

ANTIBACTERIAL TREATMENT OF GASTRIC ULCERS ASSOCIATED WITH *HELICOBACTER PYLORI*

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Abstract Background. There is a strong association between infection with *Helicobacter pylori* and gastric ulcers that are unrelated to the use of nonsteroidal antiinflammatory medications. We studied the efficacy of antibacterial therapy without medication to suppress gastric acid for the treatment of patients with *H. pylori* infection and gastric ulcers unrelated to the use of nonsteroidal agents.

Methods. Patients with gastric ulcers seen on endoscopy and with *H. pylori* infection confirmed by smear or culture were randomly assigned to receive either a one-week course of antibacterial agents (120 mg of bismuth subcitrate, 500 mg of tetracycline, and 400 mg of metronidazole, each given orally four times a day) or a four-week course of omeprazole (20 mg orally per day). Follow-up endoscopies were performed after five and nine weeks. The patients and their physicians were aware of the treatment assignments, but the endoscopists were not.

Results. A total of 100 patients were randomly assigned to treatment, and 85 completed the trial. At five weeks, *H. pylori* had been eradicated in 41 of the 45 patients in the antibacterial-treatment group (91.1 percent; 95 percent confidence interval, 82.9 to 99.3) and in 5 of the 40 in the omeprazole group (12.5 percent; 95 percent

confidence interval, 2.3 to 22.7; $P < 0.001$). The gastric ulcers were healed in 38 of the patients treated with antibacterial drugs (84.4 percent; 95 percent confidence interval, 73.9 to 95.0) and in 29 of those treated with omeprazole (72.5 percent; 95 percent confidence interval, 58.6 to 86.4; $P = 0.28$). At nine weeks, ulcer healing was confirmed in 43 of the patients receiving antibacterial therapy and in 37 of those receiving omeprazole ($P = 1.0$). The mean (\pm SD) duration of pain during the first week of treatment was 1.9 ± 2.6 days in the omeprazole group, as compared with 3.6 ± 3.0 days in the antibacterial-treatment group ($P = 0.004$). One year after treatment, recurrent gastric ulcers were detected in 1 of 22 patients (4.5 percent) in the antibacterial-treatment group and in 12 of 23 (52.2 percent) in the omeprazole group ($P = 0.001$). *H. pylori* was detected in the 1 patient with a recurrent ulcer who had received antibacterial treatment and in 10 of the 12 patients with recurrent ulcers who had received omeprazole.

Conclusions. In patients with *H. pylori* infection and gastric ulcers unrelated to the use of nonsteroidal antiinflammatory drugs, one week of antibacterial therapy without acid suppression heals the ulcers as well as omeprazole and reduces the rate of their recurrence. (N Engl J Med 1995;332:139-42.)

ABOUT 70 percent of patients with gastric ulcers are infected with *Helicobacter pylori*.^{1,2} The use of nonsteroidal antiinflammatory drugs does not increase susceptibility to infection with *H. pylori*.^{3,4} Most gastric ulcers that are not related to treatment with these antiinflammatory drugs are accompanied by antral gastritis and *H. pylori* infection, whereas about 50 percent of gastric ulcers associated with these medications are not accompanied by *H. pylori*-associated gastritis.⁵ If patients with ulcers induced by nonsteroidal antiinflammatory drugs are excluded, the prevalence of infection with *H. pylori* in patients with gastric ulcers is around 96 percent.⁶ A strong association, however, does not establish a causal relation between *H. pylori* infection and gastric ulcer disease.

In a previous study, we found that duodenal ulcers healed as well after the eradication of *H. pylori* with antibacterial therapy as they did after treatment with both antibacterial therapy and medication to suppress gastric acid.⁷ In this study, we investigated the efficacy of antibacterial therapy for the treatment of *H. pylori*-associated gastric ulcers after excluding cases related to the use of nonsteroidal antiinflammatory drugs. Our

hypotheses were that gastric ulcers not associated with these medications are causally related to *H. pylori* infection and that antibacterial therapy without additional medications can heal these ulcers and reduce the likelihood of their recurrence.

