Endoscopic Treatment of Upper Gastrointestinal Bleeding Using Haemoseal Spray: A Retrospective, Observational Study from a Tertiary Center in North India

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Abstract

Introduction United States Food and Drug Administration recently approved use of Hemospray for the management of gastrointestinal (GI) Bleeding. We report our experience with Haemoseal Spray (HS, Shaili Endoscopy) for the treatment of upper GI bleeding (UGIB).

Methods Records of patients who received HS for UGIB from January 2013 to June 2018 were studied retrospectively. Patients with UGIB from focal lesions refractory to conventional endotherapy or those with diffuse/multiple lesions not amenable to conventional endotherapy received 5cc HS spray. Primary end-point studied was clinical success, defined as control of bleeding over 24 hours. Secondary end-points evaluated included recurrence of bleeding within 7 days, in-hospital mortality, and complications secondary to HS.

Results Thirty-eight patients were treated with HS. The median age was 57 (range: 5–87) years with 27 males and 11 females. In 24 patients, HS was used as monotherapy, while it was combined with Injection/Clip/Argon Plasma Coagulation in 14. Etiology of bleeding was ulcers or erosions in 22, malignancy in 10, portal hypertensive gastropathy/gastric antral vascular ectasia in 4, and radiation gastropathy in 2. Clinical success was achieved in 32/38 (84%). All six nonresponders had coagulopathy related to chemotherapy/bone marrow transplant. Recurrent bleeding within 7 days was observed in four patients (gastric malignancy 2, radiation gastropathy 2). In-hospital mortality was seen in 8/38 (21%) of which 2(4.8%) were directly related to ongoing GI bleeding. There was no procedure-related complication.

Conclusion HS is an effective and safe tool in the endoscopic management of UGIB due to diffuse or multiple focal lesions or focal lesions refractory to conventional endotherapy.

Keywords
- endoscopic treatment
- Haemoseal Spray
- upper GI bleeding

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Introduction

Upper gastrointestinal bleeding (UGIB) is commonly associated with morbidity and mortality with a worldwide annual incidence of ~40 to 150 per 100,000 and mortality rate of 10%.[1] Common causes of UGIB include peptic ulcers, erosive gastritis, portal hypertension, malignancies, vascular malformations, and Mallory-Weiss syndrome. Endoscopic management of UGIB includes conventional methods like injection, mechanical and thermal modalities. European Society of Gastroenterology guidelines recommend a combination of two modalities for the management of peptic ulcer bleeding. With a combination of modalities, hemostasis can be achieved in 85 to 95% patients but rebleeding occurs in 5 to 10%.[2] Endoscopic therapy of difficult, diffuse, multiple or large lesions, however, remains a challenge. We report our single-center experience with Haemoseal Spray (HS) in patients with UGIB over a 5-year period.

Patients and Methods

Records of patients who received HS for endoscopic hemostasis for UGIB at our tertiary center in North India from January 2013 to June 2018 were studied retrospectively. Patients with UGIB not controlled with conventional therapy and patients not amenable to conventional therapy due to diffuse/multiple lesions were included. Conventional therapy was defined as use of intravenous proton pump inhibitor, and endotherapy with the use of 1; 10,000 epinephrine or saline injection, application of clip, or Argon Plasma Coagulation (APC) singly or in combination. Patients with known allergy to egg (as collagen powder used in the study was prepared from egg cell membrane) or multiple allergies were excluded from this study. This study was approved by the local institutional review board.

Primary end-point was clinical success, defined as control of bleeding over 24 hours. Secondary end-points studied were recurrent bleeding within 7 days, in-hospital mortality, and complications secondary to HS.

The criteria for recurrent bleeding included recurrence of hematemesis or melena, development of hemodynamic instability, drop in hemoglobin by 2 g/dL or more, transfusion requirement of 4 or more units, or presence of bleeding from the treated site at follow-up endoscopy.

UGI endoscopy was performed with Olympus gastroduodenoscope (GIFH180) within 12 hours of presentation. Nasogastric tube insertion with gastric lavage and administration of 20 mg of Metoclopramide or 25 mg of levosulpiride were routinely performed. All procedures were performed under sedation by using midazolam/fentanyl/propofol administered by anesthesiologist. During endoscopy, all attempts were made to identify the exact source of bleeding with flushing and removal of clots where feasible.

In patients with focal lesions, HS was used as salvage therapy when bleeding could not be controlled with conventional methods outlined above. In patients with multiple or diffuse lesions, HS was used as primary treatment modality. The HS kit consisted of an air pump, Haemoseal probe, a 7.5 Fr spray catheter, 230 cm in length (Shaili Endoscopy, India), and a preloaded collagen cartridge containing 5 g of powder (►**Fig. 1**). The spray catheter was passed through the working channel of the endoscope. Collagen powder was applied in short bursts through the spray catheter with an air pump. To prevent clogging of the HS catheter, care was taken to first dry the channel of the endoscope by flushing with 100 cc of air and avoiding the contact of catheter tip with the mucosa.

