ORIGINAL ARTICLE

Omeprazole before Endoscopy in Patients with Gastrointestinal Bleeding

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ABSTRACT

BACKGROUND

A neutral gastric pH is critical for the stability of clots over bleeding arteries. We investigated the effect of preemptive infusion of omeprazole before endoscopy on the need for endoscopic therapy.

METHODS

Consecutive patients admitted with upper gastrointestinal bleeding underwent stabilization and were then randomly assigned to receive either omeprazole or placebo (each as an 80-mg intravenous bolus followed by an 8-mg infusion per hour) before endoscopy the next morning.

RESULTS

Over a 17-month period, 638 patients were enrolled and randomly assigned to omeprazole or placebo (319 in each group). The need for endoscopic treatment was lower in the omeprazole group than in the placebo group (60 of the 314 patients included in the analysis [19.1%] vs. 90 of 317 patients [28.4%], P=0.007). There were no significant differences between the omeprazole group and the placebo group in the mean amount of blood transfused (1.54 and 1.88 units, respectively; P=0.12) or the number of patients who had recurrent bleeding (11 and 8, P=0.49), who underwent emergency surgery (3 and 4, P=1.00), or who died within 30 days (8 and 7, P=0.78). The hospital stay was less than 3 days in 60.5% of patients in the omeprazole group, as compared with 49.2% in the placebo group (P=0.005). On endoscopy, fewer patients in the omeprazole group had actively bleeding ulcers (12 of 187, vs. 28 of 190 in the placebo group; P=0.01) and more omeprazole-treated patients had ulcers with clean bases (120 vs. 90, P=0.001).

CONCLUSIONS

Infusion of high-dose omeprazole before endoscopy accelerated the resolution of signs of bleeding in ulcers and reduced the need for endoscopic therapy. (ClinicalTrials.gov number, NCT00164866.)

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In patients with bleeding peptic ulcers, we previously showed that infusion of a high-dose proton-pump inhibitor after hemostasis had been achieved during endoscopy reduced recurrent bleeding and improved clinical outcomes.[1] The adjuvant use of high-dose proton-pump inhibitors in endoscopic therapy has also been endorsed in two consensus statements[2,3] and confirmed in two meta-analyses.[4,5] Clot formation over arteries is pH dependent; a gastric pH above 6 is thought to be critical for platelet aggregation.[6] When given intravenously and at a high dose, proton-pump inhibitors can be used to maintain a neutral gastric pH.[7] In clinical practice, treatment with proton-pump inhibitors is often initiated before endoscopy in patients presenting with upper gastrointestinal bleeding.[8] However, there is a lack of evidence in the literature to provide support for such a preemptive approach. We hypothesized that early intravenous infusion of a high-dose proton-pump inhibitor before endoscopy would have a therapeutic effect on bleeding ulcers, reduce the need for endoscopic therapy, and result in improved clinical outcomes.

METHODS

STUDY DESIGN

This was a double-blind, placebo-controlled, randomized trial. The study protocol was approved by the ethics committee of the Faculty of Medicine at the Chinese University of Hong Kong. All patients or their legal representatives provided written informed consent for participation in the trial, according to Good Clinical Practice guidelines. There was no pharmaceutical industry support for this study. The authors vouch for the completeness and veracity of the data and data analyses.

PATIENTS

Consecutive patients who presented with overt signs of upper gastrointestinal bleeding (i.e., melena or hematemesis with or without hypotension) to the Accident and Emergency Department at the Prince of Wales Hospital in Hong Kong were evaluated by admitting residents for inclusion in the trial. Patients with hypotensive shock (systolic blood pressure ≤90 mm Hg or pulse ≥110 beats per minute) were initially resuscitated and were then considered for entry in the trial if their condition had been stabilized. Patients with continued shock despite initial volume resuscitation (refractory shock) underwent urgent endoscopy and were excluded. We also excluded patients who were younger than 18 years of age, unable to provide written informed consent, or pregnant; those with a known allergy to proton-pump inhibitors; and those who were using aspirin regularly for cardiovascular protection. Long-term aspirin users were enrolled in another randomized study, which evaluated the effect of early reintroduction of aspirin on the risk of recurrent ulcer bleeding.[9]

For patients who had bleeding ulcers associated with ingestion of nonsteroidal antiinflammatory drugs, the drugs were discontinued. Patients who had life-threatening bleeding and were using warfarin or had bleeding from an overdose of warfarin were given vitamin K or fresh-frozen plasma. Patients for whom anticoagulation was considered necessary (e.g., patients with prosthetic heart valves or pulmonary embolism within 6 months) underwent heparin therapy until the bleeding was stabilized.

