



Review of the endoscopic and medical management of non-variceal Upper Gastro-intestinal Bleeding

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Abstract

Acute Upper Gastro-intestinal bleeding(UGIB), defined as bleeding from a source that is proximal to the ligament of treitz, is a potentially life threatening medical emergency. The underlying pathophysiology of non-variceal upper GI bleeds involve either arterial haemorrhage, such as in mucosal tears or GI ulcers, or venous hemorrhage, in cases such as telangiectasias. Variceal hemorrhage is due to elevated portal pressure leading to portal gastropathy. UGIB is a common cause of admission into hospital, and it has a 6%-13%¹ hospital mortality rate. The diagnosis and management of upper gastrointestinal bleeding has evolved considerably, however despite these changes mortality has not significantly improved in the past 50 years.

Introduction

Acute Upper Gastro-intestinal bleeding(UGIB), defined as bleeding from a source that is proximal to the ligament of treitz, is a potentially life threatening medical emergency. The underlying pathophysiology of non-variceal upper GI bleeds involve either arterial haemorrhage, such as in mucosal tears or GI ulcers, or venous hemorrhage, in cases such as telangiectasias. Variceal hemorrhage is due to elevated portal pressure leading to portal gastropathy. UGIB is a common cause of admission into hospital, and it has a 6%-13%¹ hospital mortality rate. The diagnosis and management of upper gastrointestinal bleeding has evolved considerably, however despite these changes mortality has not significantly improved in the past 50 years.

Signs and Symptoms

The common findings on history of a patient with Upper GI bleeding include; weakness, dizziness, hematemesis, melena and syncope. Clinical examination is important to identify any haemodynamic compromise, and worrisome clinical signs include; tachycardia over 100 bpm, systolic blood pressure less than 90 mmHg, cold extremities,

and any other symptom of shock.

Assessment

It is important to assess patients with UGIB to identify patients with life-threatening haemodynamic compromise in order to allow for appropriate resuscitation. There is a lack of good quality studies on the initial assessment of patients with UGIB. Risk factors associated with poor outcome have been identified by descriptive cohort and case series studies. In patients with risk factors their is increased likelihood of uncontrolled bleeding, rebleeding, need for intervention and mortality.

In patients with Upper GI bleeding the main cause of mortality is comorbid disease rather than the actual bleeding itself.^{2,3}The studies show that the absence of significant co-morbidity results in mortality rates as low as 4%.^{5,6,7} Other risk factors include; Age, Liver disease, hypotension and presence of haemetamesis. Rebleeding and continued bleeding is associated with increased mortality therefore it is imperative to identify patients at high risk. The Rockall Scoring system is used clinically to predict mortality based on a combination of clinical and endoscopic findings. The initial Rockall score is derived from age(0-2), co-morbidies(0-3), and shock(0-2).

A large prospective study with 358 patients showed zero mortality for patients presenting with Acute UGIB and a score of 0-1 on the initial Rockall score, and found a significant increase in mortality in those patients with a score of 2 or higher.⁵

Patients with a score of zero have an extremely low risk of death (0.2%)⁵ and re-bleeding, and these patients may be suitable for discharge. If the initial Rockall score is higher than zero, an endoscopy is recommended within 24 hours, with results from endoscopy used to calculate a full Rockall score. Signs of bleeding or evidence of pathology further increase the risk of mortality.

In addition to the full Rockall score, the National Institute for Health and Clinical Excellence⁷ recommend that all patients with acute UGIB should have a Blatchford Score at first assessment. The Blatchford assessment aspires to identify patients who require intervention at the time of presentation into the

hospital, and uses levels of urea and haemoglobin, blood pressure, pulse rate and the presence of particular co-morbidities (e.g liver disease). Any patient with a score greater than zero is defined as being at risk of requiring intervention.

A large retrospective study⁸ found that the Blatchford system was superior at both the initial and full Rockall score in predicting the need for transfusion and endoscopic/surgical intervention and equally effective in predicting the risk of death.

Initial Management

Patients presenting with acute upper gastrointestinal bleed should receive prompt resuscitation and volume replacement if required. The recognition and management of shock is important in reducing the risk of mortality in patients. The British committee for standards in haematology recommend rapid volume restoration, using either colloid or crystalloid solutions, in order for the body to have adequate tissue oxygenation and perfusion.⁹ No studies of good quality are available in comparing colloid and crystalloid solutions in volume restoration of patients with UGIB, however using studies comparing the two solutions in the management of critically ill patients in ICU, show no statistically significant difference between the two solutions.¹⁰

Patients presenting with severe blood loss are likely to have mental state changes/confusion and these patients might not be able to protect their airway, and are at increased risk of aspiration and their are multiple recommendations suggesting elective intubation for these patients.