METHODS

All patients presenting to the Prince of Wales Hospital with dyspepsia or epigastric pain who were found to have gastric ulcers by endoscopy were eligible for the study. Patients were excluded if they were under 16 years of age, had used nonsteroidal antiinflammatory drugs in the previous three months, had had gastrointestinal bleeding within the previous four weeks, had previously undergone surgery to reduce gastric acid, or had received antibacterial therapy in the past. A gastric ulcer was defined endoscopically as a breach of the mucosa with a well-defined ulcer crater. Antral biopsies as well as biopsies around the gastric ulcers were performed to test for urease activity (Campylobacter-Like Organism [CLO] test, Delta West, Western Australia), with Gram's-stain smears and cultures to detect *H. pylori*. Patients were considered to be positive for *H. pylori* if either the culture or the smear from either the antral biopsy or the biopsy around the ulcer was positive. A positive result on the CLO test alone was not considered a sufficient criterion for a patient to be classified as positive for *H. pylori*. Patients initially classified as positive for *H. pylori* on the basis of the CLO test were reclassified as negative if the result of the CLO test was not confirmed by positive smears or cultures. The size of the ulcer was measured with an endoscopic ruler during endoscopy.

Patients were randomly assigned to one of two treatment groups with the use of sealed envelopes that contained the assignments. Treatment assignments were determined with a list of random numbers generated by computer. Both the patients and their physicians were aware of the treatment assignments, but the endoscopists were not.

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Supported by a grant (CUHK 29/93M) from the Research Grant Committee of Hong Kong.

Patients were assigned to receive either a course of bismuth subcitrate (120 mg), tetracycline (500 mg), and metronidazole (400 mg), with each medication given orally four times per day for one week, or omeprazole (20 mg per day given orally) for four weeks. In all cases, treatment was started on the day of randomization. A patient was assigned to treatment when the CLO test was positive. If infection was not confirmed by a positive smear or culture or both, the patient was classified as negative for *H. pylori* and excluded from the study.

The patients were given diary cards to record symptoms during the five weeks after their assignment to treatment. After one week of treatment, all patients were interviewed by a research nurse about compliance with the treatment, side effects, and symptoms related to the ulcer. Patients assigned to the one-week course of antibacterial therapy were then given 60 antacid tablets (Mylanta) to be taken as required.

Five weeks after randomization (i.e., four weeks after the completion of antibacterial therapy), the patients returned their diary cards and those in the antibacterial-treatment group returned any remaining antacid tablets. Follow-up endoscopy was performed to check the healing of the ulcers, and antral biopsies were repeated to obtain specimens for the CLO test, smear, and culture. If the ulcers were not completely healed, patients in the antibacterial-treatment group received antacid as necessary, and patients in the omeprazole group received omeprazole (20 mg daily) for four more weeks. A second follow-up endoscopy was performed at nine weeks. After nine weeks, all patients with persistent gastric ulcers were given omeprazole (20 mg daily) for four more weeks.

The study was approved by the ethics committee of the faculty of medicine at the Chinese University of Hong Kong. Written informed consent was obtained from all patients before they were enrolled in the trial.

Microbiologic Studies

Gram's staining was performed on minced tissue from two antral-biopsy specimens to detect gram-negative spiral organisms. The minced tissue was cultured on Columbia agar (Oxoid, Basingstoke, United Kingdom) supplemented with 5 percent horse blood and incubated for five days under microaerophilic conditions.⁸ The presence of *H. pylori* was confirmed by morphologic analysis of the colony, Gram's staining,^{9,10} and biochemical tests (for oxidase, catalase, and urease).

Statistical Analysis

The results of treatment in the two groups of patients were compared by chi-square analysis. Ulcer healing and eradication of *H. pylori* in the two groups were compared with Yates' correction or Fisher's exact two-tailed test.¹¹ The duration of symptoms was analyzed with the Mann-Whitney U test. Differences with a P value less than 0.05 were considered statistically significant.

