Efficacy of the heater probe in peptic ulcer with a non-bleeding visible vessel. A controlled, randomised study

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Abstract

A controlled, randomised study was performed to evaluate the efficacy of treatment with heater probe in the prevention of rebleeding from peptic ulcer with a non-bleeding visible vessel. One hundred and one patients were randomised into two groups: patients to be treated by heater probe (n=51) and controls without active treatment (n=50). In the heater probe group rebleeding occurred in five patients (10%) v 13 (26%) in the control group (p=0.03), with a comparative risk of 0.38 in favour of the heater probe group. The difference in proportions of successful treatment for each group was 16.2% in favour of the heater probe (95% CI=2 to 31%). Haemorrhage directly related to heater probe treatment occurred in four patients. In three of them bleeding was easily controlled by further heater probe pulses. There were no other complications and no death in the heater probe group. One patient in the control group died of pulmonary embolism. No significant differences in the length of stay in hospital, blood transfusions, surgical rates, or death were found; the design of the study, however, precluded an adequate assessment of these variables, because the heater probe was an optional rescue treatment when high surgical risk patients rebled. These results suggest that the heater probe is an effective and safe procedure in the prevention of recurrent haemorrhage in peptic ulcer with a non-bleeding visible vessel. (Gut 1993; 34: 1502-1506)

Bleeding from peptic ulcer persists or recurs early in 25% of cases,¹ which carries a high death rate related to the severity of bleeding or the need for surgical treatment. Endoscopic stigmata of recent haemorrhage allow the identification of lesions with a high risk of rebleeding. A non-bleeding visible vessel located in the crater of the ulcer has a 30-50% probability of recurrence.²⁻⁶ Therapeutic endoscopy with electrocoagulation, photocoagulation, or injection of sclerosant or vasoactive substances, has been effective in: (a) stopping active haemorrhage,^{3 7-11} (b) diminishing the rebleeding rate,^{3 4 6 7-19} (c) reducing the need of surgery,^{4 8-10 14 16 17} and (d) decreasing the death rate.^{8 10 17} These results, however, are not uniform.²⁰⁻²³

Heater probe treatment of bleeding ulcer may be better than sclerosis with alcohol for stopping acute haemorrhage.²⁴ Heater probe may be less effective, however, than epinephrine injection in the initial control of active haemorrhage.²⁵ Heater probe is not superior to YAG laser or

bipolar electrocoagulation in the immediate control of bleeding, decreasing the rebleeding rate, the need for surgery, or the death rate.^{6 26} Therefore, it remains to be proved whether the use of heater probe is better than no active treatment and a close observation of the patient.^{4-6 27 28}

The aim of this study is to evaluate the efficacy of the heater probe in preventing recurrence of haemorrhage from peptic ulcer with a non-bleeding visible vessel. A control group without active treatment allowed us to compare the results.

Methods

PATIENTS

Between November 1988 and December 1991 all consecutive patients who were bleeding and admitted to the gastroenterology unit were considered for this study. Patients were included if a gastric or duodenal peptic ulcer with a non-bleeding visible vessel was identified. The criteria for exclusion were: (a) active bleeding from the ulcer; (b) other coexistent lesions that could be the cause of bleeding; (c) malignant ulcers, and (d) patient refusal to heater probe treatment. Patients were separated according to ulcer location (gastric or duodenal) and then randomised into control and treatment groups. Randomisation was done with a table of random numbers, the allocation codes were introduced in two series of sealed envelopes according to stratification class. Patients were randomised at the time of endoscopy or within 12 hours after fulfilling the inclusion criteria. This study was approved by the ethical committee of the hospital.

DIAGNOSIS

Upper gastrointestinal bleeding was diagnosed only if haematemesis or melaenas, or both were confirmed by the hospital staff. The cause of bleeding was established by endoscopy within 12 hours of admission. To obtain a correct view of the ulcer and stigmata of recent bleeding, the lesions were gently washed to remove blood that had not adhered to the lesions.

TREATMENT

All patients in the study received the following treatment: ranitidine 50 mg intravenously three times per day, volume replacement with intravenous fluids, and blood to maintain packed cell volume above 28%. The control group did not

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receive endoscopy treatment and was studied closely. Patients in the heater probe group were treated according to the endoscopic procedure.

Endoscopic treatment – an Olympus HPU heater probe device with 3.2 mm and, occasionally, a 2.3 mm probe was used. The energy applied in each pulse was 25–30 joules. Pulses were given until the vessel had been flattened and turned dark. The treatment was only given by one of the two physicians participating in the study (JLJ and CG), both with previous experience in the use of heater probe. Coagulation was obtained by pressing in several points around and on the base of the vessel.

