Non-Variceal Upper GI Bleeding

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Introduction

Upper gastrointestinal bleeding (UGIB) is a common medical emergency linked with significant morbidity, with reported incidence of 40-150 cases per 100,000 population,\(^1,2\) and mortality generally from 10% to 14%.\(^3\) Peptic ulcer disease is the common cause of UGIB, accounting 50% of all episodes.\(^4,5\) It was reported that a decreasing annual incidence of UGIB amid a decreasing incidence of peptic ulcer bleeding, which is increasingly related to the use of low-dose aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs).\(^3,6\) The aim of this lecture is to provide updated recommendations and conflicted issues on the clinical and endoscopic management of UGIB.

Initial patient evaluation, resuscitation, and preendoscopy management

Early prompt hemodynamic resuscitation of patients with acute GI bleeding has been shown to significantly decrease morbidity and mortality.\(^7\) Immediate evaluation and resuscitation with early intravascular volume replacement using crystalloid fluids are recommended, if the patient is hemodynamic unstable. Red blood cell (RBC) transfusions should be administered to a patient with a hemoglobin level less than 7 g/dL, with a target level of 7 to 9 g/dL.\(^8\) The required volume of transfusion and target hemoglobin levels in patients with acute GI bleeding may be higher because of unstable hemodynamic conditions, inaccurate hemoglobin measures, or the presence of recurrent bleeding that leads to a rapid decrease to dangerously low hemoglobin levels.

Risk stratification tools are required for early stratification of patients into low- and high-risk categories for intervention, rebleeding and mortality.\(^9,10\) The preendoscopic Rockall and Blatchford scores use laboratory and clinical parameters to identify patients who require intervention, whereas the complete Rockall risk score use endoscopic findings to predict rebleeding or mortality.\(^11\)

It was reported that gastric irrigation failed to predict the need for endoscopic hemostasis correctly, did not improve visualization of the stomach at endoscopy, or improve clinical results such as rebleeding.\(^12\) It also should be noted that gastric lavage is a very unpleasant procedure that is not well tolerated. But, Insertion of a nasogastric tube in selected patients is considered, because the findings of aspiration may have prognostic value. Instead of gastric lavage, erythromycin (prokinetic drug) venous injection prior to endoscopy significantly improved gastric visualization, increased diagnostic yield, and decreased the need for second-look endoscopy, RBC units transfused, and duration of hospital stay.\(^13\) A single intravenous dose of erythromycin (250mg given 30-60 minutes prior to endoscopy) is safe and well tolerated, without side effects.

For patients taking anticoagulants, correcting coagulopathy is recommended but should not delay endoscopy. Most of guidelines recommend prompt reversal in all patients presenting with life-threatening bleeding, either in the case of supratherapeutic international normalized ratio (INR) elevations.\(^14\)
A meta-analysis showed that administering pre-endoscopic proton pump inhibitors (PPIs) significantly decreases the incidence of high risk stigmata of bleeding at the time of index endoscopy and the need for hemostatic procedure, but has no effect on rebleeding, need for surgery, or mortality.\textsuperscript{15} Pre-endoscopic high dose PPI therapy should be administered as soon as possible before endoscopy.

**Endoscopic management**

Early endoscopic intervention within 24 hours of onset of bleeding is recommended for most patients with acute UGIB. Early endoscopy is associated with significant reductions in length of hospital stay at low- and high-risk patient groups, compared with delayed endoscopy.\textsuperscript{16} Very early (within 12 hours) endoscopic intervention may be considered in patients at high risk; hemodynamic instability (tachycardia, hypotension) that persists despite volume resuscitation; hematemesis and fresh bloods in nasogastric aspirate; or contraindication to the interruption of anticoagulation.

The Forrest (F) classification was developed to standardize the bleeding stigmata of peptic ulcers. FIa spurting bleeding, FIb oozing bleeding, FIIa nonbleeding visible vessel, FIIb an adherent clot, FIIc black or red spot, and FIII clean base.\textsuperscript{17} It was reported that this classification was useful, predictable system to identify patients at risk of persistent bleeding, rebleeding and mortality.\textsuperscript{17} Endoscopic treatment is not indicated for patients with low-risk stigmata (FIIc or FIII).\textsuperscript{9,10} A clot in an ulcer bed warrants targeted irrigation in an attempt at dislodgement, with appropriate treatment of the underlying lesion. The role of endoscopic hemostasis for ulcers with adherent clots resistant to vigorous irrigation is controversial. Endoscopic therapy in FIIb may be beneficial in patients at high risk for rebleeding (patients with serious concomitant diseases), whereas high-dose PPI infusion without endoscopic treatment may be sufficient in patients at low risk.\textsuperscript{9} Endoscopic hemostasis is absolutely indicated for patients with high-risk stigmata (FI or FIIa).

