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Treating bleeding peptic ulcer with sustained achlorhydria

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Introduction

The high mortality associated with bleeding peptic ulcer is accounted for predominantly by the 20% of patients who continue to bleed or rebleed after the initial bleeding[1]. Complete neutralization of acid and pepsin appears to be crucial for control of rebleeding, the mode of action being prevention of dissolution of the clot which plugs the bleeding artery[2,3]. Conventional therapies comprising H_2 receptor antagonists and antacids have not been able to achieve sustained achlorhydria[4,5]. However, a combination of high dose cimetidine and continuous nasogastric antacid infusion was shown to do so in duodenal ulcer patients[6]. We recently utilized the same regimen in a randomized control trial to demonstrate that it was effective in achieving achlorhydria even in patients with peptic ulcer who were actively bleeding. Furthermore, intensive therapy led to control of bleeding in a higher proportion of patients with bleeding peptic ulcer as compared to conventional therapy. The results of that study are in press[7]; and are briefly summarized below. Of 25 patients with bleeding peptic ulcer included in the study, 12 were given conventional therapy (control group) and 13 intensive therapy (treatment group). Conventional therapy consisted of 50 mg ranitidine i.v. at 8-hour intervals whereas the intensive therapy consisted of 100 mg cimetidine i.v. every hour plus a continuous nasogastric drip of a liquid antacid at the rate of 0.5 ml/min. Gastric pH was monitored every hour using a phenaphthazine pH paper strip. The results showed that the mean gastric pH attained in patients in the treatment group was 7.88 ± 0.37 as compared to 5.00 ± 0.55 in those of the control group; the pH values were >7 on 95% of occasions in the former as compared to 8.6% in the latter. Also, final control of bleeding was achieved in a significantly larger proportion of patients in the treatment group than in the control group (92.3% vs 50%; $P<0.05$).

Having become convinced of the efficacy of the intensive therapy, we employed this regimen routinely in all subsequent patients with bleeding peptic ulcer and report our observations in the present communication.

Materials and Methods

A total of 75 patients with active bleeding from peptic ulcer admitted to the Gastroenterology Unit of our institution over a period of one and a half years were thus treated with the intensive therapy and the outcome was evaluated. Characteristics of the patients and of their ulcers were also correlated with the outcome in order to determine the factors associated with failure of control of bleeding and hence the need for surgery.

Statistical analysis

Analysis was performed using Student's 't' test, chi square analysis and Wilcoxson rank sum test. A 'P' value of <.05 was taken as significant.

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Table 1 Characteristics of patients and their ulcers treated with intensive therapy

S. No.	Characteristic	Gastric ulcer (n=21)	Duodenal ulcer (n=54)	Total (n=75)
1.	Age (yr, mean±SD)	48.81±15.90	45.44±17.14	46.39±15.90
2.	Sex ratio (M:F)	4.1:1	3.8:1	4.6:1
3.	Hb at admission (G%, mean±SD)	7.55±2.51	8.42±8.21	8.16±7.04
4.	NSAIDs users, No. (%)	4 (19%)	14 (25%)	18 (24%)
5.	Smokers, No. (%)	3 (14.1%)	21 (39.8%)	24 (32%)
6.	Size of ulcer (cm, mean±SD)	1.40±0.56	1.71±2.88	1.62±2.44
7.	Patients with SRH, No. (%)	18 (85.7%)	26 (48.1%)	44 (58.6%)

Hb = hemoglobin

Table 2 Results of treatment with intensive therapy in patients with bleeding peptic ulcer

S. No.	Characteristic	Gastric ulcer (n=21)	Duodenal ulcer (n=54)	Total (n=75)
1.	Success of therapy No. (%)	18 (84.6)	40 (72)	58 (75.4)
2.	Failure of therapy No. (%)	3 (15.4)	14 (28)	17 (24.6)
	a. Rebleeding	1 (4.7)	10 (18)	11 (14.3)
	b. Contd. bleeding	2 (9.4)	4 (7.2)	6 (7.8)
3.	Transfusion requirement (units, mean±SD)	3.10±4.35	2.96±2.96	2.99±3.35
4.	Hospital stay (days)	5.24±3.02	7.37±7.35	6.77±6.48
5.	Mortality (%)	0	5.5	4

Results

Of 75 patients treated with intensive therapy, 21 had gastric ulcers (GU) and 54 had duodenal ulcers (DU). The demographic features and factors such as major bleeding, use of non-steroidal anti-inflammatory drugs (NSAIDs) and smoking were equally distributed among the two ulcer groups. Only the frequency of signs of recent hemorrhage (SRH) was somewhat more frequent in GU than in DU (**Table 1**).