Result

Thirty-eight patients received HS in this study. The median age was 57 (range: 5–87) years with 27 males and 11 females. In 24 patients, HS was used as monotherapy (patients not amenable to conventional therapy due to diffuse/multiple lesions), while it was combined with APC/injection/clip application in 14 (patients not controlled with conventional therapy, that is, salvage therapy) (►**Fig. 2A** and **B**). All patients were kept nil by mouth following the procedure and received intravenous pantoprazole at a dose of 8 mg per hour for 24 hours.

Eighteen patients (47.4%) had underlying gastrointestinal malignancy, 8 patients (21%) had history of coronary artery disease, 6 patients (15.8%) had history of chronic liver diseases, 3 patients (7.9%) had chronic kidney disease, and 2 patients (5.2%) had cerebrovascular disease. Seven patients (18.4%) had history of antiplatelets drug ingestion either aspirin 75 mg and or clopidogrel 75 mg, two (5.2%) had history of ingestion of oral anticoagulant warfarin 2 mg, and 4 mg daily and in two patients (5.2%) there was history of nonsteroidal anti-inflammatory drug intake (►**Table 1**).

Indications were ulcers or erosions in 22, malignancy in 10, portal hypertensive gastropathy/gastric antral vascular ectasia in 4, and radiation gastropathy in 2. There were 32 (84%) inpatients, 5 of whom were admitted to intensive care unit. Among ulcers, 11 patients had esophageal ulcers,

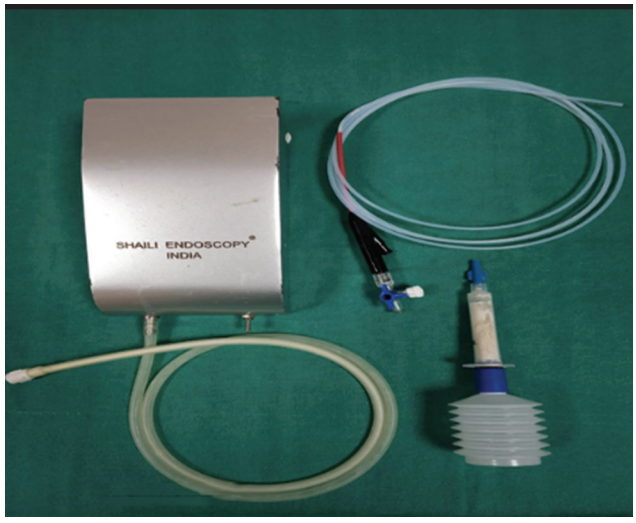

Fig. 1 Components of Haemoseal Spray (pump with connecting tubes, Haemoseal probe, Fibro protein in preloaded syringe).

Table 1 Associated comorbidities and use of drugs in patients with upper gastrointestinal bleeding

Co-morbidities and drug use	*n*(%)
Coronary artery disease	8 (21)
Chronic liver disease	6 (15.8)
Chronic kidney disease	3 (7.9)
Cerebrovascular disease	2 (5.2)
Antiplatelet drugs	7 (18.4)
Oral anticoagulants	2 (5.2)
Nonsteroidal anti-inflammatory drugs	2 (5.2)

Table 2 Causes of upper gastrointestinal bleeding

Etiology of bleeding	No. of patients (%)
Ulcers	22 (57.9)
Esophagus	
Gastroesophageal reflux disease	5 (13.2)
Infective ulcers	3 (7.9)
Post-chemotherapy ulcers Cameron	1 (2.6) 1 (2.6)
Mallory-Weiss syndrome	1 (2.6)
Stomach	
Peptic ulcers	5 (13.2)
Anastomotic ulcers	2 (5.3)
Corrosive poisoning	1 (2.6)
Duodenal	
Peptic ulcers	3 (7.9)
Malignancy	10 (26.3)
Gastric carcinoma	4 (10.5)
Gastric lymphoma	2 (5.3)
Local duodenal infiltration	4 (10.5)
Carcinoma gall bladder	2 (5.3)
Hepatocellular carcinoma	1 (2.6)
Periampullary	1 (2.6)
Portal hypertensive gastropathy/GAVE	4 (10.5)
GAVE	3 (7.9)
PHG	1 (2.6)
Radiation gastropathy	2 (5.3)

Abbreviations: GAVE, gastric antral vascular ectasia; PHG, portal hypertensive gastropathy.

8 patients had gastric ulcers, and 3 patients had duodenal ulcers (►**Table 2**).

Clinical success was achieved in 32/38 (84%). All six nonresponders had coagulopathy related to chemotherapy/bone marrow transplant. Follow-up endoscopy was done within 24 hours in 4 patients and after 24 hours in 2 patients.

