International Journal Dental and Medical Sciences Research
Volume 4, Issue 1, Jan-Feb 2022 pp 223-226 www.ijdmsrjournal.com ISSN: 2582-6018

Study of Role of pharmacotherapy in management of UGI bleed

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Submitted: 15-01-2022 Revised: 23-01-2022 Accepted: 25-01-2022

ABSTRACT
Upper gastrointestinal bleeding remains a major problem associated with high morbidity and mortality. Many decades ago, the mortality of upper GI bleed was extremely high .However, with better understanding of physiology of resuscitation , blood transfusion and adjunct role of pharmacotherapy, mortality in upper G I bleed did drop substantially. Advent of diagnostic oesophago-gastro-duodenoscopy did raise expectation of reducing the mortality but it failed to do so. However, it did help in the diagnosis. When therapeutic endoscopy came to the fore in its management, mortality did reduce little further but it has not become still zero and is hovering around 2– 15%. The management of UGI bleed can be divided into pre-endoscopic management which comprises of resuscitation and assessment, medical therapy, endoscopy both for diagnosis and therapy ,interventional radiology, surgery and followup. The UGI bleed can broadly be divided into variceal and Non-variceal bleed and both conditions have different management strategies after initial similar treatment of resuscitation and assessment. There are scoring systems for severity stratification of upper G I bleed. Many new methods are now available for endo haemostasis. In this article we would be focusing on adjunt and supportive role of pharmacoltherapy in management of UGI bleed.
Keywords UGI Bleed .Varicealbleed . NonVaricealbleed . Pharmacotherapy

I. INTRODUCTION

The incidence of upper gastrointestinal bleed is approximately 100 cases/100,000 population per year. Worldwide acute gastrointestinal bleed is a common cause of hospitalization, and it is a life-threatening situation[1].

II. METHOD

Worldwide acute gastrointestinal bleed is a common cause of hospitalization, and it is a life-threatening situation. The incidence of upper gastrointestinal bleed is approximately 100 cases/100,000 population per year [1]. Mortality rate is increased by using increasing nonsteroidal anti-inflammatory drugs and the high prevalence of Helicobacter pylori infection in patients with peptic ulcer bleeding [2]. Upper gastrointestinal bleeding is two times more common in men compared to women and increases in prevalence with age [3]. Age-related comorbid diseases often complicate the upper gastrointestinal bleeding process and are the major cause of death rather than the bleed itself. Upper GI-related mortality rates have decreased slightly over the past two decades but are still estimated to be 2–15% [4]. Mortality from peptic ulcer bleeding is still 10–13% [5]. However, appropriate management of patients has been shown to improve outcomes. In the last two decades, there have been major advances in the management of acute gastrointestinal bleed. 76 patients of UGI bleed were analysed for role various drugs used in their management.

III. DISCUSSION

Acute upper GI bleeding defined as bleeding proximal to ligament of Treitz [6]. The manifestations of upper GI bleeding are haematemesis, coffee ground vomitus and melena with or without haemodynamic compromise. In severe upper gastrointestinal bleeding, patient also gives history of Hematochezia; otherwise, it is a rare presentation in upper gastrointestinal bleeding. Hematochezia is typically associated with orthostatic hypotension. The causes of acute gastrointestinal bleeding are divided into variceal and non-variceal bleeding. The majority of episodes of acute upper gastrointestinal bleeding (AUGIB) are secondary to non-variceal causes. Peptic ulcer disease (PUD) remains the most common cause of AUGIB, despite reductions in PUD incidence and mortality over the last three decades. These reductions are largely attributable to developments in proton pump inhibitors, endotherapy, Helicobacter pylori eradication and reductions in use of nonsteroidal anti-inflammatory drugs (NSAIDs). In last two decades, the proportion of variceal bleeding is also increased due to increase in concomitant liver disorders.

