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Original Article

Haemoseal Spray for Nonvariceal Gastrointestinal Bleeding: An Initial Experience from India

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ABSTRACT

Background and Aims: The aim was to reflect the use and effectiveness of Haemoseal spray as a treatment option in gastrointestinal (GI) bleed in everyday gastroenterology practice. **Materials and Methods:** This was a single-center, retrospective observational study conducted over a period of 12 months from January 2016 to December 2016. Consecutive patients of upper or lower GI bleed where haemoseal powder was used either as salvage therapy after a failed hemostasis or as an add-on to the standard methods or as monotherapy were identified and analyzed. **Results:** Of 284 patients with GI bleed, haemoseal spray was used in 20 (7.04%) patients. Bleeding was due to duodenal ulcer in 7 (35%), gastric ulcer 3 (15%), esophageal ulcer 2 (10%), colonic postpolypectomy bleed 2 (10%), gastric carcinoma 2 (10%), Mallory-Weiss tear 1 (5%), postsphincterotomy bleed 1 (5%), gastric antral vascular ectasia 1 (5%), and portal hypertensive gastropathy 1 (5%). The nature of bleed was oozing in 17 (85%) and spurting in 3 (15%). Initial hemostasis when used as monotherapy was seen in 3/3, as add-on therapy in 6/6, and as salvage therapy in 9/11 patients. Rebleed was seen in 4 (20%) and 30-day mortality was seen in 2 (10%) patients. Rebleed rate at day 7 was more in monotherapy cases; however, the difference was not statistically significant (33.33% vs. 16.66% vs. 18.18%, $P = 0.819$). **Conclusion:** Haemoseal spray is an effective hemostatic agent in various clinical situations with GI bleeding, especially when used as salvage therapy or as add-on therapy.

KEYWORDS: *Hemospray, nonvariceal gastrointestinal bleeding, refractory gastrointestinal bleeding*

INTRODUCTION

Hemostatic powders are recently introduced modalities for the management of nonvariceal upper gastrointestinal (GI) bleeding. Experience regarding the endoscopic use of hemostatic powders has been limited with no study from India describing its use. Optimal indications are still being characterized. Safety and efficacy of hemostatic powder appear to be promising for various types of GI bleeding including those secondary to peptic ulcers, esophageal tear, gastric antral vascular ectasia (GAVE), duodenal diverticula, colonic ulcer, radiation proctitis, Dieulafoy lesion, sphincterotomy, ampullectomy, polypectomy, and endoscopic mucosal resection.[1-3] Conventional endoscopic therapies including injection, thermal, and mechanical therapies are highly effective modalities; however, they may not be feasible in patients with active multifocal bleeding sites, lesions that are notoriously difficult to access, such as ulcers on the posterior duodenal wall and coagulopathy, and malignancy-related oozing, in which contact coagulation efforts may be hampered by further tissue damage and induction of more bleeding. However, in contrast, hemostatic powders can quickly cover large areas and does not require direct contact or an *en face* view.[4] We

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here present our experience about safety and efficacy of haemoseal powder used in the management of acute upper and lower GI bleed in day-to-day practice.

Materials and Methods

Patient selection

This was a single-center, retrospective observational study conducted over a period of 12 months from January 2016 to December 2016. Consecutive patients of upper or lower GI bleed where haemoseal powder was used either as a salvage therapy after a failed hemostasis or as an add-on to the standard methods or as monotherapy were recruited in the study. The conditions that were considered ideal for using haemoseal included oozing bleeding from a tumor and bleeding involving large areas of mucosa that were not easily amenable to targeted standard therapies such as portal hypertensive gastropathy (PHG) or GAVE. Patients with hemodynamic instability where endoscopic therapy was deemed inappropriate were excluded from the study. In addition, patients in whom hemostasis was achieved without the use of hemostatic powder were also excluded from the analysis. A pragmatic approach was adopted in using haemoseal spray as the cost of this product would preclude its use as a first-line therapy even in the presence of proven benefit. To reflect the realistic practice, haemoseal was applied at the endoscopist's discretion only when more well-established conventional homeostatic endoscopic methods failed to achieve complete hemostasis or were technically not possible. To endorse day-to-day clinical practice, patients with all etiologies of nonvariceal upper and lower GI bleed where haemoseal spray was used were included in this analysis.

