

# Endoscopic injection of adrenaline versus normal saline in bleeding peptic ulcer

## A prospective evaluation

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**Summary:**

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**Background:** Endoscopic treatment is widely accepted as the most effective method for controlling acute ulcer bleeding and preventing ulcer rebleeding.

**Objective:** is to compare efficacy and safety of local endoscopic injection of adrenaline to normal saline in bleeding peptic ulcers and to identify the risk of rebleeding after successful endoscopic hemostasis.

**Patients and methods:** This is a prospective study of 77 patients with bleeding peptic ulcers were treated by local endoscopic injection of adrenaline or NS. Patients who succeeded initial hemostasis were admitted and followed for rebleeding events. Rebleeding was confirmed by urgent endoscopy followed by referral to urgent surgery. Outcome was measured directly by rebleeding rate, need for surgery, and the mortality rate and indirectly by the number of blood transfusion units and days of hospitalization. All clinical and endoscopic data of patients were collected to stratify the risk of rebleeding.

**Results:** The rebleeding rates (17.9% for NS group vs. 11.4% for adrenaline group), the need for emergency operation (10.2% vs. 5.7%), blood transfusion (3.2 units vs. 2.4 units), hospital stay (2.8 days vs. 2.7 days) and in-hospital mortality (5.6% vs. 5.7%) were not significantly different in both groups. Clinical and endoscopic analysis revealed that presence of shock, coexisting disease, large ulcer size (>2cm) and active bleeding were independent factors predicting rebleeding.

**Conclusion:** local endoscopic injection of NS and adrenaline are equally safe and effective in stopping ulcer bleeding and rebleeding. Severe bleeding, comorbidities, large ulcer size, active bleeding all are predictors of rebleeding.

**Keywords:** bleeding peptic ulcer, endoscopic injection, adrenaline & normal saline

**Introduction:**

Most ulcer bleeding is self-limited (about 80%), the remaining 20% have continued or recurrent bleeding which constitute a high-risk group with substantial morbidity and mortality (1).

Some clinical predictors of increased risk for rebleeding are age older than 60 years, clinical evidence of severe bleeding (shock, low hemoglobin value, need for blood transfusion), comorbid illness (cerebrovascular or cardiovascular diseases), the finding of fresh blood in the emesis or on per rectal examination and onset of bleeding while the patient is hospitalized (2).

The most important prognostic endoscopic features in ulcer bleeding include large ulcer (more than 2 cm), active bleeding (spurting or oozing), a visible vessel and fresh blood or a blood clot (3).

Endoscopic treatment is widely accepted as the most effective method for controlling acute ulcer bleeding and for preventing ulcer rebleeding (4).

Clinical experience suggest that various endoscopic modalities are generally equivalent in efficacy, and non-randomized studies have shown no differences in rebleeding, surgery or mortality (5, 6, 7). Injection modality is simple, widely used and

cheapest available hemostatic modality. Diluted (1:10,000) epinephrine is the only remaining agent that is widely used for injection therapy because of its safety. The proposed modes of action of adrenaline and normal saline are tamponade effect and local constricting of the blood vessel (8). The initial rate of hemostasis with adrenaline is 94% in most large series (9).

Although endoscopic treatment reduces the likelihood of ulcer rebleeding significantly, between 10-20% in patients with active bleeding and non bleeding visible vessel and 5% of patients with adherent clot will rebleed despite endoscopic intervention (10, 11).

**Aim of the study:**

The present study has two aims: to compare efficacy and safety of local endoscopic injection of adrenaline to normal saline in the bleeding peptic ulcer and to identify the risks for rebleeding after successful endoscopic hemostasis.

**Patients and methods:**

Patients with acute upper gastrointestinal bleeding were admitted in the gastroenterology and hepatology teaching hospital and underwent urgent endoscopy after initial resuscitation. Inclusion

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criteria: Patients were eligible for inclusion in this study if they have ongoing bleeding duodenal or gastric ulcers including actively bleeding ulcers "spurting or oozing", slowly oozing ulcers with or without fresh clot.

Seventy seven patients (59 males, 18 females) who met the above inclusion criteria, were then received either adrenaline or normal saline injection (according to the availability).

Techniques of therapy: Adrenaline in 1:10,000 dilution was injected around the bleeding site with a rate of 1-2 ml each until the bleeding was controlled. The amount of the N/S each site depend on the appearance of the edema of the mucosa, with the average of 5 ml each.

Follow up: Initial endoscopic failure was defined for patient who did not attain initial haemostasis. These patients were subjected to surgical intervention.

Rebleeding was suspected if there is recurrent haematemesis or the malaena continue with failure of correction of blood pressure or raising Hb level above 10 g/dl despite more than 5 units blood transfusion within 24 hours. For those patients, an emergency endoscopy was performed. If active bleeding or fresh blood clot with oozing was seen at ulcer base, rebleeding was confirmed and surgery indicated.

Outcome assessment was made by rebleeding rate, frequency of need for surgery and in hospital mortality. Indirect parameters included the number of blood transfusion and the days of hospitalization. The clinical and endoscopic data of the patients who sustained rebleeding were collected to identify the risks of rebleeding.

### Results:

Initial hemostasis and follow up:

During the study period (from January 2006 to July 2007), there were 278 patients with bleeding peptic ulcers. Of these, 77 patients who met the inclusion criteria required endoscopic treatment.

Initial hemostasis was achieved in 74 (96.1%) patients, 3 patients in whom the bleeding could not be stopped were all from actively bleeding posterior duodenal ulcers. Those were referred for emergency surgery.

