) rabeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID (RAC group); (2) omeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID without omeprazole pretreatment (OAC1 group); and (3) omeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID with 5 days of omeprazole pretreatment 20 mg BID (OAC2 group). Eradication was assessed by ¹³C-urea breath test and rapid urease test ~1 month after completion of treatment. All patients who entered this study were included in the intent-to-treat (ITT) analysis, patients who completed the study were included in the per-protocol (PP) analysis, and patients who did not undergo the ¹³C-urea breath test and rapid urease test were included in the all-patients-treated (APT) analysis.

Results: A total of 120 patients (86 men, 34 women; mean [SD] age, 55.8 [14.3] years; range, 19–86 years) were assigned to the RAC, OAC1, or OAC2 group (40 patients in each group). ITT, PP, and APT eradication rates in the

RAC group were 90%, 92%, and 90%, respectively; in the OAC1 group, 75%, 83%, and 75%; and in the OAC2 group, 85%, 90%, and 87%. These eradication rates were not significantly different between groups.

Conclusions: Eradication rates did not differ significantly between the three 5-day proton pump inhibitor-based triple therapies in this study population. However, 5-day rabeprazole-based triple therapy tends to be more effective than 5-day omeprazole-based triple therapy in the eradication of *H pylori*, and treatment with omeprazole before eradication therapy may improve the eradication rates of 5-day omeprazole-based therapy. (*Curr Ther Res Clin Exp*. 2003;64:412–421) Copyright © 2003 Excerpta Medica, Inc.

Key words: eradication therapy, *Helicobacter pylori*, omeprazole, rabeprazole.

INTRODUCTION

Clinical studies^{1–4} have shown that *Helicobacter* (formerly *Campylobacter*) *pylori* is an important causative factor for a variety of diseases of the stomach and duodenum (eg, gastritis, peptic ulceration, gastric cancer, and low-grade B-cell lymphoma of gastric mucosa-associated lymphoid tissue). Numerous therapeutic trials^{5–7} of *H pylori* eradication therapy have been reported. These studies have investigated triple therapy with a proton pump inhibitor (PPI) and 2 antimicrobial drugs. The strong antisecretory activity of PPIs is thought to play an important role in the eradication of *H pylori*, as PPI-induced high gastric pH is reported to increase the sensitivity of *H pylori* to antimicrobial agents.^{8–10}

Several investigators have studied the optimum duration of treatment of PPI-based eradication therapies. As the eradication rates of 3- to 5-day PPI-based triple therapies are reported to be significantly lower than those of 1- to 2-week therapies, a 1-week duration for PPI-based triple therapies has been recommended.^{6,7} However, previous studies^{11–13} using short-term PPI-based eradication therapies mainly have used omeprazole as the PPI. Omeprazole requires time to demonstrate its potent inhibitory action on gastric acid secretion and is reported to exhibit its maximal acid suppressive effect after several days of administration.^{14–16} Rabeprazole, a recently developed PPI, has demonstrated a faster onset of antisecretory activity and stronger antimicrobial activity than other PPIs^{14–17}; therefore, rabeprazole may yield favorable results in patients taking short-term PPI-based eradication therapy. The question of whether the faster onset of antisecretory activity of rabeprazole could shorten the duration of PPI-based triple eradication therapy has not yet been fully investigated. It also has not been established whether treatment with omeprazole before PPI-based triple therapy can compensate for the slow onset of antisecretory activity of omeprazole, with resulting improvement in the eradication rates for short-term omeprazole-based eradication therapies.

This study was performed to compare the efficacy of short-term rabeprazole-based triple therapy with that of omeprazole-based triple therapy and to determine the influence of omeprazole pretreatment in omeprazole-based short-term triple therapy.

PATIENTS AND METHODS

Patients

This 2-center, open-label, prospective, randomized study was conducted in accordance with the principles of the Declaration of Helsinki. All patients provided written informed consent prior to enrollment.

Patients who tested positive for *H pylori* and who underwent eradication therapy at the participating institutions (Shimane Medical University Hospital and Unnan General Hospital, Shimane, Japan) between August 2000 and July 2002 were eligible for the study. Patients were not eligible for the study if they had previously undergone eradication therapy or gastric surgery. Patients with malignant conditions; with severe cardiac, hepatic, renal, or hematologic disease; or who were pregnant, possibly pregnant, or lactating also were excluded.