Rescue treatment – surgery was indicated in patients of each group if bleeding recurred. Surgical risk was evaluated on admission. Patients over 65 years suffering from a severe systemic condition were considered as high risk cases. In patients with severe haemorrhage and low surgical risk, surgical intervention was carried out immediately. Surgery was performed within 24 hours if the relapse was mild. High surgical risk patients without haemodynamic changes, had heater probe treatment and, if bleeding persisted or recurred, the patient was operated on.

MONITORING

Monitoring of the patients included recording of blood pressure, heart rate, and urine output and, in haemodynamically unstable patients, measurement of central venous pressure. Values of packed cell count, haemoglobin, urea, glucose, creatinine, and electrolytes were obtained at admission. These tests were repeated 12 hours after admission and every 24 hours thereafter. Packed cell volume and haemoglobin were also measured after each bleeding episode. Characteristics and quantity of vomit, gastric aspirate, and stools were recorded. A soapy enema was given daily to avoid accumulation of faeces.

END POINTS

Rebleeding, or if absent, discharge, or death were considered the end points of the study.

DEFINITIONS

Visible vessel – a raised red or black spot protruding on the ulcer crater that does not disappear with washing.

Limited haemorrhage – the presence of unchanged packed cell volume, haemodynamic stability, lack of haematemesis, no evidence of blood in the gastric aspirate, and normal stools or only traces of melaena.

Continued haemorrhage – (a) if the volume of intravenous fluids required to restore or maintain haemodynamic stability was greater than 1000 ml/hour or 3000 ml/12 hours, (b) fresh haematemesis and, (c) haematemesis or melaenas in association with a fall in packed cell volume greater than 5% in a 24 hour period, two days after admission.

Rebleeding – bloody gastric aspirate, haematemesis or melaenas while in the hospital, after

initial control of bleeding, and the stools had become normal.

Haemodynamic stability – presence of all of the following, (a) systolic blood pressure greater than 100 mm Hg, (b) heart rate less than 100 beats/min, (c) urine output greater than 35 ml/hour and, (d) no signs or symptoms of impaired systemic perfusion.

ASSESSMENT

The efficacy of the heater probe was assessed with the results obtained at the first attempt. Data recording and assessment of results were carried out by a member of the unit who did not participate in endoscopic treatment or looked after the patients. The proportion of rebleeding in the heater group was compared with that in the control group. An intention to treat analysis was carried out.

STATISTICS

Sample size was calculated assuming 30% and 10% rebleeding rate in the control and treated groups, respectively,² and by giving values of 0.05 to an α error and 0.2 to β error. After calculation the number obtained was 48 in each group and 5% was added to compensate for non-evaluable patients. Thus, the total number including both groups was 101.

Fisher's exact test or χ^2 test with Yates's correction were used, where appropriate, to compare proportions and Student's *t* test was used for continuous variables. Confidence intervals and relative risk were also calculated.

Results

One hundred and one patients were included in the study. Thirty five had bleeding gastric ulcer and sixty six a duodenal ulcer. After randomisation 51 patients were included in the heater probe group and 50 in the control group. Table I shows the clinical data on admission.

In the heater probe group, coagulation was achieved in 49 patients. The two patients in whom coagulation was not achieved had ulcers located in the inferior and posterior wall of the duodenal bulb, respectively. The approach to the visible vessel was difficult in 10 patients. The probe was applied from the front in 32 and laterally in 17 cases. A mean of 8.4 pulses and 211 joules, were used in each patient, with the 2.3 mm probe in four cases and 3.2 mm probe in the remainder. Four patients bled during the procedure. In three of them, bleeding was finally controlled during the same session. The fourth patient required local epinephrine injection in addition to repeated heater probe pulses and was considered a failure in the final statistical analysis. In four additional patients bleeding recurred after heater probe treatment and in one of them, with high surgical risk, successful control of haemorrhage was obtained in a second thermo-coagulation session. The remaining three patients required operations. In one of these three patients the bleeding started in another ulcer not seen during the first endoscopy and therefore not treated with heater probe. Thus,

TABLE I Characteristics of patients entered into the study

	Heater probe (n=51)	Control (n=50)	p
Sex:			
Men	32	35	NS
Women	19	15	
Age (x (SD))	56.7 (17)	57.2 (14)	NS
Associated disease	19	12	NS
High risk surgical patients	12	8	NS
Ulcer location:			
Gastric	17	18	NS
Duodenal	34	32	
Initial symptoms:			
Haematemesis	19	23	NS
Melaena only	32	27	
Haemodynamics at admission:			
Pulse rate (x (SD))	89 (18)	89 (15)	NS
SBP (mm Hg; x (SD))	127 (23)	123 (25)	NS
Shock	4	7	NS
Packed cell volume <30 at admission	18	11	NS