Causes of non-variceal bleeding

1. Gastroduodenal peptic ulcer (20–50%) 2. Gastroduodenal erosions (8–15%) 3.

International Journal Dental and Medical Sciences Research
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Oesophagitis (5–15%) 4. Mallory–Weiss tear (8–15%) 5. Arteriovenous malformations/GAVE (5%) 6. Others like Dieulafoy's lesion, upper GI tract malignancy

2. Varicealhaemorrhage is usually secondary to oesophagealvariceal bleeding but can be due to gastric varices, congestive gastropathy and uncommonly ectopic varices in the upper GI tract. Initial Evaluation The main goal of initial evaluation is to assess the severity of the bleeding, identify potential source of bleeding and determine if there are conditions present that may affect subsequent management. It consists of clinical history, physical examination, blood investigations and, some cases, nasogastric lavage. This information is used to guide decision regarding triage, resuscitation, empiric medical therapy, diagnostic testing and management. No single factor is sufficiently predictive of UGIB severity to be used for patient triage. The most predictive factors are history of malignancy or cirrhosis; presentation with fresh blood hematemesis; signs of hypovolaemia including hypotension, tachycardia and haemodynamic shock; and a haemoglobin less than 8 g/dl at initial presentation. Pre-endoscopic Management The goal of treatment in massive upper GI bleeding is to correct shock and coagulation abnormalities and to stabilize the patient so that further evaluation and treatment can proceed. Resuscitation and Assessment All patients with AUGIB should be promptly assessed and triaged for early fluid/blood product resuscitation and endoscopy [6]. All patients with haemodynamic instability or active bleeding should be admitted to an intensive care unit for resuscitation and close observation. The priority should be to ensure a safe airway and to maintain adequate oxygen carrying capacity, especially in older patients with coexisting cardiopulmonary disease, the use of supplemental oxygen and transfusion of plasma expanders with the use of packed red cells if tachycardia or hypotension is present or if the haemoglobin level is less than 10 g/dl.. Two l6 or 18 gauge intravenous cannula are used for fluid resuscitation. The main aim of this treatment is reversal of both hypovolemic shock and blood loss using administration of intravenous fluids and blood components if necessary. The target haemoglobin level is 70–90 g/l. For patients being treated with anticoagulants, such as warfarin, correction of an increased international normalized ratio to ≤ 2.5 should be considered. The gastrointestinal tract is the site of haemorrhage in 41% of patients with a bleeding episode associated with warfarin therapy. Insertion of nasogastric tube is controversial in all patients with suspected acute upper gastrointestinal bleeding. However, several studies did not show any difference between those who underwent nasogastric tube lavage and those who did not with regard to mortality, length of hospital stay, surgery or transfusion requirement. The presence of red blood or coffee ground material in the aspirate also confirms the diagnosis. In 15% of cases, there is no bloody aspirate but found high risk lesions in endoscopy. Nasogastric lavage is also useful in removing particulate matter, fresh blood and clots from the stomach to facilitate endoscopy. NICE and SIGN advocate a two-step risk assessment strategy. [7]
3. Variceal Assessment The assessment is based on the presence of established varices or risk factors for portal hypertension, such as established cirrhosis, stigmata of chronic liver disease and biochemical and radiological findings. The risk stratification is done using with Blatchford and Rockall scoring systems that predict endoscopic and clinical outcomes in terms of re-bleeding and morality in acute gastrointestinal bleeding [8]

Pharmacotherapy

Acid Suppression Administration of intravenous proton pump inhibitors is recommended in all patient of suspected peptic ulcer bleeding. A strongly acidic environment leads to inhibition of platelet aggregation and plasma coagulation as well as to lysis of already formed clots. Proton pump inhibitors neutralize the acidic environment and stabilize the blood clots [11]. In long-term use, they will help in mucosal healing. A meta-analysis of 24 randomized controlled trials that evaluated proton pump inhibitors concluded that use of PPI reduces the re-bleeding, the need for repeat endoscopy for continued bleed and surgery in peptic ulcer diseases [9].

Pro-kinetics

Both erythromycin and metoclopramide have been used in patients with acute upper gastrointestinal bleeding. The main goal of using pro-kinetics is to improve gastric visualization at the time of endoscopy by clearing the stomach of blood, clots and food residue. Use of pro-kinetics agents before endoscopy will reduce the no of repeat endoscopy but does not reduce the hospital stay, need for blood products and need of surgery. Erythromycin promotes gastric emptying by acting

International Journal Dental and Medical Sciences Research
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as agonist of motilin receptors. The studies suggest that single dose of intravenous erythromycin given 20 to 120 min before endoscopy can significantly improve the visibility, shorten endoscopic time and reduce the need of second look endoscopy .