All patients underwent a physical examination before enrollment. Patients were required to cease PPI treatment for at least 4 weeks before enrollment. They were randomized to 1 of 3 treatment regimens by the envelope method at entry. (From a box containing many presealed envelopes, the investigators selected an envelope that contained the name of the treatment group to which the patient would be assigned.)

The three 5-day oral treatment regimens were as follows: (1) rabeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID (RAC group); (2) omeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID without pretreatment with omeprazole (OAC1 group); and (3) omeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID with 5 days of pretreatment with omeprazole 20 mg BID (OAC2 group). Patients in the RAC and OAC1 groups were not given placebo during the pretreatment period, and the investigators and the patients knew which regimen was being administered. All patients who entered this study were included in the intent-to-treat (ITT) analysis, patients who completed the study were included in the per-protocol (PP) analysis, and patients who did not undergo the ¹³C-urea breath test and rapid urease test were included in the all-patients-treated (APT) analysis.

Methods

Before the study began, all patients underwent upper gastrointestinal endoscopy to confirm the presence of *H pylori* infection. The status of *H pylori* infection was diagnosed using the rapid urease test, histologic examination (Warthin-Starry silver staining), culture, serologic testing (serum immunoglobulin G antibodies), and the ¹³C-urea breath test (UBT). Patients were diagnosed as *H pylori* positive if they showed positive results by ≥ 2 methods.

Eradication of *H pylori* was assessed using the rapid urease test by endoscopic biopsy specimen and the UBT at ~1 month (4–6 weeks) after completion of treatment. Patients were not allowed PPIs or antimicrobials that might influence urease activity of *H pylori* until after these tests were performed. UBT was performed as described previously,^{18–21} with minor modifications. Patients fasted for 12 hours before the examination. ¹³C-urea (100 mg) dissolved in distilled water was administered. Patients were instructed to rest in the left lateral recumbent position for 5 minutes and then to sit up for 15 minutes. Breath samples before and 20 minutes after the administration of ¹³C-urea were collected after the patient rinsed several times with mouthwash for ~20 seconds. The ¹³C-urea concentration in the breath samples was measured using a ¹³C analyzer (UbiT-IR200, Otsuka Electronics Co., Ltd., Osaka, Japan). Cases with a change in ¹³C <5% were diagnosed as negative for UBT. Patients were considered to be cured if the results of both the UBT and rapid urease tests were negative.

The *eradication rate* was defined as the number of successfully treated patients divided by the total number of treated patients. Eradication rates were assessed by ITT, PP, and APT analyses. Patients were interviewed at their first outpatient visit after completion of the therapy to clarify compliance with the therapy and ascertain whether any adverse effects (AEs) had occurred. Compliance was assessed by counting the number of tablets or capsules left after the completion of the therapy.

Statistical Analysis

Statistical analyses were performed using the chi-square test and the Mann-Whitney test when the Kruskal-Wallis test showed a significant difference. We used Stat View version 5.0 (Abacus Concepts, Inc., Berkeley, California) for the calculations. Differences of $P < 0.05$ were considered statistically significant.

RESULTS

A total of 120 patients (86 men, 34 women; mean [SD] age, 55.8 [14.3] years; range, 19–86 years) were assigned to the RAC, OAC1, or OAC2 group (40 patients in each group). These patients had the following diagnoses: gastric ulcers (or ulcer scars), 52 patients (43.3%); duodenal ulcers (or ulcer scars), 39 (32.5%); gastritis with dyspepsia, 15 (12.5%); gastric hyperplastic polyps, 7 (5.8%); gastric cancer (these patients underwent endoscopic treatment for early-stage cancer), 4 (3.3%); and gastroduodenal ulcers (or ulcer scars), 3 (2.5%). At baseline, the treatment groups differed significantly only in the ratio of men to women in the RAC versus the OAC1 group ($P < 0.05$) (Table I).

