THE USE OF HEMOSPRAY ENDOTHERAPY IN PATIENTS WITH ACUTE GASTROINTESTINAL BLEEDING: A SINGLE-CENTER EXPERIENCE

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ABSTRACT

Significance: Hemospray (TC-325) is a novel hemostatic agent recently licensed for endoscopic hemostasis of non-variceal upper gastrointestinal (GI) bleeding in the Europe and America. It acts by creating a mechanical barrier and effecting hemostasis on actively bleeding lesions via endoscopy. To our knowledge, no local report has been published yet with the use of hemospray as a treatment option for GI bleeding. This case series describes patients who were treated with hemospray at the St. Luke's Medical Center, Global City (SLMC GC).

Clinical Presentation: From 2017 to 2018, a total of 8 patients with acute GI bleeding were managed with hemospray at SLMC GC. With an age range of 36-83 years old, these patients presented with hematochezia, hematemesis or melena. 3 of the cases had a bleeding gastric mass, 3 had bleeding ulcers, while 2 had portal hypertensive bleeding.

Management: Hemospray powder was applied on the identified bleeding sites via endoscopy. The rate of successful initial hemostasis after hemospray endotherapy was 87.5% (7/8). Those treated with monotherapy had a 100% (4/4) success rate while those treated as salvage therapy at 75% (3/4). The rebleeding rate within 7 days was only 12.5% (1/8).

Recommendation: Hemospray is a novel endoscopic technique that has advantages of being non-traumatic, noncontact and can cover large areas of mucosa. This report demonstrates that hemospray is a safe and effective endoscopic therapy in achieving initial hemostasis, both as primary and salvage therapy in different etiologies of bleeding. Nevertheless, further data are needed to support its use.

Keywords: case series, hemospray, GI bleeding, hemostasis

INTRODUCTION

Gastrointestinal (GI) bleeding is a prevalent condition worldwide associated with significant morbidity and mortality. With its clinical consequences and significant influence on healthcare costs, adequate and immediate control is vital. Currently, there are various treatment modalities used to control GI bleeding which include injection of epinephrine and tissue adhesives such as cyanoacrylate, ablative therapy with contact modalities such as thermal coagulation with heater probe and bipolar hemostatic forceps, noncontact modalities such as photodynamic therapy and argon plasma coagulation, and mechanical hemostasis with band ligation, endoscopic hemoclips, and over-the-scope clips (1). In some cases, however, hemostasis is difficult to achieve, and patients may have persistent and recurrent bleeding. Recently, hemostatic powders have been added to the endoscopic armamentarium to treat GI bleeding and the one available locally is the hemospray (TC-325; Cook Medical, Winston-Salem, North Carolina, USA).

Hemospray is a proprietary inorganic powder which consists of a mineral-based compound that acts by creating a mechanical barrier and effecting hemostasis on actively bleeding lesions via endoscopy (2). It is applied during endoscopic procedures with a single-use device that delivers hemostatic powder through the channel of an endoscope. When the powdered product is delivered over the bleeding site, it interacts with moisture and forms a solid matrix with a tamponade function. Studies have shown that hemospray stopped bleeding in 95% of individuals within 5 minutes of spray (3). Re-bleeding was noted in 20% of patients, usually within 72 hours but up to 30 days after the device was used.

The aim of this case series is to evaluate the clinical efficacy of hemospray, either as monotherapy, or as part of salvage endotherapy in GI bleeding. It also aims to describe the indications as well as the complications of this novel treatment. In this report, we describe all patients managed with hemospray at St. Luke's Medical Center Global City (SLMC GC) since the time it was acquired in the endoscopy unit in 2017. To our knowledge, no local report has been published yet with the use of hemospray as a treatment option for GI bleeding. This present study provides initial experience with regard to the safety and efficacy of hemospray in the local setting.

CASE SERIES

Methods

Patients who presented with active bleeding of different origins in the upper and lower gastrointestinal tract treated with hemospray at SLMC GC were included in this case series. Data on age, sex, details of procedure and outcomes were collected through a retrospective chart review. In terms of its indication, hemospray was used either as monotherapy or as salvage therapy

at the discretion of the endoscopist. In terms of technique, hemospray was applied in short bursts from the canister, with carbon dioxide propulsion, through a 10-French catheter (Cook Medical) inserted into the working channel of a therapeutic endoscope (Olympus, Japan) to the active bleeding site. This was done until hemostasis was confirmed. Successful initial hemostasis was defined when hemospray application led to hemostasis after 3 to 5 minutes of visual inspection.