STUDY PROCEDURES

Patients were randomly assigned to receive an intravenous infusion of omeprazole (Losec, AstraZeneca) or placebo, each given as an 80-mg intravenous bolus injection followed by continuous infusion of 8 mg per hour until endoscopic examination the next morning. Identical-appearing vials of omeprazole and placebo were prepared at the School of Pharmacy under aseptic conditions, according to the International Good Manufacturing Practice Guidelines for Pharmaceuticals. The vials were sealed in packages and numbered according to a computer-generated list of random numbers in blocks of 20, without stratification. The consecutively numbered, sealed packages were delivered to the admission ward. After obtaining written informed consent for a given patient, the admitting resident opened the lowest-numbered package. Use of omeprazole or placebo was started at admission and was stopped at the endoscopy center just before endoscopy was begun. Urgent endoscopy was performed (without stopping the omeprazole or placebo) in patients with signs of ongoing bleeding (i.e., fresh hematemesis or hematochezia, hypotensive shock, or both) as judged by ward residents or attending physicians. All vials were returned to our research office at the end of the infusion period to assess whether the drug had been delivered correctly and completely. All investigators were unaware of the group assignments.

At endoscopy, gastroduodenal ulcers with spurting hemorrhage, oozing hemorrhage, or nonbleed-

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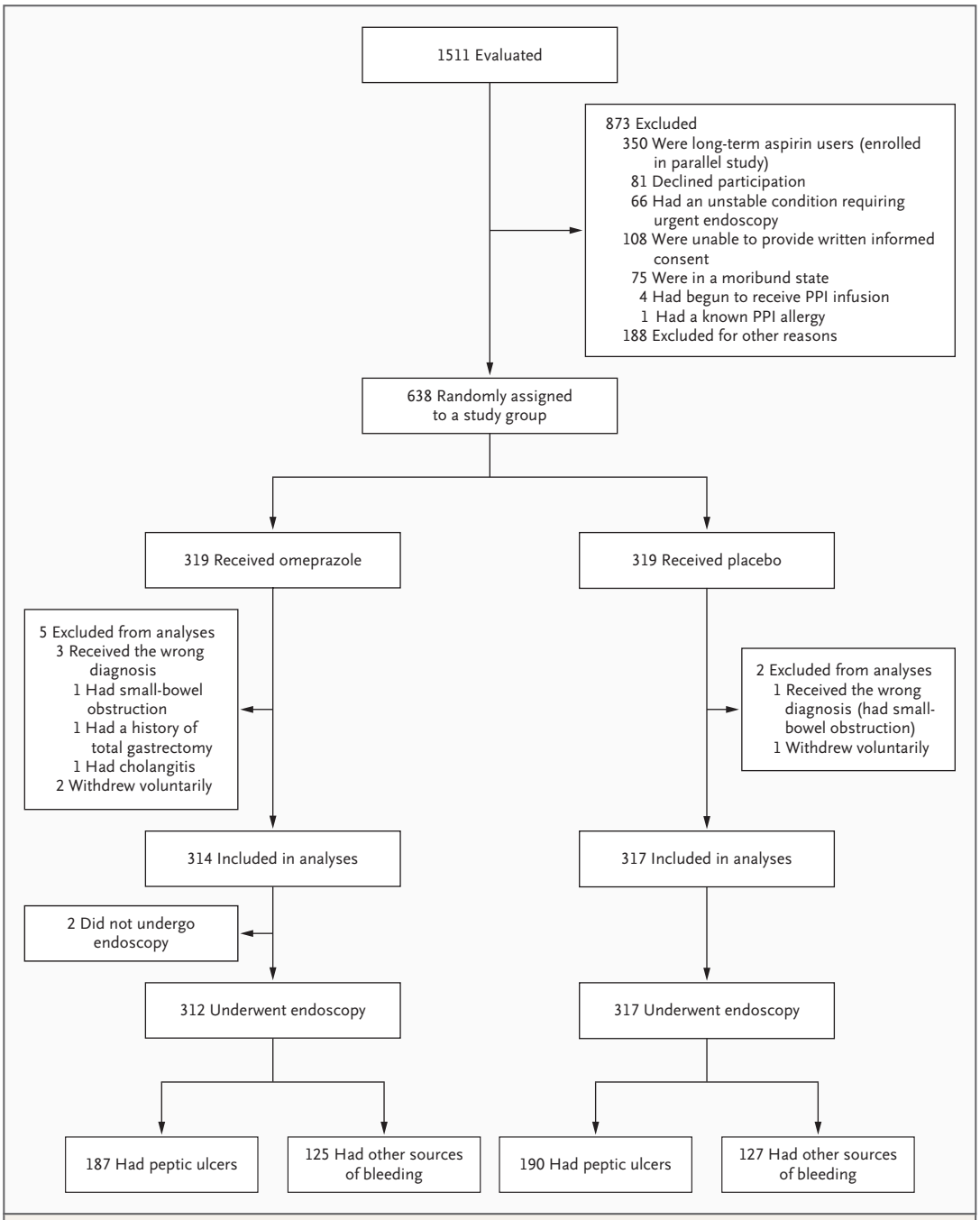