No significant differences were found in the incidence of AEs between groups. One patient in the OAC2 group (2.5%) discontinued treatment due to severe diarrhea with abdominal pain. No other severe adverse reactions were reported. All 19 patients (15.8%) who experienced mild adverse reactions—soft stools

Table I. Baseline characteristics of study patients.*

Characteristic	RAC (n = 40)	OAC1 (n = 40)	OAC2 (n = 40)	Total (N = 120)
Age, y				
Mean (SD)	55.1 (14.0)	52.5 (15.5)	59.8 (12.9)	55.8 (14.3)
Range	30–86	19–77	35–80	19–86
Sex, no. (%) of patients [†]				
Men	22 (55.0)	34 (85.0)*	30 (75.0)	86 (71.7)
Women	18 (45.0)	6 (15.0)	10 (25.0)	34 (28.3)
Diagnosis, no. (%) of patients				
Gastric ulcer [‡]	12 (30.0)	19 (47.5)	21 (52.5)	52 (43.3)
Duodenal ulcer [‡]	15 (37.5)	14 (35.0)	10 (25.0)	39 (32.5)
Gastritis with dyspepsia	5 (12.5)	5 (12.5)	5 (12.5)	15 (12.5)
Gastric hyperplastic polyp	6 (15.0)	0 (0.0)	1 (2.5)	7 (5.8)
Gastric cancer [§]	2 (5.0)	0 (0.0)	2 (5.0)	4 (3.3)
Gastroduodenal ulcer [‡]	0 (0.0)	2 (5.0)	1 (2.5)	3 (2.5)

*The three 5-day oral treatment regimens were as follows: (1) rabeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID (RAC group); (2) omeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID without omeprazole pretreatment (OAC1 group); and (3) omeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID with 5 days of pretreatment with omeprazole 20 mg BID (OAC2 group).

[†] $P < 0.05$ for ratio of men to women in the RAC group versus the OAC1 group.

[‡]Or ulcer scar.

[§]These patients received endoscopic treatment for early gastric cancer.

(4 patients [10.0%], 3 patients [7.5%], and 5 patients [12.5%] in the RAC, OAC1, and OAC2 groups, respectively) and glossitis or taste disturbance (2 patients [5.0%], 2 patients [5.0%], and 3 patients [7.5%], respectively)—completed the study.

One patient in the RAC group (2.5%), 4 in the OAC1 group (10.0%), and 1 in the OAC2 group (2.5%) did not undergo the rapid urease test or UBT after therapy. The reason that more patients were lost to follow-up in the OAC1 group than in the 2 other groups was not clarified. However, no significant between-group differences were found in the number of patients who were not assessed for *H pylori* infection after the completion of the therapy.

Patients were considered to be cured if the results of both the UBT and rapid urease test were negative. No patient had positive results on 1 test and negative results on the other.

Of the 120 patients who entered the study, 113 patients (94.2%) (excluding 6 patients [5.0%] who refused the UBT after treatment and 1 patient [0.8%] who did not complete treatment) took almost all ($\geq 95\%$) of the prescribed medication. Accordingly, 113 patients were included in the PP analysis and 119 patients were included in the APT analysis. The eradication rates for each therapeutic regimen are given in Table II. Although the eradication rates for the RAC and OAC2 regimens were higher than that for the OAC1 regimen, the

Table II. Eradication rates (95% CIs) for each of the 3 regimens.*†

Population	RAC	OAC1	OAC2
ITT	90 (80–100)	75 (61–89)	85 (73–97)
PP	92 (84–100)	83 (70–96)	90 (79–100)
APT	90 (80–100)	75 (61–89)	87 (76–98)

ITT = intent to treat; PP = per protocol; APT = all patients treated.

*The three 5-day oral treatment regimens were as follows: (1) rabeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID (RAC group); (2) omeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID without omeprazole pretreatment (OAC1 group); and (3) omeprazole 20 mg BID, amoxicillin 500 mg TID, and clarithromycin 400 mg BID with 5 days of pretreatment with omeprazole 20 mg BID (OAC2 group).

†No statistically significant between-group differences were found.

differences between the 3 regimens were not statistically significant in any analysis. Furthermore, no significant differences in eradication rates were found between male and female patients or between patients with different diseases (data not shown).

