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Management of non-variceal Upper G.I Bleed

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Abstract

Acute Upper Gastro-intestinal bleeding(UGIB), defined as gastrointestinal bleeding from a source that is proximal to the ligament of treitz, is a potentially life threatening medical emergency.Â 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 postal gastropathy.
Upper Gastro-intestinal bleeding is a common cause of acute 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 changes in initial management and the use of advanced therapeutic endoscopy mortality has not significantly improved in the past fifty years.

Introduction

Acute Upper Gastro-intestinal bleeding(UGIB), defined as gastrointestinal bleeding from a source that is proximal to the ligament of treitz, is a potentially life threatening medical emergency.Â 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 postal gastropathy.
Upper Gastro-intestinal bleeding is a common cause of acute 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 changes in initial management and the use of advanced therapeutic endoscopy mortality has not significantly improved in the past fifty 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 one hundred bpm, systolic blood pressure less than ninety mmHg, cold extremeties, and any other symptom of shock.

Assessment:-
A rapid initial assessmentÂ is important to triage patients with UGIB and to identify patients with life-threatening haemodynamic compromise in order to allow for appropriate resuscitation. 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, re-bleeding, need for intervention and mortality.
In patients with Upper GI bleeding the main cause or mortality is comorbid disease rather than the actual bleeding itself.2,3The 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.
Re-bleeding and uncontrolled bleeding is associated with higher rates of mortality therefore it is imperative to identify high risk patients. Â
The Rockall Scoring system is used clinically to predict mortality based on both 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
In the study patients with a score of zero were found to have a very low risk of death (0.2%)5 and re-bleeding, and these patients may be safely discharged. If the initial Rockall score is higher than zero, a endoscopy is recommended with 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 Excellence(NICE)7 recommend that all patients with acute UGIB should have a Blatchford Score at first assessment. The Blatchford assessment aims to identify patients who require intervention at the time of presentation into the hospital, and uses levels of urea and haemoglobin, blood pressure, heart 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 prediciting the need for transfusion and endoscopic or surgical intervention and equally effective in predicting the risk of death.

Initial Management

Patients presenting with acute upper gastrointestinal bleed should receive prompt rescusitation 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 haemotology recommend rapid volume restoration, usuing either colloid or chrystalloid solutions, in order for the body to have adequete tissue oxygenation and perfusion.9 No studies of good quality are available in comparing colloid and chrystaloid 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 require endotracheal intubation if they are deemed to be unable to protect their airway, as they are at increased risk of aspiration.
Â Patients having massive bleeds should receive blood, plateletes and clotting factors in line with hospital/local protocals for the management of major haemorrhage. The scottish intercollegiate Guidelines network(SIGN) recommend considering red cell transfusion should there be >30% volume loss. 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 ABCâ€™s have addressed it is important to assess the patients response to resuscitation and volume restoration. A clinical paper by Kaplan et al.9 found that using the patients tympanic temperature in combination with their serum bicarbonate levels allows assessment on the level of systemic perfusion. Foley catheters are important in allowing an indication of the patientsÂ urinary output and allow an assessment of the patients fluid status.

Endoscopic Therapy

Since the 1980s endoscopy has been used to achieve haemostasis 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 their 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 hemostatisis. The NICE guidelines state that patients with red or black spots/ visually clear ulcer bases do not normally require endoscopic intervention, as prognosis is good without intervention. Therapeutic endoscopy should ideally only be used on 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 scleosants 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 celcius. It has been found to have a similiar clinical effecicay 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 similiar efficacy to thermal endoscopic therapies. One of the first RCTs comparingÂ the clinical efficacy between endoscopic clipping and thermal coagulation found no stastically significant difference in clinical efficacy.12 A meta-analysis of 15 RCTs comparing the 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 where similiar for mechanical and thermal endoscopic techniques.

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 their 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 where similiar in both groups, although more complications occured 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 usuing 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 usuing either mucosal biopsies on endoscopy or by using a 13C-urea breath test. Patients with a positive 13C-urea breath test should receive a one week course of triple eradication therapy. Meta-analysis has 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. Â

Use of PPIs:-
Proton Pump Inhibitors suppress gastric acid production leading to increased gastric pH. A pH of greater than six 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 PPIâ€™s for UGIB due to ulcers found a statistically 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 PPI can accelerate resolution of bleeding and reduce need for endoscopic therapy.
Considering the results of multiple large RCTs IV PPIâ€™s appear to be a suitable pharmcalogical 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-suppresion drugs(PPIs or H2 Receptor Blockers) before endoscopy to patients with suspected non-variceal bleeding.

Tranexamic Acid and Somatostatin:-
Tranexamic acid is an anti-fibrinolytic that binds to lysine receptors on plasminogen
inhibiting its activation to plasmin, and it is used to minimise the amount of blood lost 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 high quality studies are required to identify the clinical efficacy of somatostatin in UGIB.

Conclusion(s)

Upper Gastrointestinal bleeding is a common life-threatening medical emergency which requires immediate 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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