RESULTS

From May 1992 to April 1994, 100 patients with gastric ulcers associated with *H. pylori* infection were studied; 54 patients were randomly assigned to antibacterial therapy, and 46 to treatment with omeprazole. The two groups were well matched with respect to age, sex, history of smoking, and the site and size of the gastric ulcers (Table 1). Nine patients were excluded from the analysis: four assigned to receive antibacterial therapy (one each because of unconfirmed *H. pylori* infection, loss to follow-up, a concomitant duodenal ulcer, and previous therapy for helicobacter infection) and five assigned to receive omeprazole (one because of unconfirmed *H. pylori* infection and four because of loss to follow-up). Thus, the antibacterial-treatment group included 50 patients, and the omeprazole group 41.

H. pylori was identified around the gastric ulcer in all

Table 1. Characteristics of 100 Patients with Gastric Ulcers and *H. pylori* Infection Assigned to Treatment with Antibacterial Drugs or Omeprazole.*

CHARACTERISTIC	ANTIBACTERIAL DRUGS (N = 54)	OMEPRAZOLE (N = 46)
Age — yr		
Mean	56.4	56.3
Range	26–81	32–82
Sex — M/F	40/14	33/13
History of smoking — no. of patients (%)	26 (48)	24 (52)
Location of ulcer — no. of patients		
Antrum	15	14
Angularis	30	24
Pylorus	2	2
Lesser curve	5	4
Greater curve	1	1
Body of stomach	1	1
Size of ulcer — cm	0.82±0.53	0.92±0.55

*Plus-minus values are means ±SD.

50 patients in the antibacterial-treatment group and in the antrum in 49. Of the 41 patients in the omeprazole group, 39 had *H. pylori* in both the antrum and the ulcer. One patient had *H. pylori* in the antrum alone, and one in the ulcer alone. Five patients receiving antimicrobial therapy did not complete the course of medication because of side effects, including nausea, abdominal pain, diarrhea, vomiting, and dizziness (two of these patients were lost to follow-up). These five patients were given either H₂-receptor antagonists or omeprazole. One patient in the omeprazole group violated the protocol by taking an H₂-receptor antagonist in addition to omeprazole.

Eighty-five patients (45 in the antibacterial-treatment group and 40 in the omeprazole group) completed the trial. The dropout rate (including patients lost to follow-up, those who could not tolerate the medication, and those who did not comply with the protocol) did not differ significantly between the antibacterial group (6 of 54 patients) and the omeprazole group (5 of 46, P=0.78). Since acid-suppressing medications given to the patients who could not tolerate antibacterial therapy affected ulcer healing, only patients who completed the assigned treatment were included in the analysis. We also conducted an intention-to-treat analysis that included the three patients who failed to finish the antibacterial therapy but returned for follow-up and the one patient in the omeprazole group who took an H₂-receptor antagonist.

Five weeks after randomization, eradication of *H. pylori* was documented in 41 of the 45 patients receiving antibacterial therapy (91.1 percent; 95 percent confidence interval, 82.9 to 99.3) and in 5 of the 40 patients treated with omeprazole (12.5 percent; 95 percent confidence interval, 2.3 to 22.7; P<0.001). Endoscopy at five weeks showed complete healing of the ulcers in 38 of the patients in the antibacterial-therapy group (84.4 percent; 95 percent confidence interval, 73.9 to 95.0)

Table 2. Ulcer Healing and Duration of Pain, According to Treatment Group.*

RESPONSE TO TREATMENT	ANTIBACTERIAL DRUGS	OMEPRAZOLE	P VALUE
Ulcer healing — no. of patients (%)			
Wk 5	38 (84.4)	29 (72.5)	0.28
Wk 9	43 (95.6)	37 (94.9)	1.00
Wk 13	45 (100)	38 (97.4)	0.46
Days with pain			
Wk 1	3.6±3.0	1.9±2.6	0.004
Wk 2–5	7.6±9.5	4.4±8.7	0.089

*In the antibacterial-treatment group, 45 patients completed follow-up at 5, 9, and 13 weeks. In the omeprazole group, 40 patients completed follow-up at 5 and 9 weeks, and 39 completed follow-up at 13 weeks. For details, see the text. Plus–minus values are means ±SD.

and 29 of those in the omeprazole group (72.5 percent; 95 percent confidence interval, 58.6 to 86.4; $P=0.28$). One patient in the latter group was lost to follow-up after five weeks.