Figure 1. Enrollment and Randomization of Study Patients.

The 350 patients excluded because of chronic aspirin use were enrolled in a parallel study in which regular aspirin users were randomly assigned to receive aspirin or placebo after endoscopic hemostasis of their bleeding peptic ulcers had been achieved and after adjunctive use of a high-dose proton-pump inhibitor (PPI) had been initiated intravenously.[9]

ing visible vessels (defined as protuberant discolorations) were injected with epinephrine (dilution, 1:10,000). Aliquots of epinephrine (0.5 to 1 ml) were injected around the bleeding vessel with the use of a 23-gauge sclerotherapy needle until bleeding had completely ceased. Coaptive thermocoagulation was then applied to vessels with the use of a 3.2-mm heater probe (model CD-10Z, Olympus).

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Table 1. Characteristics of the 631 Patients Included in Analyses.*

Characteristic	Omeprazole (N=314)	Placebo (N=317)	P Value
Age — yr	61.7±17.9	62.3±17.5	0.67
Male sex — no. (%)	208 (66.2)	201 (63.4)	0.46
Hemoglobin — g/dl	10.3±2.9	10.4±7.6	0.73
Hematocrit — %	0.30±0.08	0.33±0.59	0.40
No. of units of blood transfused before endoscopy			
Mean ±SD	0.76±1.11	0.85±1.21	0.26
Median (range)	0 (0–4)	0 (0–6)	0.37
Systolic blood pressure — mm Hg	116.2±20.4	117.3±21.9	0.56
Systolic blood pressure <90 mm Hg — no. of patients (%)	30 (9.6)	28 (8.8)	0.78
ASA grade — no. of patients (%)†			
I	121 (38.5)	117 (36.9)	0.78
II	126 (40.1)	125 (39.4)	
III or IV	67 (21.3)	75 (23.7)	
Coexisting illness — no. of patients			
Cirrhosis	17	19	0.86
Cancer	32	23	0.21
Cardiovascular disease	18	25	0.34
Chronic renal failure	2	3	1.00
Bleeding during hospitalization — no. of patients (%)	12 (3.8)	9 (2.8)	0.49
Risk factors for bleeding peptic ulcer — no. of patients (%)			
Use of NSAID other than aspirin	70 (22.3)	74 (23.3)	0.75
Use of warfarin	6 (1.9)	12 (3.8)	0.16
Use of aspirin	5 (1.6)	8 (2.5)‡	0.41
Previous ulcer disease — no. of patients (%)	80 (25.5)	80 (25.2)	1.00
Previous bleeding — no. of patients (%)	68 (21.7)	66 (20.8)	0.85
Use of PPI or histamine-receptor antagonist within past 4 wk — no. of patients (%)	38 (12.1)	40 (12.6)	0.90
Peptic ulcer as source of bleeding — no. of patients (%)	187 (59.6)	190 (59.9)	0.94
Duodenal ulcer	88	102	
Gastric ulcer	75	67	
Both	14	13	
Anastomotic ulcers	10	8	
Esophageal or gastric varices — no. of patients (%)	10 (3.2)	14 (4.4)	0.53