Results

From 2017 to 2018, a total of 8 patients with acute GI bleeding were treated with hemospray as shown in **Table 1**. There were 7 males (87.5%) and 1 female (12.5%) with an age range of 36-83 years old, median age of 62 years. Clinical presentation of patients varied with 3 (37.5%) patients presented with melena, 3 (37.5%) with hematochezia and 2 (25%) with hematemesis. 5 out of 8 patients (62.5%) had an upper GI bleeding while 3/8 (37.5%) had a lower GI bleeding.

Table 1. Characteristics of 8 patients treated with Hemospray for upper and lower gastrointestinal bleeding

Patient No.	Age Sex	Clinical Presentation	Origin of Bleeding	Location	Surgery /Interventional Angiography	Additional Modalities Used	Immediate Hemostasis	7-day Rebleed, day
1	57M	Anemia and melena	Gastric mass ulcerating, friable with necrosis	Corpus	None	None	Yes	No
2	42M	Hematochezia	Portal hypertensive colopathy	Ascending, transverse and descending colon	None	None	Yes	No
3	83M	Melena	Multiple Forrest IB ulcers, 0.5 cm largest	Duodenum, D1-D2	None	None	Yes	No
4	72M	Hematemesis	Gastric mass, ulcerating, with visible vessels and active bleeding	Proximal corpus	None	Epinephrine Sclerotherapy	Yes	No
5	46F	Hematemesis	Gastric mass	Cardia	None	None	Yes	No
6	67M	Melena	Gastric vascular ectasia with portal hypertensive gastropathy	Antrum	None	Argon Plasma Coagulation	Yes	No
7	67M	Hematochezia	Colonic ulcers, with oozing blood	Descending and sigmoid colon	None	Argon Plasma Coagulation	Yes	No
8	36M	Hematochezia	Colonic ulcers, multiple deep, large 5-18mm	Ascending colon	Yes (surgery 5 days after Hemospray)	Endoclip	Yes	Yes (day 5)

There was a variety of causes for bleeding identified on endoscopy. 3 (37.5%) of the 8 patients had a bleeding gastric mass, 3/8 (37.5%) had bleeding ulcers, and 2/8 (25%) had portal hypertensive bleeding. **Figure 1** illustrates the hemostatic effect of hemospray in a patient with a bleeding gastric mass *(Table 1: Patient No. 1).* He was a 57-year-old male, diagnosed case of esophageal adenocarcinoma stage III who already underwent esophagectomy 1 year prior now presenting with sudden onset melena and anemia. The initial gastroscopy done showed an ulcerating mass with recent signs of bleeding at the gastric wall and diffuse hemorrhagic gastritis. On biopsy, it revealed adenocarcinoma. Patient was scheduled for surgery for possible tumor resection but intraoperatively, peritoneal carcinomatosis with implants over the transverse colon and descending colon were found hence the surgery was deferred. Post-operatively, patient continued having melena and anemia. Due to persistent GI bleeding, a repeat gastroscopy was done where hemospray was applied to the mass achieving immediate hemostasis. No recurrence of GI bleeding was noted thereafter.

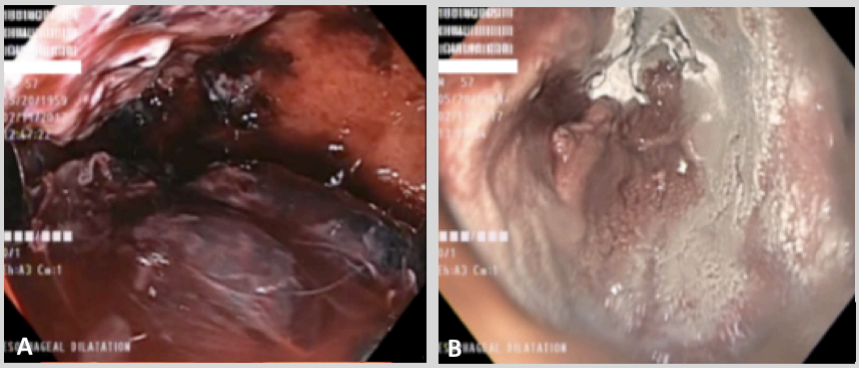

Figure 1. A Ulcerating gastric mass at the corpus. **B** Successful hemostasis after hemospray application

Figure 2 shows portal hypertensive bleeding in the colon for which hemospray was applied on the ascending, transverse and descending colon *(Table 1: Patient No. 2).* He is a 42-year-old male recently diagnosed to have liver cirrhosis on work-up after presenting with hematemesis. An initial gastroscopy showed portal hypertensive gastropathy and large esophageal varices hence rubber band ligation was done. He was stable until he presented with recurrent episodes of hematochezia. Blood transfusion and Octreotide drip was started. A colonoscopy was subsequently done which revealed multiple pinpoint vascular ectasias with signs of bleeding in the ascending, transverse and descending colon. Hemospray was applied due to the large area of mucosa affected which achieved immediate hemostasis. There was no recurrence of GI bleeding thereafter.

