Heat probe thermocoagulation and pure alcohol injection in massive peptic ulcer haemorrhage: a prospective, randomised controlled trial

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Abstract

We conducted a prospective randomised controlled trial of 137 patients with massive peptic ulcer haemorrhage over a period of 12 months to compare the haemostatic effects of endoscopic heat probe thermocoagulation and pure alcohol injection. Seventy eight patients (56.9%) were in shock at the time of randomisation to the trial. The age, sex, number of patients in shock, haemoglobin value at the time of entry to the trial, number of patients with severe medical illness, location of bleeders, and stigmata of recent haemorrhage were comparable among the heat probe, pure alcohol, and control groups. The initial haemostatic effect of the heat probe was better than that of the pure alcohol injection (44 of 45 *v* 31 of 46, $p=0.0004$). The ultimate haemostasis achieved by the heat probe group (41 of 45) was better than that of the pure alcohol group (31 of 46, $p=0.012$) and of controls (24 of 46, $p=0.0001$). The duration of hospital stay was shorter for patients in the heat probe group than for the control group (6.2 days *v* 13.8 days, $p<0.05$). The incidence of emergency surgery was less for the heat probe than the control group (three of 45 *v* 12 of 46, $p=0.027$). The mortality rate was less in the heat probe than in the control group (one of 45 *v* seven of 46, $p=0.031$). We suggest that heat probe thermocoagulation should be the first treatment of choice for arrest of massive peptic ulcer haemorrhage.

Upper gastrointestinal bleeding is a common but serious clinical problem¹⁻⁴ and its mortality rate has remained constant at 10% for the past 40 years.¹⁻⁴ About 80-90% of episodes of upper gastrointestinal bleeding stop spontaneously.^{4,5} For these patients the hospital course is relatively smooth, with a mortality rate of 4% or less.^{3,6} In patients with severe persistent bleeding, however, the mortality rate is as high as 30-40% and emergency surgical intervention is usually required.^{3,7}

In the past 10 years different methods of endoscopic haemostasis including laser photocoagulation, electrocoagulation, heat probe thermocoagulation, and injection have been tried, with varying degrees of success.⁸⁻³⁸ Laser photocoagulation is associated with drawbacks of poor tangential application, risk of perforation, optical hazard, high expense, and imperfect haemostatic effect.¹⁰ Heat probe thermocoagulation and multipolar electrocoagulation have been reported to have excellent results in the arrest of haemorrhage.¹⁰⁻²¹ Endoscopic injection for

peptic ulcer haemorrhage is easy to perform and no doubt cost effective.^{8,22-36} Unfortunately, however, only one of the reported series is a controlled study.²⁷ Fair or poor results from endoscopic injection have also been reported.^{24,31-33} Because of this a controlled trial of endoscopic injection compared with the contact probe has been needed.^{26,33-35} In this report we evaluate the haemostatic effects of heat probe thermocoagulation and pure alcohol injection in a prospective randomised controlled trial.

Materials and methods

Patients were accepted for this study if a bleeder (spurter or oozar) or a non-bleeding visible vessel in a peptic ulcer was seen during emergency endoscopic examination. The study was approved by the Clinical Research Committee of the Veterans General Hospital, Taipei, Republic of China. Informed consent was obtained from all patients before the trial. For each patient enrolled in the study, a sealed envelope was opened before therapeutic endoscopy to decide the form of treatment, which had been arranged by a statistician who was not involved in the clinical trial.

The first group of patients received heat probe thermocoagulation, the second group pure alcohol injection, and the third group (control subjects) received conservative treatment. Patients in the first and second groups in whom bleeding recurred received the same treatment again. If haemostasis could not ultimately be obtained in re-bleeders, they were removed from the study and received other forms of treatment.

In the control group emergency surgical intervention was performed if shock had not been corrected by 1500 ml blood transfusion within two hours or if the total volume of transfused blood exceeded 2500 ml within 24 hours. Patients with severe medical illness for whom surgical interventions were rejected by the surgeons were, however, excluded from the study, and they received therapeutic endoscopy for ethical reasons.

