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Management of acute upper gastrointestinal bleeding

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Abstract

The purpose of this review is to summarize the management of upper gastrointestinal bleeding (UGIB). This entity has an annual incidence of 48 to 160 cases per 100,000 adults, with a mortality rate of 10% to 14%. Classically, UGIB is divided in non-variceal hemorrhage and variceal hemorrhage, being more frequently observed the first one (80%-90%). The initial management includes investigate about the form of presentation, color and characteristics of the hemorrhage, the age of the patient, presence of coagulopathy, disease or cardiovascular risk factors, use of nonsteroidal anti-inflammatory drugs (NSAIDs), antiaggregants or anticoagulants, previous episodes of hemorrhage, endoscopy, alcohol intake, etc. However, this process must not delay the initiation of hemodynamic resuscitation in patients with patients with ongoing bleeding. To stratify these patients, risk scores including Blatchford score and Rockall score are developed.

Diagnosis is realized through endscopy, which allows definitive treatment. This treatment is improved providing pre-endoscopy as well as post-endoscopy therapy, including proton pump inhibitor (PPI) therapy. In variceal hemorrhage, if endoscopy therapy fails, balloon tamponade or transjugular intrahepatic portosystemic shunt (TIPSS) are indicated.

The purpose of this review is to summarize the initial management of acute UGIB, especially in the Emergency Department.

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Introduction

Upper gastrointestinal bleeding (UGIB) is the loss of blood through the gastrointestinal tract whose origin proximal to the Treitz angle [1]. This entity has an annual incidence of 48 to 160 cases per 100,000 adults [2-4], with a mortality rate of 10% to 14% [5]. The rates of UGIB are higher in men and the elderly, and poorly tolerated shock, with destabilisation of underlying organ disease and severe coexistent comorbidities increase the risk of mortality [6].

Classically, UGIB is divided in non-variceal hemorrhage and variceal hemorrhage. **Table 1** summarizes the main etiologies of acute UGIB [7].

Acute UGIB manifests as vomiting of blood (haematemesis) and/or passage of black, tarry stools (melena). The last one may be caused by bleeding from the small intestine downwards the duodenum. Tarry stools are usually seen if more than 50 mL to 100 mL of blood is lost per day. The passage of bright red blood per rectum (haematochezia) could be caused by severe brisk bleeding. If more than 10% to 20% of the total intravascular blood volume is lost, haemodynamically instability (hypotension, tachycardia) is observed [8].

The purpose of this review is to summarize the initial management of acute UGIB, especially in the Emergency Department.

Initial management

As we described previously, UGIB could be manifested as haemodynamically instability. Due to that, anamnesis should not delay resuscitation if it is necessary.

During the interview, it is important to ask about the quality and quantity of vomited blood (fresh red or coffee grounds), presence of melaena, syncope and alcohol consumption. Significant comorbidities, any past history of UGIB should be also known. In addition, use of non-steroidal anti-inflammatory drugs (NSAIDs), antiplatelet agents, anticoagulants, corticosteroids, and selective serotonin reuptake inhibitors (SSRIs) should be also noted due the increased risk of gastrointestinal (GI) bleeding observed with its intake [9].

Physical exploration includes documentation of cardiac frequency, blood pressure, and capillary refill time. These parameters should be monitored, including urine output and blood glucose. In addition, stigmata of chronic liver disease suggest variceal hemorrhage [7].

Attending to resuscitation, in the presence of hypovolaemic shock, should be administered 1-2 liters of crystalloids solutions [10]. Blood transfusion is also recommended if it is necessary. International consensus guidelines recommend it if the haemoglobin (Hb) level is ≤70 g/L [11]. On the other hand, some authors suggested transfusion in patients with clinical significant coexisting illness and red blood cell count of 90 g/L or delayed therapeutic intervention [12,13]. However, recent evidence has shown that adopting a restrictive transfusion strategy, and not transfusing until the Hb falls below <70 g/L, is associated with improved survival, a reduced risk of rebleeding and complications [14]. Coagulopathy should be also corrected. The National Institute for Health and Care Excellence (NICE) in a recent guideline specified the following criteria to correct it [15]:

- Platelets should only be given if the patient is actively bleeding or haemodynamically unstable and has a platelet count of $<50\times10^9$/L.

