Management of Peptic Ulcer Bleeding

Dr. Carmen Ka-man NG

MBBS, MRCP, FHKCP, FHKAM(Medicine)
Associate Consultant, Department of Medicine and Geriatrics, Princess Margaret Hospital

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded one CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 November 2009.

Upper gastrointestinal bleeding (GIB) is defined as haemorrhage proximal to the ligament of Treitz. Peptic ulcer bleeding accounts for 60% of the cases.[1] Despite advances in endoscopic treatment and pharmacotherapy, the mortality of upper GIB remains unchanged. In-hospital mortality was found to be 7.1% in 3220 patients admitted for bleeding peptic ulcers from 1993 to 2003 to a teaching hospital in Hong Kong.[2] History taking and physical examination help to define the underlying cause. It should be followed by a detailed haemodynamic assessment. Resting tachycardia (pulse $\geq$100/min), hypotension (sBP <100mmHg) and postural changes ($\uparrow$pulse of $\geq$20/min or $\downarrow$sBP $\geq$20mmHg on standing) represent a significant loss of intravascular volume. Fluid resuscitation is the first priority in patient management. Crystalloid should be infused via a large-bore catheter. Supplementary oxygen and supportive transfusion should be considered on a case to case basis.

Medical Therapy

The concept of clot stabilisation by raising the intragastric pH has led to the use of a high dose proton pump inhibitor (PPI) in acute GIB. A pH > 6 favours platelet aggregation, clot formation and inhibition of fibrinolysis.[3]

The effect of preemptive PPI before endoscopy was studied. Daneshmend had conducted a randomised study in 1147 unselected patients presenting with upper gastrointestinal bleeding. 578 patients were given omeprazole (bolus 80mg IVI, followed by 40mg IVI for three doses, then 40mg orally every 12 hours) compared to a placebo arm of 569 patients.[4] Endoscopic signs of upper GIB in the treatment group (33%) were significantly lower than in the placebo group (45%), p<0.0001. Another trial conducted in Hong Kong studied the use of PPI infusion (omeprazole 80mg IV bolus, followed by 8mg infusion / hour) before endoscopy in non-aspirin users admitted with overt signs of upper GIB.[1] The need for endoscopic treatment was lower in the PPI group (19.1%) than the placebo group (28.4%). Fewer patients had actively bleeding ulcers and more clean-based ulcers were found in the treatment group. Hospital stay was less than 3 days in 60.5% of the treatment group as compared to 49.2% in the placebo group. The Cochrane review suggested that PPI treatment initiated prior to endoscopy in patients with upper GIB significantly reduced the proportion of patients with stigmata of recent haemorrhage at index endoscopy.[6] It has no effect on the rate of rebleeding, surgery or mortality. In a cost-effective analysis, PPI reduced endoscopic therapy by 7.4% and resulted in a lower cost-effectiveness ratio per endoscopic therapy averted than the placebo.[5] The approach of preemptive PPI before endoscopic diagnosis of upper GIB is still controversial, especially in countries with high prevalence of variceal bleeding.[7]

There is more evidence of using PPI as a medical adjunct after endoscopic haemostasis for peptic ulcer demonstrating high risk stigmata of bleeding. Khuroo had shown the efficacy of omeprazole (40mg given orally every 12 hours for 5 days) in decreasing the rate of further bleeding and need for surgery in a double-blind, placebo-controlled trial of 220 patients.[8] A subgroup analysis showed positive finding in patients with non-bleeding visible vessels or adherent clots, but not in those with arterial spurting or oozing. Lau et al assessed the effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment (epinephrine injection followed by thermocoagulation) of bleeding peptic ulcers.[9] They concluded that high-dose infusion of omeprazole (80mg IV bolus, followed by infusion at 8mg per hour for 72 hours) reduced the rate of recurrent bleeding, decreased the need for endoscopic retreatment, blood transfusions, and shortened the length of hospitalisation. A systemic review of twenty-four randomised trials of PPI (oral or intravenous) compared with placebo or H2-blocker in 4373 patients with peptic ulcer bleeding showed no difference in overall mortality (3.9% vs 3.8%).[10] However, a significant reduction in rate of rebleeding (10.6% vs 17.3%) and surgery (6.1% vs 9.3%) were observed. The effect is more pronounced in studies conducted in Asian countries where all cause mortality was also found to be reduced. This may be explained by the ethnic differences in the rate of PPI metabolism, lower gastric parietal cell mass and higher prevalence of *Helicobacter pylori* infection.[11] An international trial conducted in 16 countries had tried to answer the question of ethnic difference in PPI response.[12] Intravenous esomeprazole 80mg bolus, followed by 8-mg/h infusion over 72 hours or matching placebo was given after successful endoscopic haemostasis to 764 patients with high-risk ulcer lesions. Recurrent bleeding