Hemostasis was considered to have been established if bleeding had stopped and if formerly bleeding vessels were flattened or cavitated. Clots covering ulcer craters were elevated by means of irrigation through a heater probe for up to 5 minutes or "cheese-wiring" with a mini-snare, and underlying vessels, if present, were treated. Preinjection with diluted epinephrine at the pedicle of the clot was permitted. Antral-biopsy specimens were obtained and subjected to a rapid urease test (CLO test, Delta West) and histologic examination to determine whether *Helicobacter pylori* infection was present. Bleeding esophageal and gastric varices were treated with the use of band ligation and injection of cyanoacrylate (a tissue adhesive), respectively, in addition to the use of vasoactive drugs and intravenous antibiotics.

At the end of each therapeutic procedure, the

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Table 1. (Continued.)

Characteristic	Omeprazole (N=314)	Placebo (N=317)	P Value
Other endoscopic findings — no. of patients (%)	117 (37.3)	113 (35.6)	0.68
Esophagitis, gastropathy, duodenitis, or erosions	42	40	
Mallory–Weiss tear	6	10	
Esophageal or gastric cancer	10	15	
Stromal tumor	3	1	
Dieulafoy's lesion§	3	1	
Angiodysplasia	2	0	
Other	13	11	
No clinically significant finding	36	32	
Endoscopy not performed	2	3	
H. pylori–associated bleeding peptic ulcers — no. of patients/total no. with peptic ulcers (%)¶	95/178 (53.4)	109/182 (59.8)	0.24
Symptom at presentation — no. of patients			
Melena	238	243	0.43
Hematemesis	68	61	
Both	8	13	
Duration of infusion before endoscopy — hr	14.7±6.3	15.2±6.2	0.37

* Plus–minus values are means ±SD. NSAID denotes nonsteroidal antiinflammatory drug, and PPI proton-pump inhibitor.

† The American Society of Anesthesiologists (ASA) grades are assigned as follows: I for a healthy patient; II for a patient with mild systemic disease, such as mild diabetes or hypertension or slightly limiting organic heart disease; III for a patient with severe systemic disease that is not incapacitating; IV for a patient with incapacitating systemic disease that is life threatening, such as a patient with marked cardiac insufficiency, persistent angina, and advanced pulmonary, hepatic, renal, or endocrine insufficiency; and V for a patient who is not expected to survive for more than 24 hours, with or without surgery.

‡ One of the eight patients was using both aspirin (80 mg) and clopidogrel (75 mg) daily.

§ Dieulafoy's lesion is a rare cause of acute upper gastrointestinal bleeding. It is usually found within 6 cm of the gastroesophageal junction, high in the body of the stomach or in its fundus. Histopathological examination of a resected Dieulafoy's lesion shows an unusually large and tortuous artery located just underneath the muscularis mucosae.

¶ Infection with *H. pylori* was diagnosed on the basis of a positive rapid urease test (CLO test, Delta West) or detection of the bacteria during histologic examination.

endoscopist was required to rate the difficulty of the procedure on a 10-cm visual-analogue scale (with 0 cm indicating an easy procedure, 10 cm indicating a difficult procedure, and no gradations in between). Patients who did not require endoscopic therapy were returned to the general medical ward. Those who underwent endoscopic therapy were subsequently transferred to a medical gastroenterology ward for monitoring.

Omeprazole (8 mg per hour) was infused for 72 hours after endoscopy in patients who required ulcer hemostasis. Bleeding was considered to have recurred if any of the following occurred: vomiting of fresh blood, hypotensive shock (defined as a systolic blood pressure ≤90 mm Hg or a pulse ≥110 beats per minute) with melena after stabilization, or a decrease in the hemoglobin level of more than 2 g per deciliter and a decrease in the hematocrit of more than 6% within 24 hours after a transfusion, resulting in a hemoglobin level of 10 g per deciliter or less. Patients who were judged to have recurrent bleeding underwent urgent endoscopy by endoscopists on duty. Recurrent bleeding was confirmed if the ulcer was actively bleeding (spurting or oozing hemorrhage) or if there was fresh blood in the stomach and a vessel at the ulcer base. Clots overlying ulcers were lifted, and the base of the ulcer was examined. Endoscopic therapy was repeated on the bleeding artery. Surgical intervention was deemed to be warranted if the bleeding could not be controlled by endoscopic methods or if

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there was a second recurrence of bleeding.