SBP=systolic blood pressure; NS=p>0.05.

the number of rebleeding cases in the group with heater probe treatment was five (9.8%), two from gastric and three from duodenal ulcers. Patients received a mean of 1.2 U of packed red blood cells (SD=2) and they were in hospital during a mean period of 7.4 days (SD=3.6) (Tables II and III). There were no deaths in this group.

In the control group, bleeding recurred in 13 patients (26%), six with gastric ulcers and seven with ulcer located in the duodenum. Five were poor subjects for operation, so that endoscopic treatment by heater probe was performed. Two patients required operation because of further recurrence after heater probe treatment and difficulties in reaching the lesion, respectively. In the other five rebleeding patients an operation was performed successfully. Medical treatment was considered only for the remaining three patients. Two had a mild haemorrhage and the third patient refused both operation and heater probe treatment. This patient required six packed red cells units before the bleeding

TABLE II Treatment data

	Heater probe	Control
Randomised patients	51	50
Thermocoagulation	49	—
Rebleeding	5	13
Rescue treatment:		
Heater probe only	1	3
Heater probe+epinephrine	1	—
Heater probe+surgery	—	1
Surgery only	3	6
Medical only	—	3
Transfusion:		
Packed red cell (Units; X (SD))	1.2 (2)	2 (2.5)

TABLE III Outcome of patients in heater probe and control groups

	Heater probe (n=51)	Control (n=50)
Rebleeding complication:	5	13*
Induced bleeding	4	—
Controlled by heater probe	3	—
Uncontrolled	1	—
Pulmonary embolism	—	1
Emergency surgery	3	7
Stay in hospital (days):		
Mean (SD)	7.4 (3.6)	7.7 (4.4)
Median (IQR)	6 (4)	6.5 (5)
Death	—	1

*: p=0.03 (Fisher's exact test); IQR=interquartile range.

stopped. One patient died because of pulmonary embolism during the postoperative period. An average of 2 (SD=2.5) U of packed red cells were transfused in each patient and required 7.7 (SD=4.4) days' stay in hospital (Tables II and III).

The incidence of rebleeding was lower in the heater probe treated patients than in the control group (Fisher's exact test p=0.03) with a comparative risk of 0.38 (95% CI 0.14 to 0.98). The difference in proportions of successful treatment in each group was 16.2% in favour of heater probe, with a 95% CI ranging from 2% to 31%. There were no significant differences between both groups in death, transfusion requirements, and days needed in hospital.

When the adherence to treatment is considered, the data analysis results are very similar to those seen in the intention to treat analysis (10.2% and 26% of recurrences in heater probe and in control group respectively; Fisher's exact test p=0.04). Analysis of results according to location of the ulcer showed a tendency in favour of the heater probe in both gastric and duodenal sites, but statistical significance was not reached because of the small size of subgroups.

Discussion

This study shows that treatment of bleeding ulcers with heater probe reduces the rebleeding rate compared with medical conservative management. The heater probe reached a visible vessel in 90% of the patients. The two patients in whom the lesion was not reached had ulcers located in the inferior and posterior wall of duodenal bulb. The treatment was satisfactorily performed in all patients despite some difficulties in reaching the lesion in 20% of them. In the group of patients treated with the heater probe the incidence of rebleeding was about one third of that in the control group. There was no death in the endoscopy treated group. The only complication in this group was an uncontrolled haemorrhage induced by probe manipulation. The blood transfusion requirements were similar in both groups. Differences in days spent in hospital, however, amount of blood transfused, and operations required, are difficult to analyse because heater probe was an option for rescue treatment in the control group. Endoscopic treatment has been shown to be beneficial in bleeding patients.^{10 11} Thus heater probe treatment was considered an option for rescue treatment in high risk patients. This decision was made based on ethical consideration despite the fact that the use of the heater probe as a rescue treatment would be a confounding variable in the assessment of the subsequent outcome (operation or death). Nevertheless, this strategy did not affect the results at the end point established in the methods (rebleeding).

