Routine use of Hemospray for gastrointestinal bleeding: prospective two-center experience in Switzerland

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Hemospray (Cook Medical, Winston-Salem, North Carolina, USA) is a hemostatic agent recently introduced for the management of upper gastrointestinal bleeding (GIB). To date, there is little experience with this fairly new hemostatic tool. The aim of this case series was to reflect the use and effectiveness of Hemospray as a treatment option in GIB in everyday clinical practice at two tertiary referral centers. Consecutive patients (n = 16) with active GIB of various origins were treated with Hemospray. The rate of successful initial hemostasis was 93.75 % (15 /16; salvage therapy 92.85 % [13/14]; monotherapy 100 % [2 /2]). The rebleeding rate within 7 days was 12.5 % (2/16). One patient, in whom interventional radiology also failed, had to undergo surgery as salvage therapy. The effectiveness of Hemospray in the management of GIB in various clinical situations is promising. Future multicenter randomized prospective trials for clearly defined bleeding situations are needed for greater generalizability of case series findings.

Introduction

Hemospray (Cook Medical, Winston-Salem, North Carolina, USA) is a hemostatic inorganic agent. In contact with moisture, Hemospray becomes cohesive and adhesive, creating a mechanical barrier and effecting hemostasis. Hemospray has recently been introduced for the management of upper gastrointestinal bleeding (GIB) [1]. In Europe, Hemospray is not licensed for use in the lower gastrointestinal tract and therefore current use in the lower gastrointestinal tract is "off-label." So far, preliminary experience in benign and malignant upper and lower GIB is promising although limited [1 – 5]. However, the optimal indications and technical limitations are still being characterized. We present a prospective case series regarding the use of Hemospray in daily routine for the treatment of GIB at two tertiary endoscopy centers in Switzerland, to add to the increasing experience with this promising treatment modality.

Case series

Methods

Between August 2013 and November 2013, consecutive patients with active bleeding of various origins in the upper and lower gastrointestinal tract were treated with Hemospray at two Swiss tertiary endoscopy centers. Data on sex, age, medication, details of procedure, and outcome were collected prospectively. Approval to use pseudonymized patient data was obtained from the local ethics committee.

Endoscopic hemostatic interventions (using an Olympus 1TQ scope; Olympus, Tokyo, Japan) were performed exclusively by 11 experienced staff endoscopists (St. Gallen n = 8, Zurich n = 3). They had undergone a formal theoretical and practical training in Hemospray application, organized by the Clinic of Gastroenterology and Hepatology at the University Hospital of Zurich together with Cook Medical. Each endoscopist had to pass the training before his/her first clinical application of Hemospray.

Criteria for using Hemospray. Hemospray was used either as monotherapy or as salvage therapy at the discretion of the endoscopist. The following conditions were considered to be ideal for preferring Hemospray, as first-line therapy over standard hemostatic methods: oozing bleeding from a malignant tumor; and bleeding involving larger areas of mucosa that were not easily amenable to targeted standard therapies, such as portal hypertensive gastropathy or gastric antral vascular ectasia.

Technique of Hemospray application. Hemospray was applied in short bursts from the canister,

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with carbon dioxide propulsion, through a 10-Fr catheter (Cook Medical) to the active bleeding site; this was done until hemostasis was confirmed. A burst on average contains 1 to 5 g of powder and lasts about 1 second. A maximum of 20 g (that is, four bursts) was applied. The distal end of the catheter was placed 2 to 3 cm away from the bleeding in order to prevent sticking of the catheter in moisture. **Video 1** shows the technique of Hemospray application. Successful initial hemostasis was defined when Hemospray application led to hemostasis after 3 to 5 minutes of visual inspection.

Second-look endoscopy was not performed in the standard regime, but rather only when rebleeding was assumed.

Results

In total 194 patients with upper or lower GIB presented at the two centers between August 2013 and November 2013. Of those 194, 16 patients (8.25 %; 13 men, 3 women; median age 67 years, range 40 – 87) were treated with Hemospray in that period. Details are shown in **Table 1**. Of the 16 patients, 13 (81.25 %) had significant co-morbidity, and 5/16 (31.25 %) presented with shock, needing six packs of red cells on average. All of these patients received the maximum 20 g of Hemospray.