Somatostatin and Its Analogues

Somatostatin and its analogues octreotide are used in the treatment of variceal bleeding. But they also reduce the risk of bleeding due to non-variceal causes [10]. It is not used routinely in patients with acute non-variceal bleeding, but it can be used as adjunctive therapy in some cases.

Antibiotics

Prophylactic antibiotics are recommended in cirrhotic patients because bacterial infections are present in up to 20% of patients with cirrhosis who are hospitalized with gastrointestinal bleeding. Multiple trials suggest that use of prophylactic antibiotics reduces the incidence of infectious complication and recurrent bleeding and also decreased the mortality.

Endoscopy Upper GI endoscopy is the diagnostic modality of choice for acute upper GI bleeding. Endoscopy has a high sensitivity and high specificity for locating and identifying bleeding. International consensus guidelines recommend that endoscopy should be performed within 24 h of presentation [11]. Injection Therapy Injection therapy controls the bleeding by acting like hydrostatic tamponading pressure and vasoconstriction and causes a secondary inflammatory reaction. This is an easier procedure and inexpensive. Missed injection can cause brisk bleeding and subsequently mask the visible area of the treatment. Most commonly used materials are epinephrine, 50%dextrose, ethanol and polidocanol. Most common side effect with polidocanol and ethanol is necrosis and sometimes perforation which coagulates the bleeding site. A clot in an ulcer bed should be washed, through the endoscope, to determine whether it remains adherent. Intravenous proton pump inhibitors are sufficient for adherent clot, and no endoscopic procedure is needed. One emerging modality is a haemostatic powder composed of nanoparticles of inorganic proteins that are sprayed onto the bleeding lesion. It is a suitable choice for bleeding lesions such as haemorrhagic gastritis, portal hypertensive gastropathy, gastric antral vascular ectasia, radiation-induced mucosal injury and malignancy-related bleeding [12].

Post Endoscopic Management

Proton Pump Inhibitors Continuous use of proton pump inhibitors reduces the recurrent bleeding, transfusion requirement and hospital stay but does not decrease the overall mortality of the patients [13]. Helicobacter Pylori Helicobacter pylori infection is the single most important cause for peptic ulcer disease. Identification and eradication of H. pylori infection decrease the re-bleeding rate of peptic ulcer disease. H. pylori identified by ideally during endoscopy with biopsy methods, urea breath testing or monoclonal stool antigen testing [8]. According to NICE guideline, a 7-day twice daily regimen consisting PPI and dual antibiotic therapy for eradication of H. pylori is given [14] which can be extended to 1 more week. Proton pump inhibitor is continued up to 4 weeks, but it is stopped 2 weeks before reassessment.

Management of Variceal Bleeding

Once variceal bleeding suspected octreotide, a somatostatin analogue is usually started as soon as possible. It acts as a direct splanchnic vasoconstrictor. Once initiated, octreotide should be maintained for 2–5 days. This will reduce portal pressure. It also increases systemic vasoconstriction and has been associated with myocardial infarction and small bowel necrosis. Terlipressin is a long acting safer analogue of vasopressin that can reduce mortality from variceal bleeding. It is safer than vasopressin and stimulates renal function and increases the survival time in patients with bleeding oesophageal varices. Endoscopy Urgent endoscopy should be performed within 12 h of onset of bleeding. The aim of endoscopy therapy is to reduce the variceal wall tension by obliteration of the varix. Endoscopic Sclerotherapy(EST) The principle behind sclerotherapy is to induce thrombosis of the vessel and inflammation of the surrounding tissues. In EST, injection of sclerosing agent is given either intravariceally or lumen or adjacent to the varix. The minor complications of sclera-therapy occur within 48 h of procedure that include fever, retro sternal pain, temporary dysphagia and asymptomatic pleural effusion, and other transient chest radiographic changes are very common. oesophageal varices [15].

After endoscopy, secondary prophylaxis is used to prevent rebleeding. Overall mortality rate of re-bleeding cases after endoscopy therapy is 30%. It is most common in large varices.