At nine weeks, the ulcers had completely healed in 43 of the 45 patients who received antibacterial therapy (95.6 percent; 95 percent confidence interval, 89.5 to 100) and in 37 of the 39 who received omeprazole (94.9 percent; 95 percent confidence interval, 88 to 100; $P=1.0$). The four patients whose ulcers had not healed at 9 weeks were examined again at 13 weeks. The two patients in the antibacterial-treatment group had been given omeprazole for four weeks, and their ulcers were healed. One of them remained positive for *H. pylori* infection. One of the two patients in the omeprazole group had complete healing of the ulcer after a total of 13 weeks of omeprazole therapy; the other patient was referred for surgery because the ulcer remained unhealed.

The mean (\pm SD) duration of epigastric pain during the first week of treatment was longer in the group treated with antibacterial therapy (3.6 ± 3.0 days) than in the group treated with omeprazole (1.9 ± 2.6 days, $P=0.004$). The duration of pain from the second to the fifth week after randomization was 7.6 ± 9.5 days for those receiving antibacterial therapy and 4.4 ± 8.7 days for those receiving omeprazole ($P=0.089$) (Table 2).

In an intention-to-treat analysis, ulcer healing had occurred at five weeks in 40 of 48 patients assigned to antibacterial treatment (83.3 percent; 95 percent confidence interval, 72.7 to 93.9) and in 30 of 41 assigned to omeprazole (73.1 percent; 95 percent confidence interval, 59.6 to 86.7; $P=0.36$). *H. pylori* had been eradicated in 41 patients in the antibacterial-treatment group (85.4 percent; 95 percent confidence interval, 75.4 to 95.4) and in 5 of those in the omeprazole group (12.2 percent; 95 percent confidence interval, 2.2 to 22.2; $P<0.001$). At nine weeks the ulcers had healed in 46 of the patients assigned to antibacterial therapy (95.8 percent; 95 percent confidence interval, 90 to 100) and in 38 of those assigned to omeprazole (95.0 percent; 95 percent confidence interval, 88 to 100; $P=1.0$). During the first week of treatment, the mean duration of pain was 3.5 ± 2.8 days in the antibacterial-therapy group, as compared with 2.1 ± 2.6 days in the

omeprazole group ($P=0.009$). The duration of pain in the second to fifth weeks did not differ significantly between the two groups (7.3 ± 9.6 and 4.9 ± 8.8 days, respectively; $P=0.139$).

As of August 1994, 45 patients had returned for the one-year follow-up evaluation. Recurrent gastric ulcers were detected in 1 of 22 patients in the antibacterial-treatment group (4.5 percent) and in 12 of 23 in the omeprazole group (52.2 percent, $P=0.001$). *H. pylori* was detected in the 1 patient in the antibacterial-treatment group with a recurrent ulcer and in 10 of the 12 patients in the omeprazole group with recurrent ulcers (83.3 percent). In addition, duodenal ulcers had developed in two patients in the omeprazole group within one year after treatment; both were positive for *H. pylori* infection.

DISCUSSION

Most gastric ulcers occur with chronic diffuse gastric inflammation.¹² Clinical and histologic studies have suggested that *H. pylori*-related gastritis and gastric ulcer represent a continuum of progressive disease.^{13,14} A causal relation between *H. pylori* infection and the development of gastric ulcers would be supported if the bacterial infection were treated successfully with antibacterial agents alone.