Treatment protocol

All the procedures were done by trained gastroenterologists with appropriate experience in the management of GI bleed. A total of three endoscopists were involved with the use of haemoseal spray. Both the endoscopists and the endoscopy nurses underwent a brief training session in the use of this system before its introduction in our practice. Hemostatic powder used in our study was Haemoseal Spray® manufactured by Shaili Endoscopy, India. Being a collagen powder, it is more physiological than the other available mineral powders as collagen is a fibrous protein which supports and connects body tissues, strengthens blood vessels, and plays a role in tissue development. Haemoseal spray was applied in a short burst from canister with carbon dioxide propulsion, through a 10-Fr catheter to the active bleeding site; this was done until hemostasis was confirmed. A burst on average contained 1–5 g of powder and lasted for about 1–3 s. A maximum of 20 g (that is, four bursts) was applied. An external air compressor creates the sustained force required to drive the powder from within the chamber through the catheter, resulting in the multidirectional distribution of the product onto the mucosa. As it has a wide field of distribution after application, an *en face* view of point of bleeding was not essential. Second look endoscopy was not performed routinely in all patients, rather was done only if rebleeding was presumed.

The decision to use haemoseal was made during endoscopy depending upon the endoscopic picture. Preendoscopy treatment and procedures did not affect the decision to use haemoseal spray. It was used either as (a) salvage therapy: after hemostasis failed with standard methods which included injection therapy using diluted epinephrine, heater probe electrocoagulation, and/or hemocliping or as (b) add-on therapy: along with other standard methods as a second or third agent or as (c) monotherapy: used as a sole endoscopic intervention.

Failure of treatment was defined as inability to achieve hemostasis at the end of the endoscopic procedure. Following treatment of the bleeding lesion by endotherapy, standard medical therapy was given according to the etiology of the bleed which included inpatient observation, 72-h proton pump inhibitor infusion for ulcer bleed, and blood transfusion.

Outcome measures

The primary outcome measure used for this study was successful hemostasis, which was defined as the cessation of active bleeding as visualized by the endoscopist at the time of the procedure. Secondary outcomes used for this study were rebleeding within 7 days of index endoscopy, mortality within 30 days of index endoscopy, and adverse events related to the use of haemoseal spray.

Statistical analysis

All the data were expressed as median with range or percentages. Primary and secondary outcome measures were compared between different groups using Chi-square test. A $P < 0.05$ was considered significant, and all reported P values were two-tailed. All statistical analyses were performed using SPSS statistical package, version 22.0 (IBM, Armonk, NY).

Results

Two hundred and eighty-four patients presented with upper or lower GI bleed requiring some form of endotherapy to our center in the aforesaid period. Haemoseal spray was used as a treatment modality in 20/284 (7.04%) patients. Among these, there were 16 men with a median age of 65 years (range 30–82 years). Majority of the endoscopies were done within 12 h of presentation. Initial resuscitation

with endotracheal intubation was required in six patients. Table 1 describes the baseline characteristics and outcomes of the patients treated with haemoseal spray. Of 20 patients, 12 (60%) had significant comorbidity and 3 (15%) had shock at presentation.

The bleeding lesions where haemoseal spray was used included duodenal ulcer in 7 (35%), gastric ulcer 3 (15%), esophageal ulcer 2 (10%), colonic postpolypectomy bleed 2 (10%), malignant gastric ulcer 2 (10%), Mallory-Weiss tear 1 (5%), postsphincterotomy bleed 1 (5%), GAVE 1 (5%), and PHG in 1 (5%). The nature of bleed was oozing in 16 (80%) and spurting in 4 (20%). Haemoseal spray was used by four different endoscopists giving a median experience with this product of five applications per operator.

Figure 1 depicts the distribution of patients according to the clinical scenario where hemospray was used. Haemoseal spray was used as a monotherapy in esophageal ulcer, GAVE, and PHG. It was used as salvage therapy after hemostasis failed with standard methods in duodenal ulcer and gastric ulcer bleed. It was used as an add-on therapy along with other standard methods as a second or third agent in postpolypectomy site bleed and gastric carcinoma bleed. Standard methods that were used along with haemoseal spray included injection epinephrine, heater probe, argon plasma coagulation, and/or hemoclip placement. Of 20 patients, three had undergone endoscopic hemostatic procedures in preceding 2 days at our center, and so, they were considered as rebleeding cases for which repeat endoscopy was necessary. In the remaining cases, there was no previous endoscopy done.

Figure 2 shows the comparison of rates of initial hemostasis achieved and rates of rebleed at day 7 when haemoseal spray was used in different clinical settings. Overall initial hemostasis was achieved in 18 (90%) patients. When used as monotherapy, initial hemostasis was achieved in 3 out of 3 patients, as add-on therapy in 6 out of 6 patients, and as salvage therapy in 9 out of 11 (81.81%). Of the two patients where hemostasis was not achieved despite using three endoscopic methods including haemoseal spray, one patient of gastric malignancy was treated with selective arterial embolization and the other patient of duodenal ulcer (Forrest Ia) was treated surgically. Overall rebleed within 7 days was seen in four out of 20 (20%) patients. Rebleed rates were marginally more in patients where haemoseal spray was used as monotherapy as opposed to when used as salvage therapy or add-on therapy. However, the difference was not statistically significant (33.33% vs. 18.18% vs. 16.66%, $P = 0.819$). Of rebleed