DISCUSSION

A trend in *H pylori* eradication is triple therapy, consisting of a PPI and 2 antimicrobial agents.^{5–7} Most of the recommended eradication therapy regimens are 1 week in duration because 1-week therapy improves compliance and decreases medical costs while achieving eradication rates similar to those of longer-term regimens.^{6,7} Shorter-duration regimens have been attempted, but 3- to 5-day, PPI-based triple therapies have lower eradication rates.^{11–13} The role of PPIs in these regimens has been reported to depend not only on the antimicrobial activity of the PPI but also on the PPI-induced high gastric pH environment.^{8–10} High gastric pH is considered to play an important part in successful eradication because neutral gastric pH has been demonstrated to increase both levels of antimicrobial agents in the stomach and the sensitivity of *H pylori* to amoxicillin.^{8–10} Because the time to onset of suppression of gastric acid secretion differs between PPIs,^{11–16} the time required to obtain a gastric pH high enough for successful eradication also differs. Rabeprazole has been shown to have a faster onset of antisecretory activity than omeprazole.^{14–16} Rabeprazole also has been reported to resolve symptoms more quickly than omeprazole in patients with gastroesophageal reflux disease.²² Better eradication rates with 5-day therapies for rabeprazole-based triple therapy compared with omeprazole-based triple therapy may be due to the quicker onset of the acid suppressive effect of rabeprazole. In rabeprazole-based therapy, intragastric pH may be elevated for a sufficient period on the first day of treatment to achieve eradication, whereas in omeprazole-based therapy, the intragastric pH may first reach this level several days after the start of administration. The

thioether derivative of rabeprazole also has been shown to have strong antimicrobial activity against *H pylori*.^{23–26} These characteristics of rabeprazole may favorably influence the results of short-term eradication therapies. This preliminary study demonstrated that the use of rabeprazole might shorten the duration of PPI-based eradication therapy.

In a comparative study of 3-day and 7-day rabeprazole-based triple therapies using rabeprazole 20 mg, amoxicillin 1000 mg, and clarithromycin 500 mg, all twice daily, Wong et al²⁷ reported a significantly lower eradication rate for the 3-day regimen than for the 7-day regimen. Isomoto et al²⁸ also demonstrated that the eradication rate for a 5-day regimen using rabeprazole 10 mg, amoxicillin 750 mg, and clarithromycin 400 mg, all BID, was significantly lower than the rate for a 7-day regimen. That study and the present study differed in the daily rabeprazole dosage. Therefore, the minimal dosage required to obtain an adequate eradication rate for a 5-day triple therapy is likely to be 20 mg BID. We previously reported the results of 2 studies^{19,20} of 14-day lansoprazole-based triple therapy using lansoprazole 30 mg once daily in the morning, amoxicillin 500 mg TID, and clarithromycin 400 mg BID. The eradication rates of these lansoprazole-based triple therapies were 85% to 87%, 87% to 88%, and 91% to 92% in the ITT, APT, and PP analyses, respectively. The eradication rates in the RAC and OAC2 groups in this study were similar to those of 14-day, lansoprazole-based triple therapy. Importantly, 6 of 135 patients (4.4%) with the 14-day lansoprazole-based triple therapy could not complete the treatment protocol because of severe diarrhea. Only 1 of the 120 patients (0.8%) in our study could not complete the treatment because of severe diarrhea. Thus, the 5-day RAC and OAC2 regimens investigated in this study seem to be effective for the eradication of *H pylori*, with fewer AEs. Further study is necessary to determine whether the 5-day triple therapy using rabeprazole 20 mg BID is as effective as the standard triple therapies, which have a 7-day treatment regimen.

Treatment with a PPI before PPI-based eradication therapy has been reported to reduce the *H pylori* eradication rate.^{29,30} However, 2 studies^{31,32} have shown that PPI pretreatment does not affect the efficacy of PPI-based eradication therapies. The maximal antisecretory function of omeprazole is exhibited several days after beginning drug administration.^{14–16} This slow onset of acid suppression with omeprazole may unfavorably affect the efficacy of PPI-based eradication therapies, especially those of short duration. Several investigators^{10–13} have failed to show satisfactory efficacy with short-term omeprazole-based triple therapies. A 5-day omeprazole pretreatment period was suggested to increase the eradication rate of the 5-day omeprazole-based triple therapy in this study. Treatment with omeprazole before eradication therapy may compensate for the slow onset of antisecretory function with omeprazole.