Graham et al. reported that among patients with gastric ulcers who were treated with three antibacterial drugs and ranitidine, the incidence of recurrent ulcers was significantly reduced after the eradication of *H. pylori*.¹ Labenz and Börsch used various combinations of omeprazole and antibiotics (amoxicillin, ciprofloxacin, and roxithromycin) to treat 83 people with *H. pylori*-associated gastric ulcers and found that the eradication of *H. pylori* enhanced the healing of the ulcers and reduced their recurrence.¹⁵ In both studies, patients received medications that suppressed acid production. The German Gastric Ulcer Study Group randomly assigned patients with gastric ulcers to receive omeprazole or three antibacterial drugs, including eight weeks of bismuth, and found that the eradication of *H. pylori* resulted in the healing of the ulcers.¹⁶ The Finnish Gastric Ulcer Study Group randomly assigned patients with gastric ulcers to receive bismuth (for 8 weeks) plus metronidazole (for 10 days), bismuth alone (for 10 days), or ranitidine alone (for 8 weeks)¹⁷ and concluded that the eradication of *H. pylori* improved the healing of the ulcers and prevented relapses. In both the German and the Finnish studies, however, the healing of ulcers in the groups receiving antibacterial therapy could be attributed in part to the eight-week course of bismuth.

We compared a one-week course of three antibacterial drugs but no medication to suppress acid with a four-week course of omeprazole, a proton-pump inhibitor used as the standard treatment for ulcers. Our findings in the antibacterial-treatment group establish a link between the eradication of *H. pylori* and ulcer healing, although the possibility of spontaneous healing in some instances cannot be excluded. There was a

trend toward an increased rate of healing in the antibacterial-treatment group after five weeks. The rate of healing at 9 and 13 weeks was similar in the two groups. Our findings are very similar to those in our previous study of the use of antibacterial therapy for the treatment of *H. pylori*-associated duodenal ulcers.⁷ The two studies provide evidence in support of a causal relation between *H. pylori* infection and the development of gastric and duodenal ulcers, respectively.

The relief of symptoms was significantly more rapid during the first week of treatment with the use of a medication that suppressed acid production, as compared with antibacterial therapy alone. This difference, which did not persist after the first week of treatment, was probably due to the potent acid-suppressing effect of omeprazole and the gastrointestinal side effects of treatment with three antibacterial drugs. We cannot rule out the possibility of bias in the patients' reports of symptoms, since they were not blinded to treatment. The rate of recurrent ulcers at one year was significantly higher in the omeprazole group than in the antibacterial-treatment group. Most of the patients with recurrent ulcers, including the one patient in the antibacterial-treatment group, were positive for *H. pylori* infection. Our findings are consistent with those of previous studies in which patients with gastric ulcers were treated with medication directed against *H. pylori*. These studies found that *H. pylori* infection was the most important predictor of the recurrence of ulcers.^{1,13-15}

We conclude that one week of antibacterial treatment (bismuth subcitrate, tetracycline, and metronidazole) without acid suppression heals *H. pylori*-associated gastric ulcers that are unrelated to the use of nonsteroidal antiinflammatory drugs and reduces the rate of recurrence of ulcers.