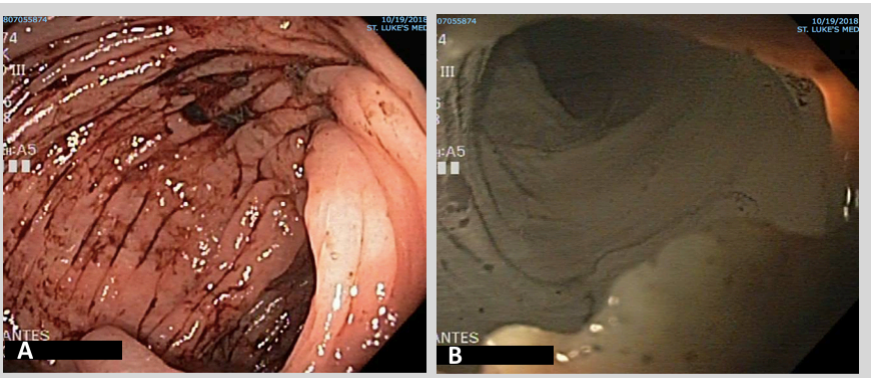

Figure 2. A Portal hypertensive colopathy with bleeding. **B** Successful hemostasis after hemospray application

Figure 3 shows a Forrest IB ulcer at the duodenum with successful hemostasis after hemospray application *(Table 1: Patient No. 3)*. He is an 83-year-old male known diabetic, diagnosed case of colon adenocarcinoma s/p right hemicolectomy who presented with few hours history of melena. Blood transfusions were done. Patient eventually underwent gastroscopy where there were noted multiple Forrest IB ulcers at the C-loop of the duodenum with the largest measuring about 0.5cm. Hemospray was applied on the identified sites of bleeding at the 1st and 2nd portion of the duodenum which afforded immediate hemostasis. There was no recurrence of GI bleeding thereafter.

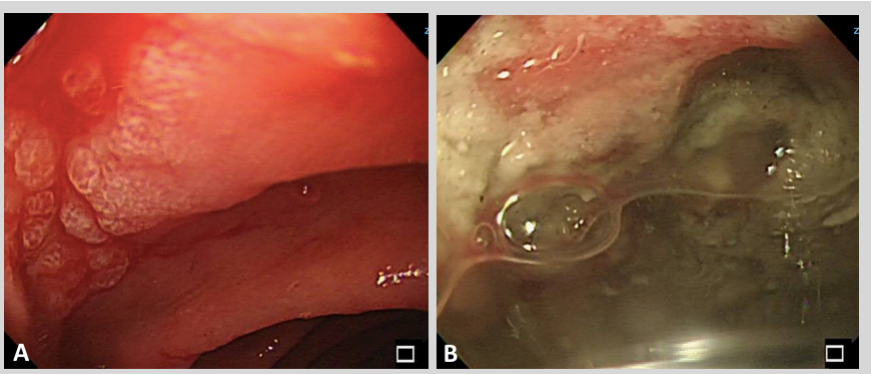

Figure 3. A Forest IB ulcer at the duodenum, D1. **B** Successful hemostasis after hemospray application

Figure 4 shows an ulcerating gastric mass in the proximal corpus with successful hemostasis after hemospray application *(Table 1: Patient No. 4)*. He is a 72-year-old male with heart failure who presented with 2 episodes of hematemesis associated with diaphoresis and dizziness. A gastroscopy done showed huge ulcerating gastric mass with visible vessels and active bleeding at the proximal corpus to part of the fundus measuring around 10cm. Injection sclerotherapy was done but did not result immediate hemostasis hence salvage therapy with hemospray employed. Bleeding subsided immediately. There was no recurrence of GI bleeding after.