After the 72-hour infusion of omeprazole, patients were given 40 mg of omeprazole orally per day for 8 weeks. Patients who had a positive rapid urease test for *H. pylori* received a 1-week course of 20 mg of omeprazole twice daily, 500 mg of clarithromycin (Klacid, Abbott) twice daily, and 1 g of amoxicillin (Amoxil, SmithKline Beecham) twice daily. These patients then received the standard dose of 40 mg of omeprazole per day for the remaining 7 weeks. We followed patients until day 30 after randomization. Research nurses contacted patients or their families. Records of hospital readmissions, clinic follow-up, and death were obtained and verified through a regional computerized hospital-record system. Eradication of *H. pylori* was confirmed with the use of a rapid urease test and histologic analysis during follow-up endoscopy at 8 weeks.

END POINTS

Our primary end point was the need for endoscopic therapy at the first endoscopic examination. Secondary end points included signs of bleeding, need for urgent endoscopy, duration of hospital stay, need for transfusion, need for emergency surgery to achieve hemostasis, and rates of recurrent bleeding and death from any cause within 30 days after randomization.

STATISTICAL ANALYSIS

We calculated that 174 patients with bleeding peptic ulcers would have to be enrolled in each group for the study to have a statistical power of 90% to detect an absolute reduction of 15% (from 30% to 15%) in the rate of endoscopic therapy with the use of preemptive infusion of high-dose omeprazole for bleeding peptic ulcers on scheduled endoscopy, with a two-sided alpha level of 0.05. Assuming that 60% of our patients presenting with upper gastrointestinal bleeding had bleeding from peptic ulcers, we then calculated that we would need to enroll a total of 290 patients in each group. In addition, we assumed that we would not be able to evaluate 10% of our enrolled patients. A minimum of 319 patients would therefore be needed in each group. One interim analysis was planned, the results of which have been published previously.[10] The level of significance of the observed difference in the primary end point did not fulfill the Peto–Haybrittle criterion (i.e., $P<0.001$) for early termination.

All analyses were based on the intention-to-treat principle. Fisher's exact test was used to analyze the primary end point, the need for endoscopic therapy, in the two groups. We calculated the effect of omeprazole as compared with that of placebo by using relative risks and the corresponding 95% confidence intervals (CIs).[11] The Kaplan–Meier method with the log-rank test was used to compare differences in the rates of recurrent bleeding and death within 30 days after randomization. All tests of significance were two-tailed, and a P value of 0.05 was considered to indicate statistical significance.

RESULTS

During a 17-month period between February 2004 and July 2005, a total of 638 patients were enrolled; 319 were randomly assigned to receive omeprazole and 319 to receive placebo (Fig. 1). Seven patients (five in the omeprazole group and two in the placebo group) were excluded from analysis: three withdrew before omeprazole or placebo was administered and four had received a misdiagnosis of upper gastrointestinal bleeding (two actually had small-bowel obstruction, one had undergone a total gastrectomy, and one had cholangitis). Two patients in the omeprazole group did not undergo endoscopy (one refused and one became moribund). Baseline demographic and clinical characteristics were similar in the two groups (Table 1).

Thirteen patients (five in the omeprazole group and eight in the placebo group) presented with aspirin-related upper gastrointestinal bleeding. They were found to have no indications for the long-term use of aspirin and were therefore not eligible for the parallel study of long-term aspirin users; instead, they were enrolled in our study. The source of bleeding was peptic ulcer in 187 of 314 patients (59.6%) in the omeprazole group and 190 of 317 patients (59.9%) in the placebo group. The mean (±SD) duration of infusion before endoscopy was 14.7±6.3 hours in the omeprazole group and 15.2±6.2 hours in the placebo group.