Non-selective Beta Blockers

At present, pharmacological therapy for secondary prophylaxis is with non-selective beta blockers, such as propranolol or carvedilol. Propranolol reduces portal pressure through splanchnic vasoconstriction and reduced cardiac output. Carvedilol has vasodilator properties due to alpha1 receptor blockade. It is more effective than propranolol to reduce the portal pressure. But carvedilol is not a drug of choice, it is an

alternative for propranolol only. Use of the non-selective beta blockers reduces the re-bleeding and decreases the mortality rates of variceal bleeding. EVL Patient should be advised elective endoscopy 2–4 weeks after EVL for varicealhaemorrhage EVL is eradication of varices. After successful eradication of varices, patient should be advised with endoscopy at 3 months, then 6 monthly thereafter . Recurrent varices should be treated with variceal band ligation until eradication. This procedure is associated with lower re-bleeding rates and a lower frequency of oesophageal strictures. EST It is performed at weekly intervals, and 4–5 sessions are usually for eradication of varices.

The management modality techniques are improved nowadays that is why surgery is not a primary therapy for UGI bleed. Use of pharmacotherapy at various stages does play significant role in overall management of UGI bleed.A good understanding of various drugs used and its side effects is essential for successful management of UGI bleed.Management of UGI bleed is multidisciplinary and a good team work is essential for better management of UGI bleed.

REFERENCES

[1]. Fallah MA, Prakash C, Edmundowicz S (2000) Acute gastrointestinal bleeding. Med Clin North Am 84:1183–1208

[2]. Sánchez-Delgado J, Gené E, Suárez D et al (2011) Has H. pylori prevalence in bleeding peptic ulcer been underestimated? A metaregression. Am J Gastroenterol 106(3):398–405

[3]. Longstreth GF (1995) Epidemiology of hospitalization for acute upper gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol 90(2):206–210

[4]. Liu NJ et al (2007) Outcomes of bleeding peptic ulcers: a prospective study. J GastroenterolHepatol23:e340–e347

[5]. Hearnshaw SA et al (2011) Acute upper gastrointestinal bleeding in the UK: patient characteristics, diagnoses and outcomes in the 2007 UK audit. Gut 10:1327–1335

[6]. Scottish Intercollegiate Guidelines Network (SIGN). Management of acute upper and lower gastrointestinal bleeding. September 2008. http://www.sign.ac.uk/assets/sign105.pdf (accessed 15/10/ 16)

[7]. National Institute for Health and Care Excellence (NICE). Acute upper gastrointestinal bleeding in over 16s: management. June 2012. https://www.nice.org.uk/guidance/cg141 (accessed 15/ 10/16

[8]. Gralnek I, Dumonceau J, Kuipers E et al (2015) Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 47:1–46

[9]. Kaviani MJ, Hashemi MR, Kazemifar AR et al (2003) Effect of oral omeprazole in reducing re-bleeding in bleeding peptic ulcer a prospective, double-blind, randomized clinical trial. Aliment PharmacolTher 17:211

[10]. Imperial TF, Birgisson S (1997) Somatostatin or octreotide compared with H2 antagonists and placebo in the management of acute nonvariceal upper gastrointestinal haemorrhage: a metaanalysis. Ann intern Med 127:1067

[11]. National Confidential Enquiry into Patient Outcome and Death (NCEPOD) (2015) Time to get control? A review of the care received by patients who had a severe gastrointestinal haemorrhage. http://www.ncepod.org.uk/2015report1/downloads/ TimeToGetControlFullReport.pdf (accessed 15/10/16)

[12]. Sung J, Luo D, Wu J, Ching JY, Chan FK, Lau JY, Mack S, Ducharme R, Okolo P, Canto M, Kalloo A, Giday SA (2011) Early clinical experience of the safety and effectiveness of Hemospray in achieving hemostasis in patients with acute peptic ulcer bleeding. Endoscopy 43:291–295

[13]. Lau J, Sung JJ, Lee KK, Yung MY, Wong SK, Wu JC, Chan FK, Ng EK, You JH, Lee CW, Chan AC, Chung SC (2000) Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. N Engl J Med 343:310–316

[14]. NICE (2014) Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. https://www.nice.org.uk/guidance/cg184/chapter/1-recommendations#helicobacter-pyloritesting-and-eradication (accessed 15/10/16)

[15]. McCarty T, Njei B (2016) Self-expanding metal stents for acute refractory esophageal variceal bleeding: a systematic review and meta- analysis. Dig Endosc 28:539–547