Recent Development of Endoscopic Treatment of Bleeding Peptic Ulcer

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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 Despite recent advances in therapy, mortality rates have remained essentially unchanged. This could be explained by the fact that patients are older and have more concurrent illnesses; it may also be due to underuse of endoscopic hemostatic techniques. The aim of this lecture is to provide updated endoscopic treatment of bleeding peptic ulcer.

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 mortalitys.7 Immediate evaluation and resuscitation with early intravascular volume replacement using crystalloid fluids are recommended, if the patients 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 endoscopic 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. A single intravenous dose of erythromycin (250 mg 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.

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. 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. 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. It was reported that this classification was useful, predictable system to identify patients at risk of persistent bleeding, rebleeding and mortality. Endoscopic treatment is not indicated for patients with low-risk stigmata (FIIc or FIII). 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. Endoscopic hemostasis is absolutely indicated for patients with high-risk stigmata (FI or FIIa). Endoscopic hemostasis can be achieved using injection, thermal, mechanical modalities, and topical therapy.

1. Injection therapy

The primary mechanism of action of injection therapy is local tamponade resulting from a volume effect. Diluted epinephrine (1:10 000 or 1:20 000 with normal saline injected in 0.5-2-ml aliquots in and around the ulcer base) may also have a secondary effect that produces local vasoconstriction. 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 another method for treating high-risk stigmata significantly reduced rebleeding, surgery, and mortality compared with epinephrine injection therapy. Sclerosing agents such as absolute ethanol, ethanolamine, and polidocanol pro-
duce hemostasis by causing direct tissue injury and thrombosis. The volume of sclerosing agents should be limited because of concerns about tissue necrosis or perforation. Another class of injectable agents is tissue adhesives including thrombin, fibrin, and cyanoacrylate glues, which are used to create a primary seal at the site of bleeding. No single solution for endoscopic injection is superior to another for hemostasis.

2. Thermal therapy

Thermal devices used in the treatment of UGIB are divided into contact and noncontact modalities. Contact thermal devices include heater probes which generate heat directly and bipolar electrocautery probes which generate heat indirectly by passage of an electrical current through the tissue. Noncontact thermal devices include argon plasma coagulation (APC) tools. Heat generated from these devices leads to edema, coagulation of tissue proteins, constriction of vessels, and indirect activation of the coagulation cascade, resulting in a hemostatic bond. Contact thermal probes (heater probe multipolar/bipolar electrocautery contact probes) and use local tamponade (mechanical pressure of the probe tip directly onto the bleeding site) combined with heat or electrical current to coagulate blood vessels, a process known as “coaptive coagulation.” The standard setting for use in achieving hemostasis in peptic ulcer bleeding is 15~20 watts, which is delivered in 8~10-second applications. Recently, hemostatic forceps have emerged as an alternative technique for endoscopic management of UGIB. Hemostasis achieved using hemostatic forceps with soft coagulation was introduced principally to manage bleeding that developed during endoscopic submucosal dissection. APC, a noncontact thermal modality, uses high frequency, monopolar alternating current conducted to the target tissue through a stream of ionized gas, without mechanical contact, resulting in coagulation of superficial tissue. As the tissue surface loses its electrical conductivity, the argon plasma stream shifts to adjacent nondesiccated tissue, which again limits the depth of tissue injury. Coagulation depth is dependent on the generator power setting, duration of application, and distance from the probe tip to the target tissue (optimal distance, 2~5 mm). No single application of endoscopic thermal coagulation is superior to another.

3. Mechanical therapy

Endoscopic mechanical therapies include clips (through-the-scope and over-the-scope) and band ligation devices. Endoscopic clips are deployed directly onto a bleeding site and typically slough off within days to weeks after placement. Hemostasis is achieved by mechanical compression of the bleeding site. Clips are available in a variety of jaw lengths and opening widths. The over-the-scope clip device includes an applicator cap, a nitinol clip, and a hand wheel. The applicator cap, with the mounted nitinol clip, is affixed to the tip of the endoscope. Clips come in three different shapes of teeth: rounded, pointed and long-pointed. Several small retrospective studies have reported that an over-the-scope clip, may have a role as rescue hemostasis therapy for severe UGIB when conventional endoscopic treatment modalities fail. Last, endoscopic band ligation devices, commonly used in esophageal variceal bleeding, have also been reported for treatment of UGIB (for Dieulafoy lesion) and involve the placement of elastic bands over tissue to produce mechanical compression and tamponade.

4. Topical therapy

Topical hemostatic sprays have been used in acute UGIB with promising results, but thus far in a limited
number of patients and without any comparative data regarding standard endoscopic hemostasis therapies. Advantages of noncontact, spray catheter delivery of hemostatic agents include ease of use, lack of need for precise lesion targeting, access to lesions in difficult locations, and the ability to treat a large surface area. Topical hemostatic sprays include TC-325, (Hemospray, Cook Medical Inc, Winston-Salem, North Carolina, USA), which is a proprietary, inorganic, absorbent powder that rapidly concentrates clotting factors at the bleeding site, forming a coagulum. The coagulum typically sloughs within 3 days and is naturally eliminated. Additional topical hemostatic sprays include EndoClot and the Ankaferd Blood Stopper. EndoClot (EndoClot Plus Inc, Santa Clara, California, USA) is a starch-derived compound that rapidly absorbs water from serum and concentrates platelets, red blood cells, and coagulation proteins at the bleeding site to accelerate the clotting cascade. Hemostatic sprays derived from plant products/extracts have also been evaluated. The overall efficacy of these topical agents is unknown in brisk arterial bleeding and may be limited because of the rapid “wash-away” effect of the hemostatic agent by ongoing blood flow. A systematic review of the current limited data suggests that Hemospray is safe and effective and may be best used in high risk cases as a temporizing measure or a bridge toward more definitive treatment.

Pharmacologic treatments

Histamine-2 receptor blocker, somatostatin, and octreotide are not routinely recommended for patients with acute UGIB. Recent 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. 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.
Conclusions

Although considerable advances have been made in endoscopic therapies for UGIB, mortality rates have remained essentially unchanged. Most of guidelines for UGIB represent a consensus of best practice based on the available evidence at the time of announcement. 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