- Fresh frozen plasma should be given if the fibrinogen level is <1 g/L or the prothrombin time (PT) or activated partial thromboplastin time is >1.5 times normal.

- Prothrombin complex should be provided to those on warfarin and actively bleeding.

- Recombinant factor VIIa should only be used when all of the above measures have failed.

Finally, all patients admitted in the Emergency Department due to UGIB should be stratified into low and high risk according to validated prognostic scales. The Blatchford score (**Table 2**) should be used in every patient on initial presentation [16]. The Rockall score (**Table 3**) may also be used, but requires the realization of an endoscopy to be fully completed [17].

Diagnosis

Diagnosis process is based in laboratory test as well as endoscopy. The first one is required to elaborate risk scores previously described and provide blood transfusion if it is necessary. In addition, lactate levels are related with outcomes [18-20]. In addition, a systematic review found that a blood urea nitrogen (BUN):Cr ratio of greater than 30 is 93% specific for a UGIB, with a positive likelihood ratio of 7.5 [21].

Endoscopy

Endoscopy is the initial procedure in patients with LGIB due to its diagnosis as well as potentially therapeutic benefits. Adequate preparation is necessary to improve the outcomes of this technique. Proton pump inhibitor (PPI) therapy is commonly given to patients prior to endoscopy; however, this treatment has been not shown to alter clinically important outcomes such as mortality, rebleeding rate and need for surgery [22]. Due to that, this treatment should not delay an early endoscopy [7]. Similar results are observed with tranexamic acid (TXA). This drug have been shown to be beneficial in critically ill trauma patients due to the significant reduce of the risk of death [23]. However, ilts role in acute UGIB remains unclear. A large study examining the potential benefit of TXA with plans to enroll 8000 patients is currently under way [24].

Early endoscopy (within 24h) provides the opportunity to realize a prompt treatment, which reduces transfusion requirements, rebleeding and need for surgery [25].

Treatment

UGIB treatment depends of the etiology. Due to that, we are going to summarize it attending to the presence or absence of variceal.

Non-variceal hemorrhage

Endoscopy provides a range of techniques to stop as well as prevent further bleeding. It includes injection (adrenaline), thermo-ablative (coagulation probes) and mechanical (clipping) therapies. Nowadays is suggested to combine these techniques to improve the outcomes [7,26]. Adrenaline injection promotes a local vasoconstriction and tamponade effect, which allows stopping the bleeding applying a thermo-ablative or mechanical therapies on the vessel.

If the initial endoscopic treatment was unsatisfactory, repeat endoscopy should be considered when initial endoscopic treatment was considered to be suboptimal or a high risk of rebleed-

ing is observed, it is suggested to repeat the endoscopy [27].

New treatments as topical haemostatic powders have been added to the therapeutic options of UGIB in selected cases. These therapies include Hemospray, Endoclot, and Blood Stopper. Hemospray effect is based in its capacity to absorb water and forms a cohesive and adhesive gel in contact with, which stops bleeding through a combination of mechanical effects (tamponade) and possible pro-coagulatory effects on platelets and clotting factors [28-30]

If endoscopic treatment fails, interventional radiology for angiographic embolisation or surgery should be realized [7].

After the endoscopy PPI therapy is suggested to be provided in patients with high-risk endoscopic lesions treated endoscopically. A meta-analysis observed that omeprazole 80 mg bolus followed by 8 mg/h infusion for 72 h decreased mortality ratio in high risk patients [31]. These results were not observed in patients with low as well as intermediate risk. .PPI treatment should be provided during 72h due to 60% to 76% of re-bleeding occurred in the first three days [32-34].

