ORIGINAL ARTICLE

Efficacy of Early *Helicobacter pylori* Eradication *vs* Continuous Pantoprazol Infusion in Prevention of Rebleeding in Peptic Ulcer Patients

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ABSTRACT

Aim: The efficacy of *Helicobacter pylori* eradication in the prevention of early rebleeding in comparison with proton pump inhibitor (PPI) infusion has not yet been elucidated. This study compares the efficacy of these two therapies in peptic ulcer bleeding patients.

Materials and methods: One-hundred and two peptic ulcer bleeding patients with confirmed *H. pylori* infection by rapid urease test and a recent stigmata of hemorrhage were treated with epinephrine injection plus argon plasma coagulation (APC) or bipolar electrocoagulation combination therapeutic endoscopy and consequently, divided into group P (intravenous pantoprazole 80 mg stat and then 8 mg/h infusion for 72 hours) and group H (omeprazole 20 mg BID, bismuth subcitrate 240 mg BID, metronidazole 500 mg BID and tetracycline 1,000 mg BID for 14 days) randomly and blindly.

Results: The average age was 51 (16-89 years) in group P and 50.96 (20-74) in group H (p = 0.96). A total of 64.7 and 52.9% of patients in each group were male, respectively (p = 0.22). The source of bleeding was gastric ulcer in 49 and 45.1% in groups P and H, respectively (p = 0.6). The other reason of bleeding was duodenal ulcer in both groups. Distribution of ulcer character (nonbleeding vessel, spurting bleeding, adherent clot and oozing) was similar in both groups (p = 0.83). The mean transfusion number was 1.61 and 1.24 in groups P and H, respectively (p = 0.11). The mean duration of hospitalization was 4.47 and 4.24 days in groups P and H, respectively (p = 0.14). There was no rebleeding, need to surgery or mortality among the study groups.

Conclusion: Early *H. pylori* eradication as an alternative to intravenous PPI could be effective in preventing early rebleeding of peptic ulcers.

Keywords: *Helicobacter pylori* eradication, Proton pump inhibitor infusion, Bleeding peptic ulcer.

INTRODUCTION

A total of 10 to 35% of patients with peptic ulcer bleeding experience rebleeding after therapeutic endoscopy.[1] Intravenous (IV) proton pump inhibitors (PPI) could stabilize the clot and control fibrinolysis by increasing gastric pH.[2] The role of early *H. pylori* eradication after patient discharge in preventing ulcer recurrence has been confirmed which could decrease the rate of ulcer recurrence to 5 to 20% in 1 year.[3] The effect of *H. pylori* eradication in preventing complication and rebleeding during hospitalization has not been investigated so far. *H. pylori* eradication may accelerate ulcer healing and decrease recurrence and complications such as GI bleeding.[4] The mechanism of ulcer treatment in decreasing rebleeding has not been completely elucidated, but according to the effects of this infection in increasing gastric acid secretion, producing gastric metaplasia as the immune response and subsiding the defending mechanism of mucosa, early eradication could be useful.[5,6] In this study, the effect of IV PPI in patients with bleeding peptic ulcer after therapeutic endoscopy has been investigated in comparison with early *H. pylori* eradication.

MATERIALS AND METHODS

Bleeding peptic ulcer patients older than 16 years who had a stigmata of recent bleeding such as active spurting (Forrest I_A), nonbleeding visible vessel (Forrest II_A), oozing or adherent clot with visible vessel (Forrest I_B, II_B, II_A) were included in the study. The exclusion criteria included esophageal varices, liver cirrhosis, malignancy, concomitant morbidity, cardiac pacemaker, nonsteroidal anti-inflammatory drug (NSAID) consumption, current therapy with anticoagulant, antibiotic or PPI and multiple ulcers.

After achieving endoscopic homeostasis with epinephrine injection (1:10,000) plus argon plasma coagulation (APC) or bipolar ECT (Table 1), two samples from the antrum and two samples from the corpus were obtained by forceps biopsy. The samples were checked for rapid urease test and all of the positive samples, according to balance block render and by submitting confounding factors such as age, gender and endoscopy results were randomly divided into two groups.