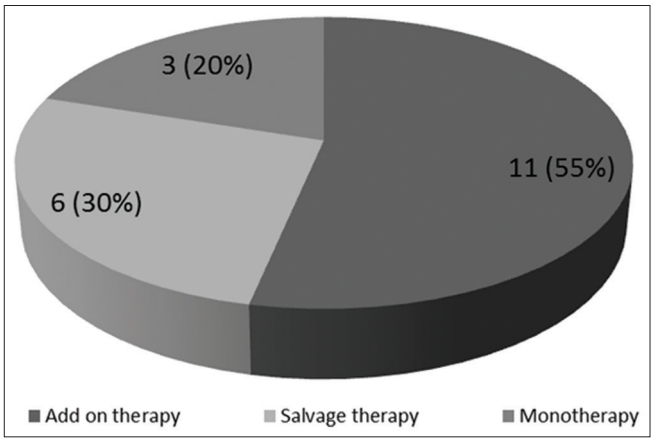

Figure 1: This pie chart shows the distribution of patients as per clinical scenario where haemoseal spray was used. It was used as an add-on therapy in 11 (55%), as salvage therapy in 6 (30%), and as monotherapy in 3 (20%) patients

Table 1: Baseline demographic, clinical characteristic and treatment outcomes of patient treated with haemoseal spray

Characteristic	n (%)
Sex (*n*)	Male 16, female 4
Age (years), median, (range)	65, (30-82)
Shock present at presentation, *n* (%)	3 (15%)
Number of red cell packs, median (range)	1 (0-7)
Etiology of GI bleed, *n* (%)	Duodenal ulcer in 7 (35%), gastric ulcer 3 (15%), esophageal ulcer 2 (10%), colonic postpolypectomy bleed 2 (10%), malignant gastric ulcer 2 (10%), Mallory-Weiss tear 1 (5%), postsphincterotomy bleed 1 (5%), gastric antral vascular ectasia in 1 (5%), and portal hypertensive gastropathy in 1 (5%)
Bleeding activity, *n* (%)	Spurting: 4 (20%) Oozing: 16 (80%)
PPI used, *n* (%)	15 (75%)
Anti-thrombotic used, n (%)	4 (20%) (warfarin in 3 patients and low molecular weight heparin in 1 patient)
Additional modalities used, *n* (%)	Injection epinephrine in 16 (80%); heater probe in 10 (50%); APC in 2 (10%); hemoclip 2 (10%)
Immediate hemostasis, *n* (%)	18 (90%)
7-day rebleed rate, *n* (%)	4 (20%)
30-day mortality rate, *n* (%)	2 (10%)
Surgery required, *n* (%)	2 (10%)

PPI=Proton pump inhibitor, APC=Argon plasma coagulation, GI=Gastrointestinal

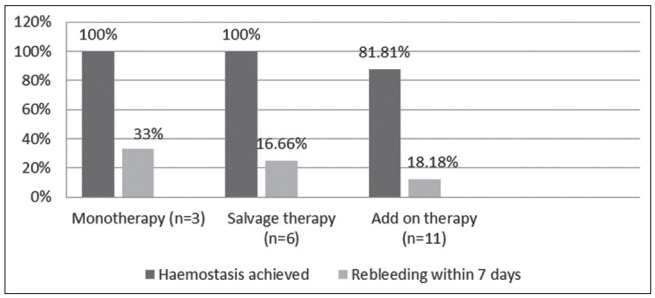

Figure 2: This bar diagram depicts that the initial rate of hemostasis was similar in all the three groups ($P > 0.05$). Although rebleed rate at day 7 was more in monotherapy group as compared to the other groups, the difference was not statistically significant ($P > 0.05$)

cases, one patient of duodenal ulcer required surgical intervention to achieve definitive hemostasis, one patient of 12 malignant gastric ulcer bleed was managed with selective embolization of the feeding artery, and two patients of gastric and duodenal ulcer were managed with repeat endoscopic hemostasis.

Thirty-day mortality was seen in 2 (10%) patients. Both the deaths were attributed to their comorbidities rather than GI bleed.

In none of the cases did the use of haemoseal spray complicate or potentiate the bleeding. In one case, the administration of the powder was hampered by occlusion of the spray catheter with activated particles. There were no reported side effects seen in association with the use of haemoseal spray.