The patients' vital signs were checked every hour for 12 hours, every two hours for 12 hours, every four hours for 24 hours until they became stable, and then four times daily. A nasogastric tube was inserted and maintained in situ until 24 hours after treatment. The haemoglobin and haematocrit values were checked every day, and a blood transfusion was given if the haemoglobin concentration dropped to less than 9 g/dl or if vital signs deteriorated. Endoscopy followed 72 hours later, and if no blood clot or haemorrhage was observed in the ulcer base, the patient

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TABLE I Characteristics of the study patients at the start of the trial

	Control group (n=46)	Heat probe group (n=45)	Pure alcohol group (n=46)
Age (yrs, mean (SEM))	57 (2.3)	58.5 (2.5)	57.9 (2.2)
Sex (M/F)	43/3	39/6	37/9
No (%) in shock	27 (58.7)	27 (60)	24 (52.2)
Haemoglobin (g/dl, mean (SEM))	8 (1.1)	8.2 (1.2)	8 (0.7)
Applied energy (J, mean (SEM))		997 (136)	
Injected volume of pure alcohol (ml, mean (SEM))			1.76 (0.17)
No (%) with severe medical disease	7 (15.2)	8 (17.8)	7 (15.2)
Stigmata of recent haemorrhage:			
No (%) with spurting haemorrhage	12 (26.1)	15 (33.3)	13 (28.3)
No (%) with oozing haemorrhage	12 (26.1)	14 (31.1)	15 (32.6)
No (%) with non-bleeding visible vessel	22 (47.8)	16 (35.6)	18 (39.1)

was discharged and followed up with endoscopy after seven days, one month, and every month until scarring of the lesion ensued.

If unstable vital signs or continued tarry or bloody stools were observed during the stay in hospital, emergency endoscopy was performed to determine whether any additional treatment was needed. Re-bleeding was defined as blood in the stomach 24 hours after treatment, bleeding in the ulcer base, presence of unstable vital signs and continued tarry bloody stools, or haematemesis after treatment.

A visible vessel at endoscopy was defined as a red or black spot raised from the ulcer base which was resistant to washing and was often associated with the freshest clot in the ulcer base. Shock was defined as systolic pressure less than 100 mmHg and a pulse rate greater than 100 bpm. The initial success of treatment was defined as haemostasis persisting for five minutes after treatment. Ultimate success of treatment was defined as lack of re-bleeding for seven days after treatment.

In the heat probe group, we used an Olympus GIF-1T10 or GIF-2T10 panendoscope and an Olympus heat probe unit to treat the patients. During treatment, the distal tip of the probe was applied directly to the bleeding site with moderate force. Initially 15–20 J/pulse were delivered, and this was increased as needed to 30 J/pulse until the red base turned black. Then the top of the probe was applied circumferentially around the bleeding site with 15–20 J/pulse for four to eight pulses. The bleeding site was observed for five minutes. At the end of this time, the bleeding site was challenged with maximal water irrigation for 10 seconds. If any further haemorrhage occurred, the above pro-

cedure was repeated until no more bleeding was seen.

In the pure alcohol injection group, we used an Olympus GIF-P10 or Olympus GIF-2T10 panendoscope and an Olympus injector NM8-L to treat the patients. We injected 99.8% alcohol (E Merck, West Germany) 0.3–0.5 ml at every quadrant and 1–2 mm away from the bleeder, with a total volume of 1–2 ml. Then we observed the ulcer for five minutes. If the bleeding had stopped, we withdrew the endoscope.

We used the ANOVA test to compare the basic data of age, volume of blood transfusion, and haemoglobin among the three groups, Kruskal-Wallis ANOVA test to compare the duration of hospital stay among the three groups, the χ^2 test, with or without Yates' correction, and Fisher's exact test, when appropriate, to compare the haemostatic effects among the three groups. A probability value of less than 0.05 was considered significant.