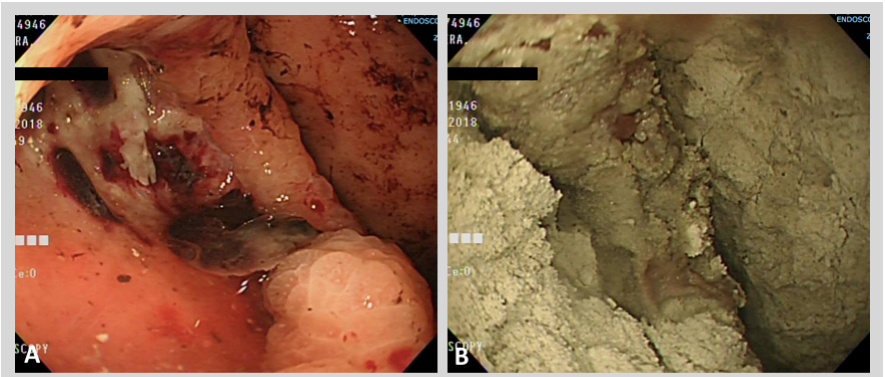

Figure 4. A Ulcerating gastric mass at the corpus. **B** Successful hemostasis after hemospray application

Patient No. 5 is a 46-year-old female, diagnosed with cervical cancer stage IV with gastric metastasis presenting with severe diffuse abdominal pain associated with hematemesis. Blood transfusions were done, and patient started on Pantoprazole drip. On gastroscopy, there was noted moderate amount of blood and blood clots with a gastric mass at the cardia which was actively bleeding. Hemospray was done which provided hemostasis. *Patient No. 6* is a known case of hepatocellular carcinoma with portal vein thrombosis who presented with hematemesis. A gastroscopy done revealed portal hypertensive gastropathy and gastric vascular ectasias. The mucosa was hyperemic with bleeding sites noted more in the antrum. Argon plasma coagulation followed by hemospray was done which afforded immediate hemostasis with no recurrence of the GI bleeding. *Patient No. 7* is the same patient as *No. 6* but readmitted few months after due to hematochezia. Colonoscopy showed ulcers with oozing and blood clots at the descending colon and sigmoid. Argon plasma coagulation was done which did not control the bleeding. Hemospray applied thereafter resulted hemostasis. There was no recurrence of GI bleeding. *Patient No. 8* is a known case of HIV who developed Burkitt's lymphoma manifesting as hematochezia. On colonoscopy, there were multiple bleeding colonic ulcers in the ascending colon noted. Due to the friable state of the mucosa and large area affected, hemospray was applied instead which afforded immediate hemostasis. However, 5 days after, the patient had recurrence of hematochezia hence was referred to surgery 5 days after hemospray endotherapy for which the patient had ileal resection. He had no recurrence of GI bleeding thereafter.

In terms of the endoscopic hemostatic methods used, of the 8 patients, 4 (50%) had hemospray as monotherapy and another 4 (50%) as salvage therapy after argon plasma coagulation, endoclipping or epinephrine sclerotherapy did not achieve hemostasis. All patients (100%) achieved immediate hemostasis. Only 1 (12.5%) patient rebled within the 7 days post-hemospray application for which he underwent surgery 5 days after hemospray endotherapy due to persistent hematochezia. No deaths occurred within 7 days after hemospray application, nor was any complication observed.

DISCUSSION

Hemospray is a new endoscopic hemostatic powder used for the treatment of GI bleeding. It that has a major advantage of covering large areas of bleeding without requiring direct contact with the bleeding source due to its aerosol delivery system. When put in contact with moisture in the gastrointestinal tract, the powder becomes cohesive and adhesive **(Figure 4).** It forms a barrier by creating a physical lattice concentrating the blood cells and clotting factors and this adheres to and covers the bleeding site achieving immediate hemostasis (4).