Discussion

GI bleeding remains a common medical emergency, with endoscopic therapies being the treatment of choice in high-risk lesions. There is a constant need for new hemostatic modalities to add to the armamentarium of the currently available therapies to widen the spectrum of lesions which can be effectively treated with endoscopy. In this study, the outcome of patients with upper and lower GI bleeding treated with haemoseal spray at a high-volume tertiary care center is being presented. The distribution of cases for which hemostatic powder was used in our study represents a typical distribution of causes of bleeding in the daily gastroenterology practice.[5]

The precise mechanism of action of various hemostatic powders available is unknown, but it is hypothesized that the powder, in contact with water or moisture, forms an adhesive covering that seals the underlying tissue, thereby producing mechanical tamponade.[1] In the next 24–72 h., this adherent coat sloughs off into the lumen and is eliminated from the GI tract. Other mechanism that is proposed includes concentration of platelets and clotting factors with activation of platelets and coagulation cascade at the bleeding site, thereby facilitating local hemostasis.[6] This has been proven in *in vitro* studies where both prothrombin time and activated partial thromboplastin are reduced in a dose-dependent way in the presence of the powder.[7] The use of these agents should be restricted only in the presence of active bleed. The collagen powder that is used in our study (Shaili's Haemoseal spray) works by interacting with body's natural coagulation cascade, resulting in the formation of fibrin clot, thus creating a physiological plug.[8,9] The Hemospray® from Cook works by forming a mechanical barrier over the bleeding site resulting in a blanket-like smothering effect.[10]

Literature search revealed a paucity of data with regard to safety and efficacy of hemostatic powder application in various clinical situations. Very few studies have been published which has prospectively analyzed the use of hemospray.[1] There has been no study from India published previously describing the use of hemostatic powder in such a wide variety of clinical scenarios as it has been done in our study. In the first multicenter prospective nonrandomized survey analyzing the effectiveness of hemospray in acute nonvariceal upper GI bleed from Europe (also known as SEAL- Survey to evaluate application of Hemospray in the luminal tract study), 63 patients were included.[11] In their study, hemospray by Cook was used as monotherapy in 55 (87%) of patients with primary rate of hemostasis being 85% and rebleeding rate at day 7 being 15%. In contrast, in our study, haemoseal spray from Shaili was used instead of hemospray. Hence, direct comparison between these two studies may not be appropriate as mechanism of action is different between these two agents. However, hemostatic powder as a treatment modality was used as a monotherapy in only 15% of cases in our study as compared to 87% in the SEAL study. This reflects the lack of consensus among gastroenterologist around the world about the definitive position of hemostatic powder in the armamentarium of agents used for endoscopic hemostasis. However, overall success rates of initial hemostasis where hemostatic powder has been used are similar across various studies published so far ranging from 85% to 95%.[9,12] In a case series of two Swiss hospitals, hemospray was used in 16 patients of upper and lower GI bleed with an initial hemostasis rate of 93% and rebleed rate of 20%.[13]

Difficult anatomical location was the most common indication for the use of haemoseal in our study. Diffuse bleed in the duodenum was the most common scenario where it was helpful. With a wide field of application, endoscopists need not have an *en face* view of the bleeding lesion to apply hemospray or haemoseal spray. There were no complications attributed to haemoseal

spray use in our study. However, certain adverse events that can happen include allergic reaction, embolization, and intestinal obstruction.[9] There has been a case report of biliary blockage when hemospray was used in a patient with postsphincterotomy bleed.[14]

It has been hypothesized that there is some risk of rebleeding in the 1st week after the initial bleeding episode, probably because the mineral matrix sloughs off from the mucosa after 24–72 h in cases where hemospray is used.[15] However, this has not been substantiated in the clinical trials. Rebleed at day 7 occurred in four patients in our study. It was seen marginally more in cases where haemoseal powder was used as a monotherapy. However, gastric malignant ulcer bleed was the most difficult to treat lesion with haemoseal in our study as both the patients where it was used eventually required radioembolization of the feeding vessel. This contrasted with Chen *et al*. and Leblanc *et al*., who reported high success rate with the use of hemospray in patients with cancer-related GI bleeding.[16,17] This may be attributed to difference in mechanism of action between these two agents. More experience with use of hemostatic powders in GI-related malignancy is required before any definite recommendations can be made.

The main limitations of our study were relatively small number of patients where haemoseal was used and observational nature of this study. However, in view of very limited experience from India regarding this new hemostatic modality, our study will contribute toward further understanding the role of hemostatic powder in day-to-day GI practice. Another limitation was that direct comparison between haemoseal powder used in our study with the hemospray used in other international studies mentioned above may not be accurate as the mechanism of action of this two agents is different.

Conclusion

Our study has demonstrated that haemoseal spray can be used as a successful agent in a range of conditions with GI bleed. The noncontact nature of this agent makes it ideal for application in conditions involving larger mucosal areas. Large multicenter randomized controlled trials are required to further define the role of this modality in day-to-day practice.

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Conflicts of interest

There are no conflicts of interest.

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