Follow-up UGI endoscopy was not routinely performed. Repeat UGI endoscopy for recurrent bleeding within 7 days was observed in 4 patients (gastric malignancy 2, radiation gastropathy 2). In-hospital mortality was seen in 8/38 (21%) patients, of whom 2/38 (4.8%) were related to active ongoing GI bleeding (►**Table 3**). There was no therapy-related complication

Table 3 Causes of mortality

Cause of mortality	No. of patients (%)
Sepsis	2 (5.2)
Bleeding related	2 (5.2)
Acute coronary syndrome	1 (2.6)
Cardiac arrhythmia	1 (2.6)
Aspiration	1 (2.6)
End-stage liver disease	1 (2.6)

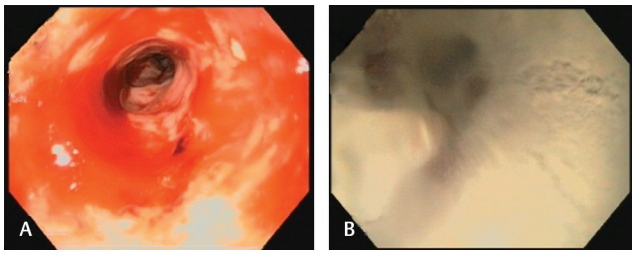

Fig. 2 (**A**) Endoscopic image showing diffuse upper gastrointestinal bleeding. (**B**) Endoscopic image of hemostasis after Haemoseal Spray in diffuse upper gastrointestinal bleeding.

Discussion

United States Food and Drug Administration recently approved the use of Hemospray for the management of GI bleeding. Various hemostatic powders are available for use during endoscopy, that is, Ankaferd Blood Stopper, Hemospray (TC-325), Endoclot Polysaccharide Hemostatic System, and HS.[3-6] Hemospray (Cook Medical, Winston-Salem, North Carolina, United States) consists of an inorganic powder that becomes cohesive and adhesive on coming in contact with moisture, thus forming a stable mechanical barrier and sealing the site of bleeding. Due to its composition, it is neither absorbed nor metabolized within the mucosa, hence minimizing the risk of systemic toxicity.[4] HS consists of collagen that is the major protein of the extracellular matrix. It activates intrinsic coagulation pathway as well as platelet activation. Collagen acts as a scaffold in tissues because of its stiff, triple-stranded helical structure.[7] Collagen binds with platelets via the glycoprotein IV/IX/V receptors, exposing procoagulant phospholipids and leading to thrombosis.[8] Collagen also accelerates reparative processes and initiates wound healing through activation of inflammatory cells and tissue vascularisation.[9] Collagen has also been shown to stimulate angiogenic growth factors and epithelial cell migration and proliferation, leading to re-epithelialization.[10-12]

Efficacy of Hemospray has been demonstrated in bleeding from peptic ulcers, cancer, and postbanding variceal ulcers.[5,13,14] The first multicenter prospective nonrandomized survey analyzing the effectiveness of Hemospray in acute nonvariceal upper GI bleed from Europe (SEAL study) demonstrated successful immediate hemostasis in 85% and a rebleeding rate of 15% in nonpeptic-ulcer bleeding.[15] Prasad et al who pioneered use of HS in India reported initial hemostasis in 90% of patients with peptic ulcer and rebleeding rate of 20%.[7] In another study from India, initial hemostasis was

seen in 90% of cases with rebleeding in 20%.[16] A recent study from Canada on 86 applications of Hemospray could achieve immediate hemostasis in 88.4%, but the rebleeding rate was high at 33.7%.[17] This may be attributed to higher prevalence of Forrest 1A and 1B ulcers in their series. A randomized control trial compared use of Hemospray and endoscopic clip application in patients with nonvariceal UGIB, majority of whom had bleeding from peptic ulcer.[18] Hemostasis was achieved in 100% patients with Hemospray as compared with 90% with hemoclip (p = 0.487). However, during second-look endoscopy, 5/20 (25%) patients required an additional hemostatic procedure.

In our study, clinical success was achieved in 84% patients with rebleeding rate of 10%. The lower clinical success in our study is possibly due to use in a wide variety of causes of UGIB including difficult to treat patients with gastric malignancies. Recent guidelines from International Consensus Group recommend use of hemostatic powder like TC-325 as a temporizing therapy to stop bleeding when conventional endoscopic therapies are not available or fail, in patients with actively bleeding ulcers.[19] However, monotherapy with TC-325 in patients with actively bleeding ulcers is not advisable.

Generally, all the homeostatic powders are considered safe. Transient abdominal discomfort due to rapid air insufflation and gastric distension, reported by others, was not seen by us. Allergic reaction to egg protein used for synthesis of HS, though unreported, remains a possibility with HS.[7]

All hemostatic powders are simple to use. Moreover, they can be used for control of bleeding from areas difficult to access with endoscopic injection, clip, or other direct methods. Availability and cost are the two major concerns, especially in our country. HS is available for about Rs 15,000/- while other hemostatic powders are not available.

Our study has few limitations. This is a retrospective analysis and a single-center experience with small number of subjects.

Conclusions

HS is an effective, safe, and cost-effective tool in the endoscopic management of UGIB. Well-designed prospective multicenter studies are required to ascertain the efficacy and safety of HS to establish its role as hemostatic agent and acceptance in every endoscopy unit.

Conflict of Interest
Nil.

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