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CORRECTION

Antibacterial Treatment of Gastric Ulcers

To the Editor: Sung et al. (Jan. 19 issue)¹ reported that in patients with *Helicobacter pylori* infection and gastric ulcers unrelated to the use of nonsteroidal antiinflammatory drugs, "one week of antibacterial therapy without acid suppression heals the ulcers as well as omeprazole and reduces the rate of their recurrence." The authors imply that they have proved that therapy directed against *H. pylori*, and not against ulcers, cures ulcers. There are a number of ways to accelerate ulcer healing without using antisecretory drugs (such as sucralfate or bismuth subcitrate). In our view, Sung et al. actually showed that two regimens that had previously been shown to accelerate ulcer healing were approximately equally effective. Their description of bismuth subcitrate as an antibacterial agent is very misleading, because it is an extremely effective antiulcer agent independently of its antimicrobial activity. Colloidal bismuth subcitrate is an effective antiulcer agent whose effectiveness is not limited to ulcers associated with *H. pylori*.^{2,3} Other bismuth preparations do not appear to have similar behavior with respect to experimental ulcers. For example, histochemical staining has been used to compare the ability of bismuth subnitrate, bismuth subcarbonate, bismuth subsalicylate, and colloidal bismuth subcitrate to coat experimental gastric ulcers in rats.³ When colloidal bismuth subcitrate was administered, bismuth was deposited in a uniform layer covering the ulcer base. The histochemical staining of the ulcer base was negative with the other bismuth salts and remained negative even when the concentrations of bismuth subcarbonate or bismuth subnitrate were increased by a factor of 5. Subsequent studies have demonstrated important differences between different formulations of bismuth subcitrate; colloidal bismuth subcitrate is effective in preventing ulceration in Shay rats, whereas noncolloidal bismuth subcitrate is not.⁴

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To the Editor: Sung et al. randomly assigned patients to receive either omeprazole or a course of bismuth subcitrate, tetracycline, metronidazole, and antacid tablets (Mylanta). The amount of antacid taken by the patients is not reported, nor is it clear whether they were allowed to take their own antacids. Bismuth compounds and antacids both have ulcer-healing properties equivalent to those of ranitidine.^{1,2} It is possible that the combination of bismuth and antacids may have resulted in substantial healing of the relatively small (average size, <1 cm), uncomplicated ulcers in this study, independently of any antibacterial effects. Study of a group of patients treated with bismuth and antacids alone would be required to rule out this possibility.

The authors do not explain how they determined that *H. pylori* had been eradicated. In their inclusion criteria, a positive Campylobacter-Like Organism test alone was not considered definitive evidence of infection; a confirmatory smear or culture was required. In the United States, the gold standard for the diagnosis of *H. pylori* infection includes antral biopsy for histologic analysis after the application of special stains.³

It is also not clear how the one-year follow-up evaluation was conducted. Did all patients undergo endoscopy again, or only those with symptoms? Was the endoscopist blinded to the patients' original treatment groups? This information is important for the interpretation of the data.

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To the Editor: How many patients with gastric ulcer did Sung et al. exclude before they identified 100 patients with ulcers associated with *H. pylori* for the study? What was meant by the statement that "patients were excluded if they . . . had received antibacterial therapy in the past"? Does this mean they were excluded if they had received antibacterial therapy for ulcer disease or antibacterial therapy for any

reason within the preceding six months, or is there some other explanation?

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To the Editor: Of the 40 patients treated with omeprazole alone, *H. pylori* was eradicated in 5. This somewhat surprising outcome may represent a false negative result due to the redistribution of *H. pylori* from the antrum to the body and fundus of the stomach that occurs during omeprazole therapy.¹ This effect of omeprazole considerably lessens the sensitivity of antral biopsy for detecting *H. pylori* in patients who are taking the drug.

Using a one-week regimen of bismuth subcitrate, tetracycline, and metronidazole, Sung et al. found in an intention-to-treat analysis that *H. pylori* was eradicated in 41 of 48 patients (85.4 percent). We believe the intention-to-treat analysis should include all 51 patients who were randomized and fulfilled the entry criteria. The inclusion of these patients would decrease the rate of eradication of *H. pylori* to 80.4 percent.

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To the Editor: The 95 percent confidence intervals in the article by Sung et al. are expressed as accurate to 0.1 percent, when in fact they vary from the exact 95 percent confidence intervals by 1.0 to 4.1 percent.

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The authors reply:

To the Editor: We excluded patients who had used nonsteroidal antiinflammatory drugs, those with ulcer bleeding in the previous four weeks, and those who had received antibacterial therapy for *H. pylori* infection in the past. During the two-year study period, 1233 patients with gastric ulcers were seen in our unit. Of these, 920 presented with bleeding gastric ulcers. The remaining 313 patients had nonbleeding gastric ulcers, including 32 who had taken nonsteroidal antiinflammatory drugs, 72 with a negative urease test, 58 with concomitant duodenal ulcers, 44 who were older than 70 years and had premorbid conditions, 4 who had previously received anti-helicobacter therapy,

and 3 who were offered surgery for gastric-outlet obstruction. These patients were excluded from the study. Thus, 100 patients were studied.