To our knowledge, this is the first study to suggest that the timing of the onset of the antisecretory function of PPIs may influence the results of short-term PPI-based eradication therapy, although gastric pH monitoring was not performed during eradication therapy in this study.

There are several limitations to interpreting the results of this study because neither the male-female ratio nor the number of patients with different gastric diseases was equally distributed between the 3 treatment groups. Therefore, we compared the eradication rates between male and female patients and between patients with different diseases and did not find any significant differences in eradication rates in these comparisons. However, these differences of distribution of sex and gastric diseases between groups might have affected the results of this study. Furthermore, large-scale studies are required to confirm whether omeprazole pretreatment can shorten the duration of use of combined antimicrobial agents.

CONCLUSIONS

Eradication rates did not differ significantly between the three 5-day PPI-based triple therapies in this study population. However, 5-day rabeprazole-based triple therapy tends to be more effective than 5-day omeprazole-based triple therapy in the eradication of *H pylori*, and treatment with omeprazole before eradication therapy may improve the eradication rates of 5-day omeprazole-based therapy.

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REFERENCES

1. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet*. 1984;16:1311–1315.
2. Graham DY. Treatment of peptic ulcers caused by *Helicobacter pylori*. *N Engl J Med*. 1993;328:349–350.
3. Parsonnet J, Friedman GD, Vandersteen DP, et al. *Helicobacter pylori* infection and the risk of gastric carcinoma. *N Engl J Med*. 1991;325:1127–1131.
4. Isaacson PG, Spencer J. Is gastric lymphoma an infectious disease? *Hum Pathol*. 1993;24:569–570.
5. Pounder RE. New developments in *Helicobacter pylori* eradication therapy. *Scand J Gastroenterol*. 1997;223(Suppl):43–45.
6. Lind T, Veldhuyzen van Zanten S, Unge P, et al. Eradication of *Helicobacter pylori* using one-week triple therapies combining omeprazole with two antimicrobials: The MACH I Study. *Helicobacter*. 1996;1:138–144.
7. Lind T, Megraud F, Unge P, et al. The MACH2 study: Role of omeprazole in eradication of *Helicobacter pylori* with 1-week triple therapies. *Gastroenterology*. 1999;116:248–253.