Control of bleeding was however, achieved in a equally high percentage of patients in both ulcer groups (75.4%) (**Table 2**). Seventeen patients in whom intensive therapy failed to control the bleeding were subjected to surgery. These patients did not differ from those who responded to medical therapy (no surgery group) with regard to age, admission hemoglobin, percentage using NSAID, smoking history, and site and size of ulcers (**Table 3**). A comparison of the ulcer characteristics in these patients with those in whom bleeding was controlled by treatment revealed that 87% of patients requiring surgery had SRH whereas only half of the patients not requiring surgery had SRH. Moreover, all three patients with a spurter required surgery whereas only 56.2% of patients with a visible vessel at the ulcer base required surgery. Interestingly, 85.8% of patients having an adherent clot had arrest of the bleeding with intensive therapy (**Table 3**). No side effects of drug therapy were encountered in any patient. Three of the operated patients died during the postoperative period, bringing the overall mortality to 4% in the total group of 75 patients.

Discussion

With final control of bleeding occurring in 75.4% of peptic ulcer patients with bleeding, the results of the prospective trial of the intensive regimen were quite as expected from our earlier randomized controlled trial[7]. Furthermore, they have instilled confidence in us that this intensive therapeutic regimen is practical and can be utilized to advantage in any hospital setting. Only a quarter of the patients given the intensive therapy in the present series required emergency surgery with an overall mortality of 4%. Although we had no control group in the present series, these latter

Table 3 Patients requiring surgery versus those not requiring surgery: Characteristics of patients and their ulcers

S. No.	Characteristic	Surgery (n=17)	No surgery (n=58)
1.	Age (yr, mean±SD)	50.00±18.93	45.26±16.44
2.	Hb at admission (g%, mean±SD)	6.54±2.40	7.71±2.78
3.	NSAID users, No. (%)	5 (29.4)	13 (22.1)
4.	Smokers, No. (%)	6 (34.8)	18 (30.6)
5.	Site of ulcer, No. (%)		
	a. GU	3 (17.4)	18 (30.6)
	b. DU	14 (82.6)	40 (68.4)
6.	Size of ulcer (cm, mean±SD)	1.26±0.62	1.93±4.19
7.	Patients with SRH, No. (%) (n=44)*	15 (87)	29 (49.3)**
	a. visible vessel (n=16)	9 (56.2)	7 (43.8)
	b. adherent clot (n=21)	3 (14.2)	18 (85.8)
	c. oozing (n=4)	0	4 (100)
	d. spurter (n=3)	3 (100)	0
8.	Mortality, No. (%)	3 (17.4)	0

*:'n' under this column refers to the total no. of patients with 'SRH'
**: $P<0.005$

figures are very impressive compared to those of a series of 33 patients with bleeding peptic ulcer who were treated in the same unit with the conventional regimen during the year preceding the start of the controlled trial of the intensive regimen; of those 33 patients, 15 (43.3%) required surgery with an overall mortality of 15.1% (unpublished data). We, therefore, believe that utilization of the intensive therapy has resulted in a substantial reduction in the need for emergency surgery and the overall mortality in our patients with bleeding peptic ulcer.

A comparison of 17 patients who required surgery with 58 patients who responded to intensive medical therapy revealed that there was no difference in the two groups as regards age, admission hemoglobin, percentage using NSAIDs, smoking history, and site and size of ulcers. Jones et al[11] similarly failed to show any correlation between these factors and the need for surgery. The majority (87%) of patients in the 'surgery group' had SRH as compared to only 50% in those not requiring surgery. All patients with a spurter and half the patients with a visible vessel required surgery whereas 85.8% of patients with a clot on the ulcer base responded to medical treatment (**Table 3**). This is in conformity with the observations made by other workers who have also found a significant increase in the incidence of rebleeding and need for surgery in patients with a visible vessel or spurter, but not in those with nonarterial stigmata such as an adherent clot[12].

Sustained achlorhydria can thus clearly be maintained by using a continuous nasogastric antacid infusion with an hourly bolus intravenous cimetidine and with this treatment the rate of control of bleeding was higher and the need for surgery and the overall mortality lower in the treatment group. We therfore strongly recommend its use in clinical practice.

Summary

A controlled randomized study and a subsequent prospective therapeutic trial have demonstrated the efficacy of an intensive therapy comprising hourly intravenous injections of 100 mg of cimetidine along with a continuous nasogastric infusion of a liquid antacid at the rate of 0.5 ml per minute in achieving achlorhydria and controlling bleeding in patients with bleeding peptic ulcer. We recommend that this regimen should be routinely employed for treating patients with bleeding peptic ulcer, at least in center that do not practise topical therapeutic modalities for control of bleeding.

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