Results

Between August 1987 and July 1988, a total of 1240 patients visited the emergency department with a chief complaint of upper gastrointestinal bleeding. Nine hundred and thirty of these patients underwent emergency endoscopy within 12 hours of arrival. We failed to identify bleeders in eight patients. We found peptic ulcers with bleeding (oozing or spurting) or non-bleeding visible vessels in 141 other patients. We explained the details of this clinical trial to each patient and his or her family before emergency endoscopy was performed. Four of the 141 patients refused to enter the trial.

The age, sex, number of patients in shock, haemoglobin values, number of patients with severe medical illness, and stigmata of recent haemorrhage in the three groups were not statistically different (Table I).

We enrolled 46 patients in the control group. Twenty four of them had an uneventful course over the following weeks, except for two who had re-bleeding episodes three to four days later which subsided spontaneously (Table II). Conservative management of the other 22 patients failed, as shown by continuing bleeding. Twelve of these 22 patients underwent emergency surgery; one patient underwent transcoeliac artery embolisation; five patients with severe medical illness underwent therapeutic endoscopy (four for heat probe and one for pure alcohol haemostasis) for ethical reasons; two patients died of unrelated medical illness; and two patients died of massive haemorrhage while awaiting surgery.

In the heat probe group, 44 patients (97.8%) achieved initial haemostasis. The only patient in whom this failed was withdrawn from the study. Of the 44 patients who had achieved initial haemostasis, eight (18.2%) re-bled within seven days. These eight underwent a second heat probe thermocoagulation and five (62.5%) attained ultimate haemostasis. In the end ultimate haemostasis was achieved in 41 patients (91.1%) (Table II).

In the pure alcohol group, 31 patients (67.4%) achieved initial haemostasis. Two of them re-

TABLE II Comparison of results in heat probe (HP) thermocoagulation, pure alcohol (PA), and control groups in patients with massive peptic ulcer haemorrhage

	Control group (n=46)	Heat probe group (n=45)	Pure alcohol group (n=46)
No (%) with successful initial haemostasis		44 (97.8)	31 (67.4)**
No (%) with rebleeding		8 (18.2)	2 (6.5)*
No (%) with successful repeat haemostasis		5 (62.5)	2 (100)*
No (%) with ultimate haemostasis	24 (52.2)	41 (91.1)	31 (67.4)#
Blood transfusions (U, mean (SEM))	7.1 (1.1)	7.5 (1.2)	5.7 (0.7)*
No (%) receiving emergency surgery (%)	12 (26.1)	3 (6.7)	2 (4.3)†
Days in hospital (mean (SEM))	13.8 (2.4)	6.2 (0.7)	9.0 (1.1)##
Mortality rate	7 (15.2)	1 (2.2)	0 (0)††

*p>0.05, **p=0.0004.
†p=0.0024 (p=0.027 between controls and HP, p=0.009 between controls and PA).
#p=0.0002 (p=0.0001 between controls and HP, p=0.012 between PA and HP).
##p<0.05 between HP and controls. Others: p>0.05.
††p=0.002 (p=0.031 between controls and HP, p=0.018 between controls and PA).

TABLE III The ability to stop bleeding in relation to the location of the peptic ulcers among the three groups

Location of bleeders	Control group (n=46)	Heat probe group (n=45)	Pure alcohol group (n=46)	
Cardia	—	1/1	2/2	NS
Body of stomach	4/9	12/14*	8/16*	*p=0.045
Antrum	3/8*	8/8*	4/5	*p=0.013
Duodenal bulb	17/28*	18/19*	17/23	*p=0.0083
Marginal ulcer	0/1	2/3	—	NS

bled within seven days of the injection. These two patients achieved ultimate haemostasis after the second injection treatment. Fifteen patients who had failed to achieve initial haemostasis were withdrawn from the study and underwent heat probe thermocoagulation. Thirteen of these patients achieved ultimate haemostasis; the two others underwent surgery (Table II).