Patients having massive bleeds should receive blood, platelets and clotting factors in line with hospital/local protocols for managing massive bleeding. The Scottish Intercollegiate Guidelines Network (SIGN) recommend considering red cell transfusion should there be >30% volume loss. Current evidence suggests using a restrictive blood transfusion strategy and aiming for a target haemoglobin of between 7 and 9 g/dL.

SIGN and NICE both recommend that patients with platelet counts lower than 50 x 10⁹/litre should be offered platelet transfusion, and those patients with fibrinogen levels of less than 1g/litre or a INR/APTT greater than 1.5x their normal value should receive fresh frozen plasma. The NICE guidelines recommend not using recombinant factor VIIa except when all other methods have failed.

Once the patients "ABC's" have addressed it is important to assess the patients response to

resuscitation and volume restoration. A study by Kaplan et al.⁹ indicated that using the patients skin temperature in combination with their serum bicarbonate and lactate levels allows assessment on the level of systemic perfusion. Foley catheters are important in allowing continual evaluation of urinary output and hence a guide to renal perfusion.

Endoscopic Therapy

Since the 1980s endoscopy has been used to achieve hemostasis for bleeding ulcers and varices, and the techniques used have continually evolved, with endoscopy now being the main method of diagnosing and managing acute active haemorrhage due to ulcers, with 85-90% of patients responding to endoscopic therapy. Initially endoscopic techniques used included; injection of adrenaline, heater probe/bipolar electrode/laser coagulation. Newer techniques introduced include; endoscopic banding/clipping and argon plasma coagulation.

A large number of RCTs have demonstrated that early endoscopic therapy has reduced rates of; rebleeding, need for emergency interventions and requirement of blood transfusions. However there is not a major statistical reduction in mortality, which may be due to co-morbidities being the major determinant in survival as opposed to the achievement of hemostasis. The NICE guidelines state that patients with black or red spots/ clean ulcer base do not normally require endoscopic intervention, as prognosis is good without intervention. Endoscopic therapy should only be delivered to actively bleeding lesions, non-bleeding visible vessels and ulcers with an adherent blood clot.

Adrenaline/Sclerosant Injection:-

Endoscopic injection of adrenaline into/around areas of bleeding have been found to significantly reduce the risk of rebleeding. The hemostatic effect of adrenaline is due to the vessel vasoconstriction that it induces, and the subsequent platelet aggregation. An adrenaline injection causes a reduction in the volume of bleeding, allowing better visualisation of the ulcer/lesion allowing mechanical/thermal techniques to be used.

RCTs have looked into the effects of using 20,30 and 40ml injections of adrenaline, but no significant difference in the rate of initial hemostasis was found between the three groups. However increased rates of epigastric pain were found particularly in the 40ml groups and hence studies have concluded that the optimal volume of adrenaline is 30ml.¹¹

Injection of sclerosants such as alcohol, polidocanol,

and sodium tetradecyl sulfate are also effective in producing hemostasis, however the use of sclerosants is associated with higher levels of complications, such as tissue necrosis and perforation, compared to the use of adrenaline injections.

Thermal:-

Heater probe coagulation involves the use of electrodes surrounded by a titanium casing and covered with protective material such as Teflon. The probes heat up to 250 degrees celsius. It has been found to have a similar clinical efficacy as adrenaline injections. Risk of complications such as widespread tissue necrosis and mucosal perforation are rare.

Mechanical:-

Endoscopic clipping allows closure of bleeding vessels, and available data shows that it has similar efficacy to thermal endoscopic therapies. One of the first RCTs comparing the clinical efficacy between endoscopic clipping and thermal coagulation found no statistically significant difference in clinical efficacy.¹² A meta-analysis of 15 RCTs comparing the different endoscopic techniques found that definitive hemostasis was higher with clipping (86.5%) than injection (75.4%), and that it was also superior in reducing the need for emergency surgery/interventions. The meta-analysis found that rates of rebleeding/mortality and the need for surgery were similar for mechanical and thermal endoscopic techniques.

Hemostatic Powders:-

Recently the use of hemostatic powders being delivered through the working channels of the endoscope has started being a new way of controlling Upper GI Bleeding. The hemostatic powders currently being used are the Hemospray, EndoStop and the Ankaferd Bloodstopper.

The main advantage of using these powders is that offers more flexibility when dealing with lesions that are hard to access and less precision is required overall compared to other techniques.

The exact mechanism by which these powders produce hemostasis is not fully understood but the scientific hypothesis behind how these powders work is by mechanical tamponade.

Large scale RCTs are required in order to determine if the use of hemostatic powders will significantly change practice but early case reports and smaller studies do show potential for the use of hemostatic powders in a variety of different scenarios.

Combination:-

Multiple RCTs have found that combinations of

endoscopic therapies superior to the use of any single endoscopic therapy, without any significant increase in complications.

For the endoscopic treatment of non-variceal UGIB, NICE recommends a combination of endoscopic therapies rather than monotherapy with adrenaline. The SIGN guidelines for the management of UGIB recommend combinations of endoscopy with adrenaline and the use of either thermal or mechanical modalities.