was found to be significantly less within 72 hours, at 7 days and 30 days. It showed a trend towards fewer surgery and lower all-cause mortality. The efficacy of PPIs in preventing recurrent peptic ulcer bleeding should not be race-specific and could be applied universally.

Endoscopic Therapy

Timing of endoscopy is a balance between clinical need and resources. It is usually scheduled in the following endoscopic session, within 24 hours of admission. Endoscopic intervention decreased rates of further bleeding, surgery, and mortality in patients with high-risk endoscopic features,[13] defined as Forrest class I and IIa/b lesions. (Table 1)[14]

In case of torrential upper GIB, the stomach could be filled with clots. By inducing gastric emptying, 250mg erythromycin given intravenously 20 minutes before endoscopy, had resulted in an empty stomach in 82% (42/51) compared with 33% (18/54) in the placebo group ($p<0.001$).[15] Endoscopic duration was shortened. By infusion of erythromycin 30 to 90 minutes before endoscopy, at 3mg/kg over 30 minutes, image quality was significantly improved.[16] Both studies showed a reduction in the need for a second-look endoscopy. It is, however, not used routinely in all upper GIB patients.

A variety of endoscopic haemostatic techniques are available. They include injection, thermal therapy and mechanical treatment. A direct comparison of the various modalities is difficult.[17] The method used depends on the location of the vessels and local expertise. Adrenaline monotherapy is inferior to other monotherapies in preventing rebleeding. Adding a second haemostatic method to adrenaline injection achieves a better result than stand alone adrenaline injection therapy.[18] However, dual endoscopic therapy had no advantage over thermal or mechanical monotherapy in improving patient's outcome.[19]

Injection Method

Diluted adrenaline (1:10 000) is the most widely used injection substance. It causes vasoconstriction and provides volume tamponade. Initial haemostasis is satisfactory but an unacceptably high rebleeding rate is observed since the injected fluid dissipates rapidly. The use of sclerosants (polidocanol, ethanolamine, alcohol and hypertonic glucose) for non-variceal bleeding is out of favour. It can cause transmural necrosis. Its injection in the proximal stomach, especially the fundus, is contraindicated due to risk of late perforation.

Thermal Method

The bipolar probe and the heater probe achieve haemostasis by occluding the vessel through compression, followed by sealing it with heat (coaptive coagulation). Arteries associated with visible vessels have a mean external diameter of 0.7mm (0.1 - 1.8mm).[20] Contact thermal therapy can coaptively coagulate arteries which are less than 2mm in diameter.[21] Argon plasma coagulation is the representative non-contact thermal method for coagulation. It delivers a stream of argon gas to conduct heat for electrocoagulation. It is especially effective in treating vascular lesions.

Mechanical Method

Endoclips provide at the spot mechanical clamping of the vessels. Newer models allow reopening and repositioning. It is difficult, if not impossible, to be placed tangentially. The deploying mechanism is weakened with the scope in retroflexion. Hence lesions in the fundus pose a challenge to therapy.

Table 1. Forrest classification of peptic ulcers in upper GIB.

Forrest class	Endoscopic appearance	Risk of rebleeding %
Ia	Arterial spurting	100
Ib	Arterial oozing	17-100
IIa	Non-bleeding visible vessel	8-81
IIb	Sentinel clot	14-36
IIc	Haematin covered flat spot	0-13
III	Clean base	0-10

Surgery

A history of peptic ulcer disease, previous ulcer bleeding, shock at presentation, active bleeding at endoscopy, large ulcers of >2cm in diameter, large bleeding vessel ($\geq$2mm) and ulcers at the lesser curvature of stomach or over the posterior / superior duodenal bulb are predictors of endoscopic treatment failures. [7]

The aim of emergency surgery is not to cure the disease but rather to stop the bleeding.[7] It is employed in selected groups of patients. They include patients suffering from profuse blood loss rendering an unstable haemodynamics despite intravascular replacement with fluid and blood products, patients who may not tolerate recurrent or worsening bleeding and patients whose endoscopic interventions are ineffective.