The initial haemostasis was better in the heat probe group than in the pure alcohol group ($p=0.0004$). Re-bleeding rates in the heat probe and pure alcohol groups were 18.2% (eight of 44) and 6.5% (two of 31) respectively ($p=0.087$). With the second treatment for re-bleeders we achieved an ultimate haemostatic rate of 62.5% (five of eight) in the heat probe group and 100% (two of two) in the pure alcohol group ($p=0.41$). The ultimate success rates in the control, heat probe, and the pure alcohol groups were 52.2% (24 of 46), 91.1% (41 of 45), and 67.4% (31 of 46), respectively. Heat probe thermocoagulation was better than conservative treatment or pure alcohol injection in achieving ultimate haemostasis ($p=0.0001$, $p=0.012$, respectively). There was no statistically significant difference in the haemostatic effects between the pure alcohol and the control groups ($p=0.2$) (Table II).

The duration of hospital stay was significantly less in the heat probe group compared with the control group (6.2 days v 13.8 days, $p<0.05$). Emergency surgery for persistent or recurrent bleeding was required in 12 (26.1% of the control subjects and in three patients (6.7%) in the heat probe group. The heat probe group had a statistically lower emergency surgery rate than the control group ($p=0.027$).

Seven patients in the control group died – as the result of surgical complications in two, failure of embolisation to halt bleeding in one, severe exsanguination in two, and severe medical illness in two. One patient from the heat probe group and none from the pure alcohol group died of massive haemorrhage. The mortality rate was significantly lower in the heat probe group than in controls (one of 45 v seven of 46, $p=0.031$). No complications related to therapeutic endoscopy were observed in the heat probe or pure alcohol groups.

After analysing the ability to halt bleeding in relation to the location of the bleeding among

three groups, we conclude that the heat probe thermocoagulation was effective in any site of the stomach and duodenum whereas pure alcohol injection was less effective (Table III). An investigation into the relation between haemostatic effects and the stigmata of recent haemorrhage among the three groups showed that the heat probe group achieved a better haemostatic result than control subjects in ulcers with spurting haemorrhage ($p=0.0018$, 95% confidence interval on difference=0.32–0.92) and oozing haemorrhage ($p=0.004$, 95% confidence interval on difference=0.72–1.28), and a better result than the pure alcohol group in ulcers with spurting haemorrhage ($p=0.0037$, 95% confidence interval on difference=0.26–0.86). In patients with non-bleeding visible vessels there was no statistically significant difference in haemostasis achieved among the three groups (Table IV).

Discussion

Since 1978 heat probe thermocoagulation has been reported as an excellent means of achieving haemostasis.^{10–19 34} Pure alcohol injection has also been reported to be highly effective in achieving haemostasis.^{8 22–28} Some questions have been raised, however, about injection therapy.^{12 33} The detailed sites of bleeders were not mentioned,^{22–27} and the number of massive haemorrhages reported was small.^{8 22 24 26} Therefore, a randomised controlled trial has been needed to evaluate the haemostatic effect of injection therapy.^{26 33–35}

In our series massive haemorrhage was apparent in most patients. Seventy eight (56.9%) patients were in shock at the time of entry to the trial. The average volume of blood transfusion in the three groups was 7.1 U (control subjects), 5.7 U (pure alcohol group), and 7.5 U (heat probe group).

The ultimate haemostatic rate of the heat probe group in our series was high, up to 91.1% (41 of 45). This result is similar to those reported by other authors^{10 17} and in our previous uncontrolled series.^{11–14} The ultimate haemostatic rate of pure alcohol injection in our series was 67.4% (31 of 46). This result is lower than those reported by some authors^{8 10 22–28} but is comparable with our previous report and those of other authors.^{12 31 32}

In reports discussing the haemostatic effect of endoscopic injection, Leung and Chung²² found that it was difficult to inject bleeders located on the floor or posterior wall of the duodenal bulb; Sugawa *et al*⁸ excluded two patients in their series because of a poor tangential approach; Panes *et al*²⁷ also excluded seven patients for the same reasons. The 15 patients who failed to achieve haemostasis in our series included nine with spurting haemorrhage and six with bleeders that were difficult to approach en face (two bleeders located over the posterior wall of the duodenal bulb, two over the posterior wall of the midbody of the stomach, and two over the lesser curvature of the high body of the stomach). Failure to manage the difficult to approach bleeders and spurting bleeders are two main causes for the low haemostatic rate achieved in the pure alcohol group. In the heat probe group we had no such