Of the 314 patients in the omeprazole group, 60 (19.1%) required endoscopic treatment, as compared with 90 of the 317 patients (28.4%) in the placebo group (relative risk for the omeprazole group, 0.67; 95% CI, 0.51 to 0.90; $P=0.007$). Among patients with peptic-ulcer bleeding, 42 of 187 pa-

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Table 2. Outcomes for the 631 Patients Included in the Analyses.*

Outcome	Omeprazole (N=314)	Placebo (N=317)	P Value	Relative Risk (95% CI)
Endoscopic therapy — no. of patients (%)	60 (19.1)	90 (28.4)	0.007	0.67 (0.51–0.90)
Endoscopic therapy for bleeding peptic ulcers — no. of patients/total no. with peptic ulcers (%)	42/187 (22.5)	70/190 (36.8)	0.002	0.61 (0.44–0.84)
Volume of injected diluted epinephrine — ml	9.2±6.0	10.5±7.0	0.31	
No. of pulses of heater probe — median (range)	5 (2–16)	6 (2–18)	0.01	
Endoscopic therapy for other sources of bleeding — no. of patients (%)	18 (5.7)	20 (6.3)	0.87	0.90 (0.49–1.68)
Endoscopic signs of bleeding in peptic ulcers — no. of patients	187	190		
Active bleeding	12	28	0.01	0.44 (0.23–0.83)
Nonbleeding visible vessel	23	31	0.30	0.75 (0.45–1.24)
Clot with underlying vessel	7	11	0.47	0.65 (0.26–1.63)
Flat, pigmented spot	25	30	0.56	0.85 (0.52–1.38)
Clean base	120	90	0.001	1.35 (1.13–1.63)
Urgent endoscopy — no. of patients	7	6	0.79	1.18 (0.40–3.44)
For bleeding peptic ulcers	4	3		
For other causes of bleeding	3	3		
Hospital stay — days				
Total	1402	1570		
Mean ±SD	4.5±5.3	4.9±5.1	0.24	
Median (range)	3 (1–43)	3 (1–54)	0.003	
Hospital stay <3 days — no. of patients (%)	190 (60.5)	156 (49.2)	0.005	1.23 (1.07–1.42)
Death within 30 days — no. of patients (%)	8 (2.5)	7 (2.2)	0.78	
Difficulty with endoscopic therapy†	4.2±2.6	4.8±2.7	0.28	
Units of blood transfused	1.54±2.41	1.88±3.44	0.12	
Emergency surgery — no. of patients/total no. with peptic ulcers (%)	3/187 (1.6)	4/190 (2.1)	1.00	
Partial gastrectomy — no. of patients	1	1		
Vagotomy and pyloroplasty	2	1		
Ulcer excision	0	1		
Omental patch repair (for a perforated duodenal ulcer)	0	1		
Recurrent bleeding within 30 days — no. of patients (%)	11 (3.5)	8 (2.5)	0.49	
Bleeding peptic ulcers	8	7		
Bleeding Mallory–Weiss tear	2	0		
Esophageal varices	1	1		

* Plus–minus values are means ±SD. CI denotes confidence interval.
† Difficulty was reported on a 10-cm visual-analogue scale, with 0 cm indicating an easy procedure and 10 cm indicating a difficult procedure, with no gradations in between.

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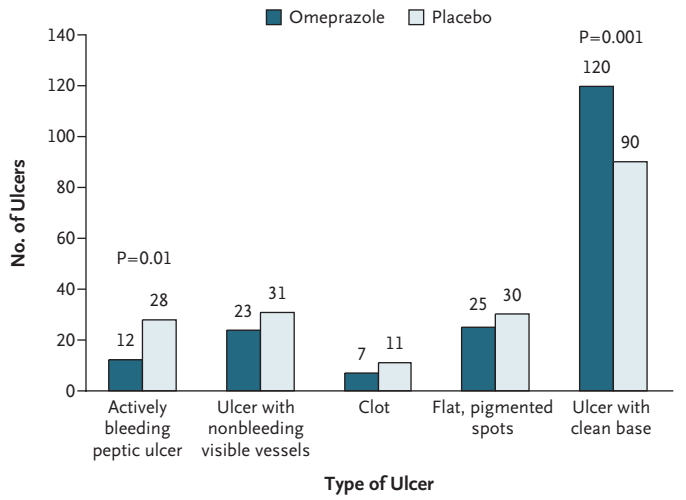

Figure 2. Numbers of Ulcers Found during the First Endoscopic Examination.

A total of 187 patients in the omeprazole group and 190 patients in the placebo group had ulcers.