Management of Patients after first or failed endoscopic treatment:-

Patients who are either deemed to be at high-risk of rebleeding, or who are known to have re-bleed require urgent intervention to reduce the risk of mortality. The NICE guidelines recommend repeat endoscopy and appropriate treatment to any patient; at high risk of rebleeding, known to have rebleed, or when there is doubt that adequate hemostasis was achieved in the first endoscopy.

An RCT randomised patients who rebleed after initial endoscopy to either repeat endoscopy or operative surgery, and found that clinical outcomes were similar in both groups, although more complications occurred in the group who underwent surgery.¹³

The NICE guidelines recommend that unstable patients who rebleed after initial endoscopy should be offered prompt treatment with interventional radiology. Percutaneous angiography allows localisation of bleeding segments and allows the simultaneous embolisation of these points using coils, poly-vinyl alcohol and gelatine sponges. Small descriptive studies have advocated the use of interventional radiology, and have shown that there is high rates of clinical success with low rates of re-bleeding and low rates of complication. An RCT comparing percutaneous angiography and surgery found similar clinical efficacy.¹⁴

If an unstable patient is unable to receive prompt interventional radiology, then they should be referred urgently to surgery.

Medical Management

Patients presenting with UGIB due to a peptic ulcer should receive testing for *Helicobacter Pylori* using either mucosal biopsies on endoscopy or by using a urea breath test. Patients who test positive for *H Pylori* should receive a one week course of eradication therapy. Systematic reviews have shown that *H Pylori* eradication is superior than anti-secretory non-eradication therapies in preventing further

episodes of UGIB from a peptic ulcer. The SIGN and NICE guidelines recommend a further three week ulcer healing treatment after one week of eradication therapy.

Use of PPIs:-

Proton Pump Inhibitors suppress gastric acid production leading to increased gastric pH. A pH of greater than 6 optimises platelet aggregation and clot formation, thereby protecting an ulcer clot from fibrinolysis.¹⁵ A meta-analysis of 24 randomised control trial looking at the use of PPI's for UGIB due to ulcers found a significant reduction in the risk of re-bleeding and the use of surgical/endoscopic intervention.¹⁶ A study by Lao et al.¹⁷ has demonstrated that high dose IV proton pump inhibitors can accelerate resolution of bleeding and reduce need for endoscopic therapy.

Considering the results of multiple large RCTs IV PPI's appear to be a suitable pharmacological therapy in patients with acute bleeding due to a Upper GI ulcer. This is confirmed by both the SIGN and Nice guidelines, both recommending high dose IV PPIs after endoscopic therapy.

However there is a lack of clinical evidence supporting the use of PPIs in patients pre-endoscopically. In one meta-analysis, pre-endoscopic use of PPI in a patient with UGIB found no benefit in mortality/rebleeding or use of surgical/endoscopic intervention.¹⁸ Further studies are required to identify whether PPI use before endoscopy produces better clinical outcomes. Due to lack of data the NICE guidelines discourage the use of acid-suppression drugs(PPIs or H2 Receptor Blockers) before endoscopy to patients with suspected non-variceal bleeding.

Tranexamic Acid and Somatostatin:-

Tranexamic acid is an antifibrinolytic that inhibits the activation of plasminogen to plasmin, and is used to reduce blood loss during surgery and in certain medical conditions. Very few trials have been carried out on the role of antifibrinolytics in the treatment of UGIB. From the limited data available it is possible that Tranexamic acid may be of benefit in the treatment of UGIB but large robust studies are required in order to identify whether the use of Tranexamic acid is suitable in the treatment of UGIB.

Somatostatin is a peptide hormone, which has been found to achieve vasoconstriction in the blood vessels. Small individual trials have shown that somatostatin and its analogues could reduce the risk of rebleeding and need for surgery. Further studies are required to identify the clinical efficacy of somatostatin in UGIB, currently it is not recommended for routine use unless

in settings where endoscopy is unavailable.

Conclusion

Upper Gastrointestinal bleeding is a common life-threatening medical emergency which requires prompt investigation and management. It is important to stratify patients to identify those who require more urgent treatment, and it also important to identify patients who are hemodynamically compromised and to start prompt resuscitation and volume restoration in these patients.

Endoscopy is an important tool in the investigation and management of UGIB, and patients who require endoscopic treatment should receive a combination of endoscopic therapies. Mucosal biopsies should be taken to identify if H.Pylori is present, and treatment to eradicate H.Pylori should be started if its presence is confirmed.

IV Proton Pump Inhibitors should be started on suitable patients post-endoscopically.

Further studies are required to identify whether PPI use pre-endoscopically has any clinical merit. Studies are also required to identify whether traneximic acid and somatostatin serve any clinical use in the treatment of UGIB.

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