8. Grayson ML, Eliopoulos GM, Ferraro MJ, Moellering RC Jr. Effect of varying pH on the susceptibility of *Campylobacter pylori* to antimicrobial agents. *Eur J Clin Microbiol Infect Dis.* 1989;8:888–889.
9. Hunt RH. pH and Hp-gastric acid secretion and *Helicobacter pylori*: Implications for ulcer healing and eradication of the organism. *Am J Gastroenterol.* 1993;88:481–483.
10. Sachs G, Shin JM, Munson K, et al. Review article: The control of gastric acid and *Helicobacter pylori* eradication. *Aliment Pharmacol Ther.* 2000;14:1383–1401.
11. Trevisani L, Sartori S, Caselli M, et al. A four-day low dose triple therapy regimen for the treatment of *Helicobacter pylori* infection. *Am J Gastroenterol.* 1998;93:390–393.
12. Moayyedi P, Langworthy H, Tompkins DS, et al. The optimum 5 day therapy against *Helicobacter pylori*. *Gastroenterology.* 1997;112(Suppl):A223. Abstract.
13. Catalano F, Branciforte G, Catanzaro R, et al. *Helicobacter pylori*-positive duodenal ulcer: Three-day antibiotic eradication regimen. *Aliment Pharmacol Ther.* 2000;14:1329–1334.
14. Williams MP, Sercombe J, Hamilton MI, Pounder RE. A placebo-controlled trial to assess the effects of 8 days of dosing with rabeprazole versus omeprazole on 24-h intragastric acidity and plasma gastrin concentrations in young healthy male subjects. *Aliment Pharmacol Ther.* 1998;12:1079–1089.
15. Williams MP, Pounder RE. Review article: The pharmacology of rabeprazole. *Aliment Pharmacol Ther.* 1999;13(Suppl 3):3–10.
16. Saitoh T, Fukushima Y, Otsuka H, et al. Effects of rabeprazole, lansoprazole and omeprazole on intragastric pH in CYP2C19 extensive metabolizers. *Aliment Pharmacol Ther.* 2002;16:1811–1817.
17. Gardner JD, Perdomo C, Sloan S, et al. Integrated acidity and rabeprazole pharmacology. *Aliment Pharmacol Ther.* 2002;16:455–464.
18. Miwa H, Ohkura R, Nagahara A, et al. [¹³C]-urea breath test for assessment of cure of *Helicobacter pylori* infection at 1 month after treatment. *J Clin Gastroenterol.* 1998;27(Suppl 1):S150–S153.
19. Adachi K, Ishihara S, Hashimoto T, et al. Efficacy of sucralfate for *Helicobacter pylori* eradication triple therapy in comparison with a lansoprazole-based regimen. *Aliment Pharmacol Ther.* 2000;14:919–922.
20. Adachi K, Ishihara S, Hashimoto T, et al. Efficacy of ecabet sodium for *Helicobacter pylori* eradication triple therapy in comparison with a lansoprazole-based regimen. *Aliment Pharmacol Ther.* 2001;15:1187–1191.
21. Adachi K, Fujishiro H, Mihara T, et al. Influence of lansoprazole, famotidine, roxatidine and rebamipide administration on the urea breath test for the diagnosis of *Helicobacter pylori* infection. *J Gastroenterol Hepatol.* 2003;18:168–171.
22. Holtmann G, Bytzer P, Metz M, et al. A randomized, double-blind, comparative study of standard-dose rabeprazole and high-dose omeprazole in gastro-oesophageal reflux disease. *Aliment Pharmacol Ther.* 2002;16:479–485.
23. Tsuchiya M, Imamura L, Park JB, Kobashi K. *Helicobacter pylori* urease inhibition by rabeprazole, a proton pump inhibitor. *Biol Pharm Bull.* 1995;18:1053–1056.
24. Tsutsui N, Taneike I, Ohara T, et al. A novel action of the proton pump inhibitor rabeprazole and its thioether derivative against the motility of *Helicobacter pylori*. *Antimicrob Agents Chemother.* 2000;44:3069–3073.
25. Kawakami Y, Akahane T, Yamaguchi M, et al. In vitro activities of rabeprazole, a novel proton pump inhibitor, and its thioether derivative alone and in combination with other antimicrobials against recent clinical isolates of *Helicobacter pylori*. *Antimicrob Agents Chemother.* 2000;44:458–461.

26. Ohara T, Goshi S, Taneike I, et al. Inhibitory action of a novel proton pump inhibitor, rabeprazole, and its thioether derivative against the growth and motility of clarithromycin-resistant *Helicobacter pylori*. *Helicobacter*. 2001;6:125–129.
27. Wong BC, Wong WM, Yee YK, et al. Rabeprazole-based 3-day and 7-day triple therapy vs. omeprazole-based 7-day triple therapy for the treatment of *Helicobacter pylori* infection. *Aliment Pharmacol Ther*. 2001;15:1959–1965.
28. Isomoto H, Furusu H, Morikawa T, et al. 5-Day vs. 7-day triple therapy with rabeprazole, clarithromycin and amoxicillin for *Helicobacter pylori* eradication. *Aliment Pharmacol Ther*. 2000;14:1619–1623.
29. Labenz J, Leverkus F, Börsch G. Omeprazole plus amoxicillin for cure of *Helicobacter pylori* infection. Factors influencing the treatment success. *Scand J Gastroenterol*. 1994;29:1070–1075.
30. Bayerdörffer E, Miehke S, Mannes GA, et al. Double-blind trial of omeprazole and amoxicillin to cure *Helicobacter pylori* infection in patients with duodenal ulcers. *Gastroenterology*. 1995;108:1412–1417.
31. Annibale B, D'Ambra G, Luzzi I, et al. Does pretreatment with omeprazole decrease the chance of eradication of *Helicobacter pylori* in peptic ulcer patients? *Am J Gastroenterol*. 1997;92:790–794.
32. Adamek RJ, Szymanski C, Pfaffenbach B. Pantoprazole suppresses *Helicobacter pylori* without affecting cure. *Helicobacter*. 1999;4:266–271.

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