Infection with *H. pylori* was considered to have been eradicated if the results of the Campylobacter-Like Organism test, smears, and cultures were negative five weeks after randomization (i.e., four weeks after the completion of antibacterial therapy). After ulcer healing was confirmed by endoscopy, the patients were asked to return for a one-year follow-up evaluation. All patients were offered a repeated endoscopy by an endoscopist blinded to their previous treatment.

We acknowledge that bismuth subcitrate and antacids are effective ulcer-healing agents that might have caused healing of the ulcers in the triple-therapy group (bismuth subcitrate, tetracycline, and metronidazole). Previous data have shown that 70 to 90 percent of ulcers heal when treated with bismuth for four to eight weeks.^{1,2,3} Multiple mechanisms are involved in the ulcer-healing action of bismuth, but suppression of *H. pylori* is one of the most important.⁴ The relatively low relapse rate after treatment with bismuth as compared with H₂ antagonists supports this hypothesis.^{1,2} In our study, bismuth subcitrate was given for seven days as part of the triple therapy. One week of bismuth subcitrate alone is unlikely to achieve the high healing rate — 84.4 percent — noted in the antibacterial-treatment group in our study.

Antacid (Mylanta) was given freely to our patients for symptomatic relief. We did not count the tablets consumed.

As Dr. Fagan observed, a number of the 95 percent confidence intervals were not accurate. We have recalculated them using the exact method rather than one involving approximation (Table 1).⁵

Table 1. Corrected 95 Percent Confidence Intervals for the Results of Triple Therapy and Omeprazole Therapy, According to a Standard Analysis and an Intention-to-Treat Analysis.

Table 1. Corrected 95 Percent Confidence Intervals for the Results of Triple Therapy and Omeprazole Therapy, According to a Standard Analysis and an Intention-to-Treat Analysis.*

VARIABLE	OMEPRAZOLE	BISMUTH, METRONIDAZOLE, AND TETRACYCLINE
Standard analysis		
No. of patients	40	45
Ulcer healing at 5 wk — no./total no. (%)	29/40 (72.5)	38/45 (84.4)
Published 95% CI — %	58.6–86.4	73.9–95
Corrected exact 95% CI — %	55.9–84.9	69.9–93
Cumulative ulcer healing at 9 wk — no./total no. (%)	37/39 (94.9)	43/45 (95.6)
Published 95% CI — %	88–100	89.5–100
Corrected exact 95% CI — %	81.4–99.1	83.7–99.2
Eradication of <i>H. pylori</i> at 5 wk — no./total no. (%)	5/40 (12.5)	41/45 (91.1)
Published 95% CI — %	2.3–22.7	82.9–99.3
Corrected exact 95% CI — %	4.7–27.6	77.9–97.1
Intention-to-treat analysis		
No. of patients	41	48
Ulcer healing at 5 wk — no./total no. (%)	30/41 (73.2)	40/48 (83.3)
Published 95% CI — %	59.6–86.7	72.7–93.9
Corrected exact 95% CI — %	56.6–85.1	68.9–91.8
Cumulative ulcer healing at 9 wk — no./total no. (%)	38/40 (95)	46/48 (95.8)
Published 95% CI — %	88–100	90–100
Corrected exact 95% CI — %	81.8–99.1	84.5–99.3
Eradication of <i>H. pylori</i> at 5 wk — no./total no. (%)	5/41 (12.2)	41/48 (85.4)
Published 95% CI — %	2.2–22.2	75.4–95.4
Corrected exact 95% CI — %	4.6–27	71.6–93.4

*In our original study we used the following formula to calculate the 95 percent confidence intervals: estimator $\pm 1.96 \times$ the standard error. CI denotes confidence interval.

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