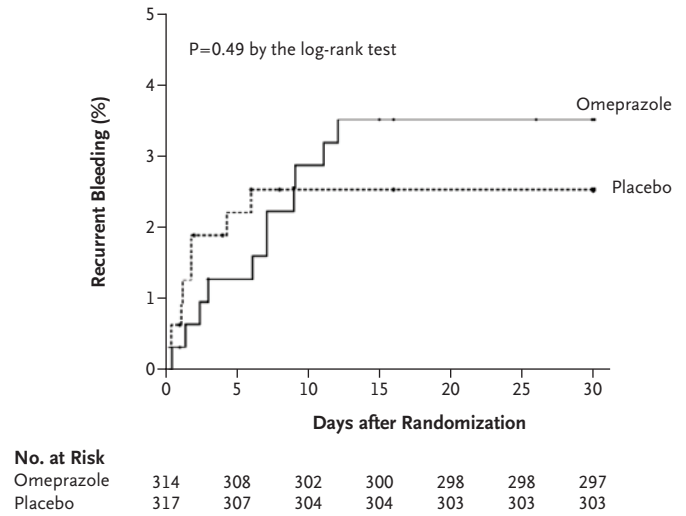

Figure 3. Kaplan–Meier Estimates of the Cumulative Percentages of Patients with Recurrent Bleeding.

tients (22.5%) in the omeprazole group and 70 of 190 patients (36.8%) in the placebo group required endoscopic treatment (relative risk, 0.61; 95% CI, 0.44 to 0.84; P=0.002) (Table 2). The mean volume of injected epinephrine was lower in the omeprazole group than in the placebo group (9.2±6.0 ml vs. 10.5±7.0 ml, P=0.31), as was the median number of pulses of heater probe used (5 [range, 2 to 16] vs. 6 [2 to 18], P=0.01).

Among patients with peptic-ulcer bleeding observed during the first endoscopic examination, actively bleeding peptic ulcers were seen less frequently in patients given omeprazole before endoscopy than in those given placebo (in 12 of 187 [6.4%] vs. 28 of 190 [14.7%], P=0.01) (Fig. 2). In addition, more ulcers with clean bases were seen in the omeprazole group than in the placebo group (in 120 of 187 [64.2%] vs. 90 of 190 [47.4%], P=0.001). The numbers of nonbleeding visible vessels, clots, and flat, pigmented spots did not differ significantly between the two groups.

Urgent endoscopy was required for seven patients in the omeprazole group and six patients in the placebo group (P=0.79). Episodes of hypotensive shock (defined as systolic blood pressure ≤90 mm Hg or a pulse ≥110 beats per minute) occurred during the infusion period in 18 patients in the omeprazole group and 24 patients in the placebo group (P=0.35). The mean number of units of blood products transfused was 1.54±2.41 in the omeprazole group and 1.88±3.44 in the placebo group (P=0.12). Three of 187 patients (1.6%) in the omeprazole group and 4 of 190 patients (2.1%) in the placebo group underwent emergency surgery owing to failure to achieve hemostasis during endoscopy. Recurrent bleeding occurred within 30 days after endoscopic therapy in 11 patients (3.5%) in the omeprazole group and 8 patients (2.5%) in the placebo group (P=0.49 by the log-rank test) (Fig. 3). The hospital stay was significantly shorter in the omeprazole group (median, 3 days [range, 1 to 43] vs. 3 days [1 to 54], P=0.003). The hospital stay was less than 3 days for 190 patients (60.5%) in the omeprazole group and 156 patients (49.2%) in the placebo group (P=0.005).

Eight patients (2.5%) in the omeprazole group and seven patients (2.2%) in the placebo group died within 30 days after randomization (P=0.78 by the log-rank test) (Table 3). Causes of death in the omeprazole group were disseminated cancer (four patients), small-bowel infarction (one patient), peritonitis (one patient), variceal bleeding (one patient), and myocardial infarction (one patient). Causes of death in the placebo group were pancreatic cancer (two patients), bleeding stomach cancer (one patient), colon cancer (one patient),

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Table 3. Incidences of Serious Adverse Events.*