Group P was treated with 80 mg IV bolus injection of pantoprazole and then continuous IV infusion 8 mg/h for 72 hours. Group H had received *H. pylori* eradication regimen including omeprazole 20 mg BID, tetracycline 1,000 mg BID, metronidazole 500 mg BID and bismuth subcitrate 240 mg BID for 14 days. The patients risk score was determined according to Rockall score and rebleeding was defined as hematemesis, repeating melena, higher than 2 gr/dl decrease in hemoglobin level, pulse rate higher than 90 beat/min or a sudden drop in blood pressure.

RESULTS

Overall, 102 patients were enrolled in the study between February, 2009 and December, 2011. They were divided into two groups (each group consisting 51 patients) (Table 2). Average age in group P and H was 51.1 and 50.96 years, respectively (p = 0.96). In group P, 62.7% of the patients were younger than 60 years and 37.3% were older than 60 years in comparison with 66.7 and 33.3%, respectively in group H (p = 0.67).

In group P, 64.7% of the patients were male and 35.3% female in comparison with 52.9 and 47.1 in group H, respectively (p = 0.22) (Table 3). In group P, the site of bleeding was the duodenum in 51% and the stomach in 49%. Bleeding site was in the duodenum in 54.9% and in the stomach in 45.1% in group H. According to the hemodynamic status, 43.1% of group P patients and 39.2% of group H patients were stable (Table 4). Orthostatic hypotension was seen in 56.9% of group P and 60.8% of

Table 1: Endoscopic methods for hemostasis (p = 0.21)				Total
		Protocol		
		Bipolar	*APC*	
Group H	Count	15	36	51
	% within group	29.40%	70.60%	100.00%
Group P	Count	21	30	51
	% within group	41.20%	58.80%	100.00%
Total	Count	36	66	102
	% within group	35.30%	64.70%	100.00%

Table 2: Classification of risk scores between groups (p = 0.84)				Total
		Risk score		
		Intermediate	*High*	
Group H	Count	23	28	51
	% within group	45.1%	54.9%	100.00%
Group P	Count	24	27	51
	% within group	47.1%	52.9%	100.00%
Total	Count	47	55	102
	% within group	46.1%	53.9%	100.00%

Table 3: Demographic characteristic of patients			
Baseline characteristics and results: Characteristic			
Age, years: mean (SD)	*Group H*	*Group P*	*p*
Gender: M/F, n/n	51.10 (19.39)	50.96 (15.90)	0.96
3 age groups, <40/40-60/>60: n/n/n	18/22/11	15/19/17	0.22
Hemodynamic : normal/orthostatic	32/19	34/17	0.67
Hypotension: n/n	22/29	20/31	0.68
Location of ulcer, stomach/duodenum: n/n	25/26	23/28	0.69
Risk score, intermediate/high: n/n	23/28	24/27	0.84
Endoscopic protocol: bipolar/APC: n/n	15/36	21/30	0.21
Packed cell transfusion: mean (SD)	1.61 (1.2)	1.24 (1.12)	0.11
Hospital days: mean (SD)	4.47 (0.85)	4.24 (76)	0.14
Rebleeding episode: n	0.00	0.00	----
Need to surgery: n	0.00	0.00	----
Mortality: n	0.00	0.00	----
Drug side effects: n	0.00	0.00	----

Table 4: Characteristic of bleeding peptic ulcer between groups (p = 0.84)							Total
			Ulcer				
			Clot	*Nonbleeding*	*Oozing*	*Spurting*	
Group	H	Count	15	16	17	3	51
		% within group	29.40%	31.40%	33.30%	5.90%	100.00%
Group	P	Count	19	14	16	2	51
		% within group	37.30%	27.50%	31.40%	3.90%	100.00%
Total		Count	34	30	33	5	102
		% within group	33.30%	29.40%	32.40%	4.90%	100.00%

group H patients (p = 0.68). There was no case of shock in any of the groups.