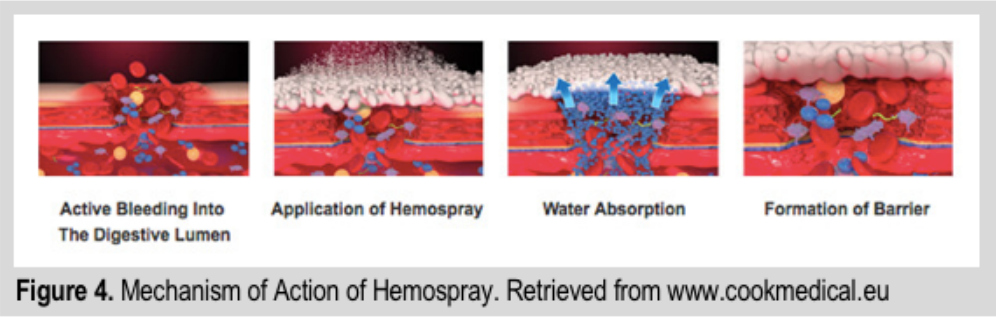

Figure 4. Mechanism of Action of Hemospray. Retrieved from www.cookmedical.eu

Hemospray was acquired by the SLMC GC Institute of Digestive and Liver Diseases last February 2017 and since then, there were 8 patients who were treated using hemospray as either primary monotherapy or salvage therapy. In this case series, hemospray was successfully used as monotherapy in a patient with a gastric mass, duodenal ulcer, and portal hypertensive colopathy. In contrast, it was used as salvage therapy in a patient with portal hypertensive gastropathy, gastric vascular ectasia, gastric mass and multiple colonic ulcers. These patients were initially treated with argon plasma coagulation, endoclipping or epinephrine sclerotherapy but did not achieve hemostasis, hence the use of hemospray. It is remarkable to note that only 1 patient with multiple colonic ulcers had rebleeding within 7 days post-hemospray necessitating emergency exploratory laparotomy due to the recurrence of massive hematochezia. Overall, with these 8 cases, different causes and locations of GI bleeding responsive to hemospray were demonstrated – from ulcers to masses and portal hypertensive bleeding to either upper or lower GI tract. These kinds of cases were actually common and typical of the usual cases seen in daily practice, hence, we appreciate the potential of this novel treatment as an addition to the gastroenterologist's usual endoscopic armamentarium. With the hemospray's efficacy and immediate hemostasis as shown in this report, the possible range of application of treatment in different causes or locations of bleeding are deemed promising.

In terms of its indications, studies have shown that hemospray is beneficial to patients with oozing bleeding from a malignant tumor, bleeding involving larger areas of mucosa (e.g. hemorrhagic gastritis, portal hypertensive gastropathy or gastric

antral vascular ectasia), and bleeding on sites not easily accessible to targeted standard therapies (5). Apparently, these indications were actually the same reasons of the endoscopists who did hemospray in this case series. Currently, there are only recommendations but no actual set indications for the use of hemospray. It is usually by the endoscopist's experience and discretion that this tool is utilized. It is likely that new or novel indications and innovations will emerge regarding this technique.

Hemospray has already been licensed for use in the endoscopic hemostasis of non-variceal upper GI bleeding (NVUGIB) in the Europe, Canada and USA. In the Asia-Pacific region, a recently published guideline entitled *Asia-Pacific Working Group Consensus on NVUGIB 2018 Update* has stated that endoscopic hemostatic powder spray such as hemospray is a useful treatment for temporary control of bleeding in NVUGIB when definitive hemostasis cannot be achieved (6). Likewise, patients with bleeding from upper gastrointestinal malignancy may also have benefit from hemostatic powder spray treatment. However, with the lack of RCTs and large-scale studies in the Asia-Pacific region, the level of evidence of this guideline was considered only low. On the other hand, hemospray has not been licensed yet for use in the lower GI tract and therefore current use in the lower GI tract is considered 'off-label.' The feasibility of hemospray for colonic application was demonstrated by a variety of case reports which have shown hemospray is safe and effective as well (7). In this case series, there were 3 patients who presented with lower GI bleed – 2 patients with colonic ulcers and 1 with portal hypertensive colopathy. All 3 had immediate hemostasis but one of the patients with colonic ulcer had rebleeding day 5 post-hemospray application. This may probably be explained by the large size of these multiple ulcers at 5-18mm and its friable state in the ascending colon. Likewise, recurrent bleeding may be expected to occur in hemostatic powders since these do not directly induce healing of the underlying and is sloughed off within 2-3 days, leaving behind a clean remnant which can be prone to bleed again (8). In view of these high-risk cases which are prone to recurrent bleeding, hemospray could probably be best used as a temporary measure or a bridge toward more definitive therapy instead. Other benefits of hemospray as supported by evidence are cancer-related GI bleeding and bleeding related to portal hypertension (9). In this case series, 3 patients had cancer-related GI bleeding and 2 with portal hypertensive bleeding. All 5 patients achieved immediate hemostasis with hemospray with no rebleeding.

In terms of its safety, there was no adverse event noted in all the 8 patients treated in the study. However, there are potential complications identified in published studies. There is risk of thromboembolism in patients with variceal bleeding with low venous pressure and numerous collateral shunts (8). It also has a risk of perforation and obstruction in diverticular bleeding with thin mucosal wall and narrowed bowel edema (10). Gastrointestinal obstruction is a possible risk as the powder is sloughed off and passing through the small intestine. Although some studies reported cases of mortality after application of hemospray, the causes of death were not directly due to GI bleeding itself but from other complications of their underlying or co-morbid illness (11).

CONCLUSION

Hemospray is a promising novel endoscopic technique that has advantages of being non-traumatic, noncontact and can cover large areas of mucosa. This report demonstrates that hemospray is a safe and effective endoscopic therapy in achieving initial hemostasis, both as primary and salvage therapy in different etiologies of bleeding. Nevertheless, further data are needed to support its use in the local setting.

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