It should be pointed out that in our control group, the incidence of rebleeding was 26%, which is less than the 30 to 50% seen by others.^{2 4-6} Our definition of visible vessel is widely accepted.^{29 30} The endoscopic concept of visible vessel includes several stages of the same lesion and even various types of lesions. It is interesting also that slight changes in the colour

of the so called visible vessel are associated with a different risk of rebleeding ranging from 18 to 50%.^{2 30-32}

In uncontrolled studies, the use of heater probe in active bleeding ulcers or in ulcers with stigmata of recent haemorrhage, achieves haemostasis in 75 to 100% of cases, and in 69 to 86% of patients the control of bleeding is definitive.³³⁻³⁶ Randomised controlled trials have shown similar results. Compared with other endoscopic treatment used to stop bleeding, the heater probe seems better than pure alcohol sclerosis⁴ but less effective than epinephrine injections.²⁵ No significant difference was seen when compared with laser YAG or bipolar electrocoagulation.^{6 24 26} With the heater probe the complication rate was less than 5%.^{6 25 27} Difficulties in reaching the bleeding point have been reported in 20% of cases.²⁵ Thus, because of inaccessibility two to nine per cent of ulcers were excluded from randomisation.^{6 24 27} Ulcers located in the posterior or lower walls of the duodenal bulb and in the upper portion of the lesser curvature of the stomach are the most difficult to reach.^{24 26 37 38} Problems in gaining access to lesion must be taken into account in the final evaluation of any of the endoscopic types of treatment. The current data are insufficient to establish the suitability of the heater probe compared with other types of endoscopic treatment.

Previous studies have not shown that the heater probe is less effective than other types of endoscopic treatment, whose efficacy is already proved.^{10 11} Although the benefit of the heater probe *v* medical treatment alone has not been established, it seems more effective. There are only two studies published in complete form in which the results showed statistical difference. Fullarton *et al*²⁷ obtained definitive haemostasis in 20 (100%) of the treated patients *v* 22% failures in the control group ($p=0.05$). Lin *et al*,⁴ after one or two sessions of thermocoagulation, achieved a significant lower rate of rebleeding, emergency operation, death, and days in hospital compared with control patients. In a third study⁵ in ulcers with a non-bleeding visible vessel, heater probe treatment did not improve significantly the rebleeding or death rates compared with controls. Finally, the results of Matthewson *et al*⁶ suggest that the heater probe has some advantages over conservative treatment in preventing rebleeding and decreasing the number of operations. The analysis of the results, however, did not show a statistical difference. Nevertheless, these two last studies^{4 6} cannot exclude a real benefit for the heater probe. In the Matthewson trial with a comparative risk or rebleeding of 0.82 in treated *v* control patients the β error probability was 0.54. In the report by Lin *et al*, the comparative risk was 0.56 and the β -error 0.29. In these two studies the statistical power is lower than the conventional 80% required to reject a true effectiveness with statistical confidence. In addition, the results of two different studies have been published in abstract form,^{28 39} one of these claiming a therapeutic benefit for heater probe.²⁸

This study, including estimation of sample size and the methods used, was aimed at avoiding problems with statistical evaluation of the

results. The inaccessible lesions were included in the final analysis as the aim was to evaluate this procedure according to the intention to treat. Only the results from the first treatment with the heater probe were included in the statistical analysis although a definitive control of the bleeding was achieved sometimes after additional sessions. Finally, rebleeding from a previously missed and non-treated ulcer was considered a failure.

A meta analysis including our data and data obtained from previous publications^{4-6 27 39} was performed to further evaluate the effectiveness of the heater probe, according to the DerSimonian-Laird method in rates differences estimation and the Mantel-Haenszel-Peto method by odds ratio.⁴⁰ The results of the meta analysis suggest that the heater probe is useful in the treatment of bleeding ulcers. The combined total number of patients included in the above mentioned studies is 428, 220 treated and 208 in the control group. The mean rate of recurrent or continued bleeding in control groups was 37%. In the heater probe group the incidence of bleeding was lowered to 14% (pooled rate difference 95% CI = -0.23 (0.08)) and the typical odds ratio of uncontrolled haemorrhage was 0.29 (95% CI = 0.19 to 0.45) favouring the heater probe. In ulcers with a non-bleeding visible vessel, the mean rate of rebleeding was 33% in control groups, the reduction as a result of treatment 19% (pooled rate difference 95% CI = 0.19 (0.09)) and the odds ratio 0.37 (95% CI = 0.21 to 0.65).

In summary, this study shows that compared with medical treatment the heater probe reduces the rebleeding rate in a non-bleeding visible vessel by 62%, there was no death, and complications were minimal. Our results suggest that heater probe is an effective and safe procedure in the prevention of recurrent haemorrhage in peptic ulcer with a non-bleeding visible vessel.

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