Event	Omeprazole (N=314)	Placebo (N=317)	P Value
	no. of patients (%)		
Recurrent bleeding within 30 days after randomization	11 (3.5)	8 (2.5)	0.49
Disseminated cancer†	3 (1.0)	4 (1.3)	1.00
Emergency surgery	3 (1.0)	4 (1.3)	1.00
Pneumonia	3 (1.0)	1 (0.3)	0.37
Myocardial infarction	1 (0.3)	0	0.50
Septicemia	0	1 (0.3)	1.00
Peritonitis from ulcer perforation	1 (0.3)	0	0.50
Hepatic failure	1 (0.3)	0	0.50
Respiratory failure	0	1 (0.3)	1.00
Subarachnoid hemorrhage	0	1 (0.3)	1.00
Hypoglycemia	0	1 (0.3)	1.00
Small-bowel infarction and peritonitis	0	1 (0.3)	1.00
Death within 30 days after randomization	8 (2.5)	7 (2.2)	0.78

* A serious adverse event was defined as an adverse medical occurrence that was life threatening, required hospitalization or prolongation of hospitalization, or resulted in persistent disability or death.
† Disseminated cancer in the omeprazole group included colon cancer, prostate cancer, and lung cancer. Disseminated cancer in the placebo group included stomach cancer, pancreatic cancer, malignant non-Hodgkin's lymphoma, and colon cancer.

subarachnoid hemorrhage (one patient), variceal hemorrhage and hepatic failure (one patient), and nosocomial pneumonia (one patient). None of the serious adverse events (Table 3) were judged by investigators to be related to omeprazole or placebo.

DISCUSSION

Our findings reaffirm that optimal acid suppression facilitates clot formation over arteries in bleeding peptic ulcers. On endoscopy, fewer cases of actively bleeding peptic ulcers were seen among patients who had received omeprazole than among those who had received placebo. Early administration of high-dose omeprazole reduced the need for endoscopic therapy. In addition, omeprazole appears to accelerate the resolution of signs of bleeding. More patients in the omeprazole group than in the placebo group had ulcers with clean bases. Early administration of omeprazole therefore permitted more patients to be discharged early. Among our patients awaiting endoscopy, omeprazole stabilized clots, prevented recurrent bleeding, and initiated healing. Because patients in both groups received an infusion of high-dose omeprazole after hemostasis had been achieved, the rates of recurrent bleeding were low. The rate was marginally higher in the omeprazole group. No significant differences were detected between the two groups in any clinical outcomes.

Daneshmend et al. performed a multicenter clinical trial to examine the effect of acid suppression before endoscopy.[12] Bolus injections of omeprazole or placebo were used during the first 24 hours, followed by an oral regimen. Signs of bleeding were found in 33% of patients receiving omeprazole, as compared with 45% of patients given placebo — a finding that was similar to ours. The times to endoscopy, need for therapy, and specific signs of bleeding were not reported.

In a placebo-controlled clinical trial that did not involve endoscopic therapy, Khuroo et al. found that recurrent bleeding was less frequent in patients with nonbleeding visible vessels and clots who were given oral omeprazole than in those given placebo.[13] This finding provides support for the notion that acid suppression confers clot stability among patients with ulcers. However, the same omeprazole treatment did not reduce the rate

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of recurrent bleeding among patients with ulcers that were actively bleeding on endoscopy.

Several factors limit the generalizability of our findings. First, we excluded long-term aspirin users who had coexisting cardiovascular conditions. Another ongoing clinical trial in our hospital focused on this subgroup of patients,[9] preventing their inclusion into our study. The effect of high-dose omeprazole on clot stability in patients taking aspirin is unknown. Patients enrolled in our study may therefore have been at low risk. Second, our findings may not be applicable to geographic areas with a higher prevalence of variceal bleeding than that in Hong Kong. In Hong Kong, the source of upper gastrointestinal bleeding is peptic ulcer in approximately 60% of patients.[14]

In patients with upper gastrointestinal bleeding, early endoscopy (usually defined as endoscopy performed within 24 hours after admission) should be the standard of care in most hospitals. In selected high-risk patients, early endoscopy involving therapy stops bleeding and potentially saves lives. Early endoscopy also permits low-risk patients to be discharged early from the hospital. We do not propose using high-dose proton-pump inhibitors as a replacement for early endoscopy. In patients awaiting endoscopy, however, we recommend the preemptive use of high-dose intravenous omeprazole. Although we did not perform a cost analysis, early administration of high-dose omeprazole may prove to be a cost-saving approach owing to reduced use of hospital resources.

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