Although only epinephrine injection therapy is more effective than medical treatment in patients with high-risk stigmata, it provides suboptimal efficacy and should be used in combination with second method. Epinephrine plus an another method for treating high-risk stigmata significantly reduced rebleeding, surgery, and mortality compared with epinephrine injection therapy.\textsuperscript{18} No single solution for endoscopic injection is superior to another for hemostasis. No single application of endoscopic thermal coagulation is superior to another. Thermal coagulation, clips, or injection therapy other than epinephrine should be used in patients with high-risk stigmata, alone or in combination with epinephrine injection. New endoscopic hemostasis modalities (topical hemostatic sprays and over-the-scope clips) are emerging as possible alternative endoscopic hemostasis when bleeding is refractory or not amenable to standard endoscopic treatments.\textsuperscript{19} Second-look endoscopy is not routinely recommended. Second-look endoscopy does not appear to be cost-effective, however, may be considered in selected patients at high risk for rebleeding.\textsuperscript{20} In cases of rebleeding, a second endoscopic hemostasis is usually recommended.

**Pharmacologic treatments**

Histamine-2 receptor blocker, somatostatin, and octreotide are not routinely recommended for patients with acute UGIB.\textsuperscript{10} Recent the meta-analysis found significant benefit in rebleeding, surgery, and mortality with intravenous high-dose PPI therapy after endoscopic hemostasis, whereas lower or intermittent doses were associated with significant benefits in rebleeding but not surgery or mortality compared with placebo.\textsuperscript{21} Thus, intravenous high-dose PPI treatment should be used in patients with high-risk stigmata who have undergone successful endoscopic hemostasis. Patients should be discharged with a prescription for a usual single-dose oral PPI for certain duration.
Management after successful endoscopic hemostasis

Patients at low risk stigmata after endoscopy can be fed within 24 hours. Most patients who have undergone successful endoscopic hemostasis for high-risk stigmata should be hospitalized for at least 72 hours thereafter. In the patients for whom primary or repeated endoscopic therapy has failed, percutaneous angiographic embolization or surgery should be considered. Patients with peptic ulcers bleeding should be tested for H. pylori infection and receive eradication therapy if it is present, with confirmation of eradication. Because peptic ulcer remains the most frequent cause of acute UGIB and H. pylori infection remains the primary cause of peptic ulcer disease. When H. pylori is eradicated successfully, the risk of ulcer rebleeding is reported to be extremely low. However, the false-negative rate of H. pylori infection is higher if the test is performed at the time of the acute bleeding as compared to later follow-up. Re-testing for H. pylori should be performed in those patients with a negative test in the acute setting. Documentation of successful H. pylori eradication should be recommended.

Postdischarge, Aspirin, and NSAIDs

In patients with previous ulcer bleeding who require an NSAID, it should be recognized that taking with a NSAID plus PPI or a COX-2 inhibitor alone is associated with a clinically important risk for recurrent bleeding. In these patients, the PPI plus COX-2 inhibitor is recommended to reduce the risk for rebleeding from that of COX-2 inhibitors alone. In patients receiving low-dose aspirin and develop acute ulcer bleeding, aspirin therapy should be restarted as soon as the risk for cardiovascular complication is thought to outweigh the risk for bleeding. In patients receiving low dose aspirin for primary cardiovascular prophylaxis who develop peptic ulcer bleeding, withholding aspirin and re-evaluating the risks/benefits of ongoing aspirin use in consultation with a cardiologist, and resuming low dose aspirin following ulcer healing or earlier if clinically indicated, are recommended. In patients receiving low dose aspirin for secondary cardiovascular prophylaxis who develop peptic ulcer bleeding, aspirin should be resumed immediately following index endoscopy if the risk of rebleeding is low (FIIc, FIII). In patients with high risk peptic ulcer (FIIa, FIIb, FIIa, FIIb), early reintroduction of aspirin by day 3 after index endoscopy is recommended. In patients receiving dual antiplatelet therapy who develop peptic ulcer bleeding, continuing low dose aspirin therapy is recommended. Early cardiology consultation should be obtained regarding the timing of resuming.

Conclusions

Management of the patient presenting acute UGIB is important, despite recent advances in therapy, mortality rates have remained essentially unchanged to at 6-8%. Most of guidelines for UGIB represent a consensus of best practice based on the available evidence at the time of announcement. Further well designed, controlled studies may be needed to clarify conflicted results. Endoscopists should be aware recently guideline or consensus for UGIB, and try to improve clinical outcomes, such as rebleeding and mortality in patients with acute UGIB.

References