The mean number of transfusions was 1.61 unit in group P and 1.24 in group H (p = 0.11). The mean duration of hospitalization in groups P and H was 4.47 and 4.24 days, respectively (p = 0.14).

STATISTICS

According to recurrence rate of 22% in group P[7] and 4% in group H,[8] the sample size of 51 patients in each group was determined to achieve the accuracy rate of 90%. For determining differences between mean values, t-test was used. A p-value of less than 0.05 was considered statistically meaningful. The effect of treatment on rebleeding, need for transfusion and duration of admission was determined by using a multivariate logistic regression ratio. This study has registered in IRCT (Iranian Registry of Clinical Trials) as number IRCT201108073836N2.

DISCUSSION

The risk of rebleeding in patients with bleeding peptic ulcer is higher than noncomplicated ulcer disease.[9] Almost one-third of patients with bleeding peptic ulcer during 1 to 2 years and 40 to 50% of them during 10 years will experience rebleeding if given no treatment.[10] So the two strategies of '*H. pylori* eradication' and 'maintenance antisecretory therapy' would be effective in preventing ulcer recurrence and complication. The previous studies had focused on therapeutic PPI infusion after endoscopic homeostasis in treatment of bleeding peptic ulcers and had reduced the rate of rebleeding [number of need to treat (NNT): 13; 95% confidence interval (CI): 9-25; odd ratio (OR): 0.49; 95% CI: 0.37-0.65].[11,12]

In patients who have had experienced peptic ulcer bleeding, *H. pylori* eradication has been accompanied with a lower risk of rebleeding in comparison with maintenance antisecretory therapy. In three studies on 470 patients, it has been shown that the risk of rebleeding in *H. pylori* eradication group is 1.6% and in patients who receive maintenance antisecretory regimen this risk is 5.6% (OR: 0.25, 95% CI: 0.08-0.76, NNT: 20, 95% CI: 12-100).

In another study, acceleration in *H. pylori* eradication resulted in the decreased rate of readmission of patients with peptic ulcer. This study also showed that early *H. pylori* eradication during first 6 months after peptic ulcer, would be accompanied with a lower risk of hospitalization due to complication of ulcer in comparison with late eradication (181-365 days or >365 days) (HR = 0.57; CI: 0.54-0.59; p < 0.001 for early eradication in less than 6 months in

comparison with late therapy from 181 to 365 days, HR = 1.68; CI: 1.51-1.86; p < 0.001; and after 365 days, HR = 1.74; CI: 1.67-1.80; p < 0.001).[13,14]

No study has investigated the effect of continuous IV PPI infusion on the rate of rebleeding, need to surgery and mortality in comparison with immediate early *H. pylori* eradication in patients with bleeding peptic ulcer after endoscopic homeostasis. In this study, patients with bleeding peptic ulcer who were treated with endoscopic homeostasis by combination of adrenalin injection and APC or bipolar were randomly divided into two groups: *H. pylori* eradication and IV PPI infusion. The results of this study have not showed any difference in the rate of rebleeding, duration of admission, blood transfusion, need to surgery or mortality as primary and secondary outcome in the first week and first month between the two groups. The mean rebleeding rate with PPI infusion was 6.7%. This rate has been reported 13% with continuous pantoprazole infusion[15] and in our study; this figure was significantly lower than the previous studies. The reason of this difference could be explain by lesser number of patients in our study, the lower number of patients with spurting bleeding, use of combination endoscopic homeostatic therapy, exclusion of patients who consumed NSAID and also genetic or geographic reasons.

CONCLUSION

This study confirms the importance of early *H. pylori* eradication in patients with bleeding peptic ulcer who have stigmata of hemorrhage and have received therapeutic endoscopy. Our findings showed that in this group of patients, early *H. pylori* eradication could be as effective as IV PPI infusion in preventing rebleeding, need to surgery and mortality and also due to the lower cost could be a good therapeutic alternative.

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