The remaining 74 patients, who sustained initial hemostasis, completed the follow up after endoscopic therapy, 11 (14.8%) patients rebled; 7 patients in the 1<sup>st</sup> day, 2 patients in the second day and 2 patients in the third day.

Of those who rebled, 7 patients underwent emergency surgery and 4 patients died.

Table (1) shows the clinical characteristics of the studied patients.

Table (1): Clinical characteristics of the studied patients

No. of patients	77	100%
Age: Range	16-90	
Mean	53.7±43	
Smoker	25	32.4%
Presentation:		
Hemostasis and malaena	63	81.8%
Malaena	14	18.1%
Ethanol habit	0	0%
Preceded abdominal pain	13	16.8%
NSAIDs users	43	55.8%
Past history of PUD	7	9.0%
Coexisting disease	16	20.7%
Shock	11	14.2%
Bleeding site:		
Ant. DU	41	53.2%
Post. DU	30	38.9%
Gastric Ulcer	6	11.6%
Bleeding type:		
Active bleeding	46	59.7%
Fresh clot with ooze	23	29.8%
Slow oozing	8	10.3%

Normal saline versus adrenaline injection:

The success of endoscopic hemostasis between two groups was equal. The rate was 95.1% (39/41) for N/S group and 97.21% (35/36) for adrenaline group (p-value 0.9).

The clinical and endoscopic characteristics of the 74 patients who sustained the initial response (39 patients treated with N/S injection and 35 patients treated with adrenaline injection) were compatible in age, sex, location of ulcer, and severity of bleeding.

Seven of 39 patients (17.9%) in the N/S group and 4 of 35 patients (11.4%) in the adrenaline group experienced a clinically significant rebleeding, stratified the criteria for emergency surgery and were operated on.

The difference in the rebleeding rates failed to reach a statistical significance (p-value 0.3).

There was no significant difference in the blood transfusion requirement, emergency surgery, hospital stay and mortality between the two groups, table (2).

Table (2): The outcome of patients in the two groups

Characteristics	NS group	Adrenaline group	p-value
No. of patients	39	35	
Rebleeding	7 (17.9%)	4 (11.4%)	0.325
Surgery	5 (10.2%)	2 (5.7%)	0.39
Mortality	2 (5.6%)	2 (5.7%)	0.44
Blood unit transfused (mean)	3.2±1.7	2.4±2.0	0.069
Hospital stay	2.8±1.4	2.7±1.4	0.896

Predictors of rebleeding:

The eleven patients who rebled within the 72 hours of endoscopic therapy were compared to 63 who didn't rebleed with respect to clinical and endoscopic parameters.

A significant independent association with rebleeding was found for the presence of ease, large ulcer size and actively bleeding ulcer. No statistical

significance was found for the age, sex, ulcer site and NSAIDs use.

Table (3) shows the clinical and endoscopic data between rebleeding and non-rebleeding group.

Table (3): The clinical and endoscopic data of rebleeding and non-rebleeding group

Characteristics	rebleeding group	Non rebleeding group	p-value
No. of patients	11	63	
Age mean	54.5±17.7	47.4±15.7	0.221
Gender			
Male	10 (90.9%)	47 (74.6%)	0.22
Female	1 (9.1%)	16 (25.4%)	
Hb. on presentation	8.2±1.0	9.6±1.1	0.000
NSAIDs use	8 (72.7%)	35 (55.6%)	0.234
Shock	6 (54.5%)	3 (4.8%)	0.001
Coexisting disease	6 (54.5%)	10 (15.8%)	0.018
Total blood use	4.4±0.9	2.5±1.9	0.002
Large Bleeding ulcer size (> 2cm)	9 (81.8%)	12 (19%)	0.000
Ulcer site			
Ant. DU	7 (63.6%)	34 (54.0%)	0.547
Post. DU	4 (36.4%)	23 (36.5%)	
Gastric U	0	6 (9.5%)	
Bleeding type			
Active	10 (90.9%)	33 (57.1%)	0.05
Clot with ooze	1 (9.1%)	22 (30.2%)	
slow ooze	0	8 (12.7%)	

#### Discussion:

In our study, the N/S was as effective as adrenaline in stopping the bleeding from ulcer (95.1% versus 97.2%, p-value > 0.05) at time of endoscopy.

The total rebleeding rate was 14.8 (11/74) with 9.4% (7/74) need for surgery and 5.4% (4/74) in hospital mortality. These values are in keeping with those from other series (12,13,14).

In the present study, there was no significant difference in the outcome of the patients who sustained initial hemostasis in the N/S and adrenaline group as measured by transfusion requirement, the need for emergency surgery, hospital stay and in hospital mortality (p-value > 0.05).

Several studies have defined factors that predict rebleeding after endoscopic therapy. These factors were related to high risk ulcers (ulcer size, bleeding stigmata, ulcer position), signs of massive bleeding or to patient characteristics (age, comorbidities, NSAIDs use) (15).

Choudari and colleagues found no differences in outcome of patients in different age groups (<60, 61-74, >75 years) treated endoscopically (16). Other study documented that older age does not predict failure of endoscopic therapy but associated with increase mortality (17).

Our series showed consistent correlation of rebleeding risk with the clinical features of severe bleeding, ulcer size  $\geq 2$  cm with active bleeding character. Factors related to ulcer site were not significant in our analysis.

The age was not a significant predictor of either rebleeding or the mortality, which can be interpreted by the approximate age of the majority of studied patients (< 60 years).

#### Conclusion:

The present study shows that N/S and adrenaline are equally effective and safe in the endoscopic therapy of bleeding peptic ulcers. It also defined the features of severe bleeding, comorbidities, large ulcer size and active bleeding type; all are predictors of rebleeding and mortality.

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