In addition, a urease test should be routinely performed at the time of endoscopy in patients with peptic ulceration to despite Helicobacter pylori infection. H. pylori eradication is effective in reducing recurrent peptic ulcer bleeding and is more effective than PPI therapy alone [35]. If urease test is positive, it is recommended togive PPI therapy for at least 3 weeks after eradication [36]. Finally, if antiplatelet and anticoagulant agents need to be given after resolution of UGIB, concomitant treatment with omeprazole significantly reduced the rate of ulcer bleeding with no significant increase in cardiovascular events [37].

Variceal hemorrhage

Endoscopic therapy

In oesophageal varices, variceal band and sclerotherapy provide similar results iin terms of rebleeding rate, mortality rate and rate of death due to rebleeding [38]. Due to that, hospital conditions, operator experience, and the characteristics of esophageal varices should be considered to choice the treatment.

Gastric varices may be classified according to their location and relationship to oesophageal varices. Gastroesophageal varices (GOV) type 1 are defindes as those that continue from oesophageal varices and extend for <5 cm along the lesser curvature of the stomach. If gastroesophageal varices extend towards the fundus along the greater curvature are defined as GOV type 2. On the other hand, isolated gastric varices (IGV) are not in continuation with oesophageal varices and may be in the fundus (IGV type 1) or anywhere distally (IGV type 2) [7]. A Cochrane review observed cyanoacrylate superglue injection is more effective than band ligation in terms of initial haemostatic control, rebleeding rate, need for blood transfusion and treatment-induced ulcer bleeding. However, due to the very low quality of the evidence, authors did not provide a preference of treatment [39].

Pharmacotherapy for variceal bleeding

Vasoactive drugs reduce portal hypertension by decreasing portal blood flow. These treatments include terlipressin and somatostatin or its analogues (such as octreotide). Terlipressin treatment is preferred due to it is the only one to have shown a reduction in mortality [40]. However, recent studies observed similar results in both treatments in oesophageal varices as well as gastric varices [41,42]. Both treatments should be started promptly if variceal bleeding is suspected and continued after endoscopy for at In addition, cirrhotic patients with variceal bleeding which have sepsis on admission, should be also treated with antibiotic. This effect is produced due to its capacity to mitigate the sepsis-induced systemic endotoxin release, which promotes an increase in portal pressure due to local vasoconstriction and a rise in intrahepatic vascular resistance [43]. Antibiotics which could be given include ceftriaxone, norfloxacin, ciprofloxacin or other broad spectrum antibiotics such as tazocin.

Like non-variceal hemorrhage, PPI therapy is commonly employed after variceal band ligation due to the decrease of the risk of bleeding [44] as well as the decreased number of ulcers after variceal banding [45].

Rescue therapy for variceal bleeding

10%–20% of variceal bleeding continues despite combined pharmacological and initial endoscopic therapy. If there is cardiovascular compromise, balloon tamponade with a Sengstaken–Blakemore tube can be life-saving. This technique is also effective in massive variceal bleeding where endoscopy fails to identify or adequately treat bleeding varices. Successful outcomes are observed in around 80% of patients. However, complications including aspiration, tube migration and oesophageal necrosis or perforation occur in as many as 20% [46].

In patients with variceal bleeding, an hepatic venous pressure gradient (HVPG) of >20 mmHg is associated with failure to control bleeding as well as higher rate of rebleeding and higher 1-year mortality [47]. Transjugular intrahepatic portosystemic shunt (TIPSS) is the percutaneous placement of a stent between the hepatic vein and intrahepatic segment of the portal vein in order to reduce portal pressure. A reduction in HVPG to <12 mm Hg or by 20% from the baseline value reduces the risk of variceal haemorrhage and improves survival. Complications of this treatment include hepatic encephalopathy due to systemic exposure to toxin-containing blood and heart failure due to the sudden increase in cardiac preload [48].