TABLE IV The ultimate haemostatic effects among the three groups in relation to stigmata of recent haemorrhage

Stigmata of recent haemorrhage	Control group (n=46)	Heat probe group (n=45)	Pure alcohol group (n=46)	
Spurting haemorrhage	3/12†	13/15†#	4/13#	†p=0.0018 #p=0.0037
Oozing haemorrhage	6/12*	14/14*	12/15	*p=0.0040
Non-bleeding visible vessel	15/22	14/16	15/18	NS

problem. Since the side of the distal tip of the probe can be applied to thermocoagulate the bleeder, tangential probe application is more feasible than pure alcohol injection.^{10 12 20} In our series, the haemostatic rate for the heat probe group was better than that for the pure alcohol group for bleeders located over the posterior wall of the gastric body or duodenum (15 of 15 v four of 8, $p=0.015$).

With regard to the volume of pure alcohol needed to stop the haemorrhage, Sugawa *et al*⁸ suggested that a volume of less than 1 ml be used to avoid perforation. We believe that this volume may be too little to arrest a spurting bleeder¹² and therefore we injected 1–2 ml pure alcohol around each bleeder and up to 3.5 ml in two cases without perforation. A larger volume of other solutions (eg, hypertonic saline, epinephrine, or polidocanol) may be more effective in arresting spurting haemorrhage.³⁶

In ulcers with spurting haemorrhage, the special irrigation system of the heat probe enabled us to irrigate and compress the bleeder simultaneously, thus ensuring compression of the bleeder before thermocoagulation.^{10 12 20} The heat sink effect was thus diminished⁹ and damage to the normal mucosa was also avoided.⁹ A total of 40 patients with spurting haemorrhage entered our study. This number of patients is larger than those reported by other authors.^{10 15 17 22–25 29} Patients with peptic ulcer and spurting haemorrhage have an 85% incidence of further haemorrhage and a mortality rate of 50%.^{39 40} They usually require surgery or therapeutic endoscopy.^{34 39 41} In our control subjects spurting haemorrhage subsided spontaneously in only three of 12. The other nine patients required either surgical intervention or therapeutic endoscopy. In our opinion patients with peptic ulcer and spurting haemorrhage comprise a more severely ill group, for whom immediate aggressive management is needed.

Peptic ulcer patients with oozing haemorrhage have a mortality rate of 13.3% – four to five times that of patients whose ulcers have a clean base.⁴⁰ In our control subjects, half (six of 12) with oozing haemorrhage could be managed conservatively. In ulcers with oozing haemorrhage, the haemostatic effect was significantly better in the heat probe group than in the control group. Although the haemostatic effect was better in the pure alcohol group than in the control group, the difference was not statistically significant, perhaps because of the small number of patients. We suggest that patients with oozing peptic ulcers be treated with heat probe thermocoagulation as the first treatment of choice.

The re-bleeding rate for peptic ulcers with a visible vessel was estimated to be 33–100%.^{42–46} Whether a peptic ulcer with a non-bleeding visible vessel needs aggressive treatment remains a matter of controversy.^{39 43 44 46 47} In the control group, 11 (50%) patients re-bled and seven (31.8%) patients required surgery or therapeutic endoscopy. The ultimate haemostatic rates in peptic ulcer patients with non-bleeding visible vessels were better (though not statistically significant) in the heat probe and pure alcohol groups than in the control group. The number of patients may be too small to result in a statistic-

ally significant difference and should be increased to 107 for each group to be statistically significant (alpha error: 0.05, beta error: 0.10).

We conclude that therapeutic endoscopy is necessary in peptic ulcers with oozing or spurting haemorrhage. Heat probe thermocoagulation can achieve a much higher haemostatic rate, shorten the length of hospital stay and reduce the incidence of surgery and mortality. It should therefore be the first treatment choice in the management of peptic ulcers with spurting and oozing haemorrhage. We also look forward to a larger series of controlled trials to determine whether non-bleeding visible vessels require aggressive management.

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