Risk Score

Various risk scoring systems were designed to risk stratify patients with acute GIB into appropriate and cost-effective levels of care. The two most widely employed are the Rockall score and the Glasgow-Blatchford score.

The Rockall score (RS) was derived from 4185 admissions of patients older than 16-year old for upper GIB and validated with an additional 1625 patients' data. It was published in 1996 and revalidated a year later.[22, 23] It comprises the pre-endoscopic clinical score and the complete score after addition of the two endoscopic variables. It has a minimum score of 0 and a maximum score of 11. (Table 2) The primary intent of the study is to predict mortality. (Table 3) At high score, it loses the discrimination power and tends to overestimate. It is useful in demonstrating low rebleeding risk and low mortality in individuals with low score.[24]

The Glasgow-Blatchford score (GBS) assesses clinical data presented upon admission to predict the need for clinical intervention (transfusion and endoscopic intervention).[25] The study was conducted on 1748

patients from 19 hospitals and revalidated prospectively in another 197 adult patients. The score ranges from 0 to 23. (Table 4) From the full risk score, a fast-track screening procedure was derived. Patients fulfilling all of the following were classified as having low risk for clinical intervention, namely blood urea less that 6.5 mmol/L, haemoglobin more than 130g/L for men or 120g/L for women, systolic blood pressure 110 mm Hg or higher, and pulse less than 100 beats per min.

These two scoring systems were tested prospectively in patients admitted to four hospitals in the United Kingdom with upper GIB.[26] Sixteen percent (105/649) and 28% (184/657) scored 0 by GBS and RS respectively. No intervention and no death was recorded in the low-risk group identified by a GBS of 0. One death and 44 interventions (21 endoscopic or surgical) and 23 transfusions were noted in 32 (17%) of patients with an admission RS of 0. In phase 2 of this study, GBS low-risk criteria were used to assess 572 consecutive patients presenting to A&E departments at two hospitals. Overall, 123 (22%) individuals were identified as low risk, with 84 (68%) of this group managed as outpatients. All patients were offered outpatient endoscopy but only 23 (40%) attended. None of the non-attendees was readmitted for upper GIB or died in 6 months. Among those who returned for endoscopy, none had malignant disease, varices or ulcers that required intervention. GBS was superior to RS for prediction of need for intervention or death. It helps to identify patients who are safe to be managed as outpatients. GBS reduces admissions for upper GIB and allows more appropriate use of in-patient resources.

Table 2. Rockall Risk Score.

Variable	Score			
	0	1	2	3
Age	< 60 years	60 - 79 years	≥ 80 years	
Shock	'No shock' sBP ≥ 100, pulse <100	'Tachycardia' sBP ≥ 100, pulse ≥ 100	'Hypotension' sBP < 100	
Co-morbidity	No major comorbidity		Cardiac failure, ischaemic heart disease and major comorbidity	Renal / liver failure Disseminated malignancy
Diagnosis	Mallory-Weiss tear, no lesion identified and no SRH	All other diagnoses	Malignancy of upper GIT	
Major SRH	None or dark spot only		Blood in upper GIT, adherent clot, visible or spurting vessel	

sBP, systolic blood pressure; SRH, stigmata of recent haemorrhage.

Table 3. Observed rebleeding and mortality by Complete Rockall

	Score								
	0	1	2	3	4	5	6	7	8+
Re-bleed (%)	4.9	3.4	5.3	11.2	14.1	24.1	32.9	43.8	41.8
Deaths (total %)	0	0	0.2	2.9	5.3	10.8	17.3	27	41.1

Table 4. Blatchford Score.

Admission risk marker	Score component value
Blood urea (mmol/L)	
≥6.5 <8.0	2
≥8.0 <10.0	3
≥10.0 <25.0	4
≥25	6
Haemoglobin (g/L) for men	
≥120 <130	1
≥100 <120	3
<100	6
Haemoglobin (g/L) for women	
≥100 < 120	1
<100	6
Systolic blood pressure (mm Hg)	
100 - 109	1
90 - 99	2
<90	3
Other markers	
Pulse ≥ 100 (per min)	1
Presentation with melaena	1
Presentation with syncope	2
Hepatic disease	2
Cardiac failure	2

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