Secondary prevention of variceal haemorrhage

Without additional therapy, patients affected by a variceal bleeding episode have a 60% chance of rebleeding within 1–2 years with a 33% mortality [7]. β-blockers such as propranolol and carvedilol has been shown to significantly reduce rebleeding and mortality [49,50]. The combination of this type of drugs and nitrates is superior to β-blocker monotherapy but is associated with more side effects and is poorly tolerated [51]. In addition, periodic gastroscopy with or without band ligation if it is necessary have been observed to significantly reduce the median rebleeding rate to around 32% [52]. Patients who rebleed despite optimal pharmacological and endoscopic therapy or those who are intolerant to that approach, can be considered for TIPSS.

Tables

Table 1: Main cause of acute upper gastrointestinal bleeding. UGIB: Upper gastrointestinal bleeding. NSAIDs: non-steroidal anti-inflammatory drugs

NON-VARICEAL UGIB (80-90%):	VARICEAL UGIB (10-20%)
Gastroduodenal peptic ulcer (40-50%): It is the most frequent cause. Mainly by Helicobacter pylori and intake of (NSAIDs).	**Hemorrhage due to esophageal varicose veins *(75%)* or gastric varicose veins (10%):** They are frequently observed in cirrhotic patients with a mortality rate of 30%. High risk of sepsis and spontaneous bacterial peritonitis.
Acute lesions of the gastroduodenal mucosa (erosive and hemorrhagic gastritis) (10-15%): Caused by unsuccessful endoscopic therapy, prolonged use of NSAIDs, stress and alcohol intake.	**Hemorrhage due to gastropathy of portal hypertension:** It is very rare. It is produced by dilatation of venules and capillaries of mucosa and gastric submucosa in the absence of erosive or inflammatory phenomena, which is characteristically associated with portal hypertension.
Mallory-Weiss syndrome (15-20%): In patients with a history of vomiting with intense arches that lead to hemorrhages and even perforation. Lacerations occur in the gastroesophageal junction. It yields spontaneously in most cases.	
Esophagitis (5-10%): Uncommon cause. It usually presents as occult hemorrhage. Endoscopic treatment is useful in case of ulcerations or bleeding visible vessels.	

Table 2: Blatchford score. Scores of 0-3 points are patients categorized as low risk. These patients may be discharged with an upper digestive endoscopy in 24-48 hours. Score values higher than 3 points require an urgent upper gastrointestinal endoscopy.

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	
• ≥12.0 <13.0	1
• ≥10.0 <12.0	3
• ≥10.0	6
Haemoglobin (g/L) for women	
• ≥10.0 <12.0	1
• ≥10.0	6
Systolic blood pressure (mmHg)	
• 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

Table 3: Rockall score. Scores <2 points are patients categorized as low risk. Scores between 3-4 points implies intermediate risk. Finally, scores higher than 5 are patients categorized as high risk. However, patients categorized as low risk but present blood in the stomach, hematocrit less than 30% or hypotension increase its score to intermediate risk.

ROCKALL SCORE				
Variable	**Score**			
	0	1	2	3
Age	No shock	Pulse >100, Systolic blood pressure >100 mmHg	Systolic blood pressure <100 mmHg	
Shock	No shock	Pulse >100, Systolic blood pressure >100 mmHg	Systolic blood pressure <100 mmHg	
Comorbidity	Nil major		Heart failure, ischaemic heart disease, major comorbidity	Renal failure, liver failure, metastatic cancer
Endoscopy	None disturbs or Mallory–Weiss	All other diagnoses	Gastrointestinal malignancy, blood, adherent clot, spurting vessel	

Conclusions

UGIB represents approximately 48 to 160 cases per 100,000 adults, with a mortality rate of 10% to 14%. A correct anamnesis to determine the severity as well as the prognosis of the hemorrhage is necessary, but this not may delay the initiation of hemodynamic resuscitation. Blatchford score as well as Rockall score are useful tools to determine the patient risk. Diagnosis is determined by endoscopic techniques which should be realized as soon as possible. In addition, this technique provides the possibility to perform a definitive treatment in non variceal hemorrhage as well as variceal hemorrhage. In addition, after the endoscopy treatment, both etiologies have been observed to increase its outcomes applying PPI therapy. If endoscopy treatment fails in variceal hemorrhage, balloon tamponade or TIPSS are indicated.

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