There was a variety of causes for bleeding (**Table 1** and **Table 2**). Four of the 16 patients had ulcer disease (25 %), and in 13/16 of cases (81.25 %) the bleeding was oozing in nature. **Fig. 1** illustrates the hemostatic effect of Hemospray in a patient with oozing bleeding after insertion of a percutaneous endoscopic gastrostomy. **Fig. 2** and **Video 1** show spurting bleeding (Forrest Ia) from an ulcer in the duodenum. After a failed attempt at hemostasis using the Coagrasper forceps, application of Hemospray was successful.

Of the 16 patients, four (25 %) had undergone endoscopic hemostatic treatment at our centers within the preceding 2 days, and these cases therefore counted as re-bleedings or hemostatic failures for which repeat endoscopy was necessary. In the remaining cases there was no previous endoscopy. In 14/16 cases (87.5 %) Hemospray application was salvage therapy after failed hemostasis with standard methods such as injection, clipping, heater probe, or argon plasma coagulation in the same endoscopic session (**Table 1** and **Table 2**). In this group with Hemospray as salvage therapy, the rate of successful initial hemostasis was 13/14 (92.85 %) (**Table 2**). The rate of initial hemostasis with Hemospray as monotherapy was 2/2 (100 %) (**Table 2**).

The rebleeding rate within 7 days was 2/16 (12.5 %). Both patients twice had previously had oozing bleeding and both needed repeat endoscopy within 24 hours (**Table 2**). In one patient interventional radiology also failed and the patient had to undergo

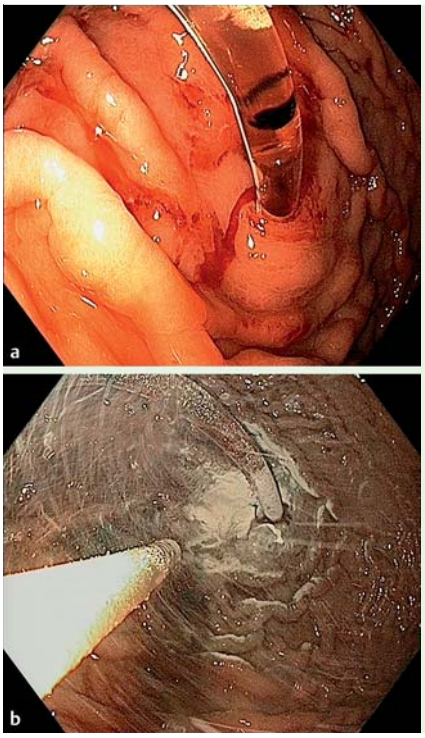

Fig. 1 **a** Oozing bleeding after insertion of a percutaneous endoscopic gastrostomy tube (15 Charriere). Epinephrine and Beriplast was injected but hemostasis was not achieved. **b** Successful hemostasis after Hemospray application.

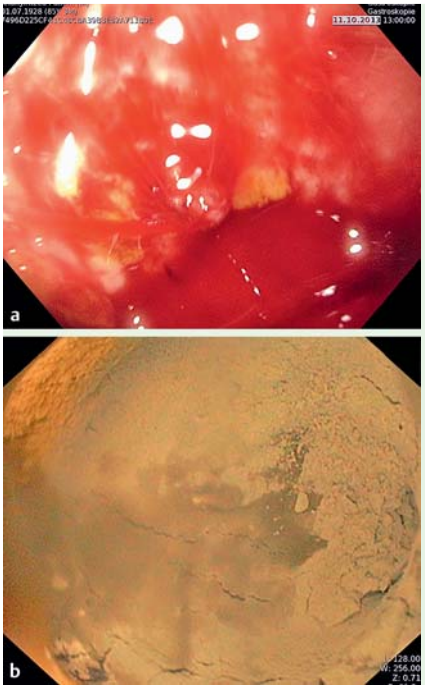

Fig. 2 **a** Spurting bleeding (Forrest Ia) from ulcer in the duodenum. **b** Use of the Coagrasper did not achieve hemostasis, but successful hemostasis after Hemospray application is shown.

Video 1

Technique of Hemospray application in the setting of spurting bleeding (Forrest I a) from an ulcer in the duodenum, after use of a Coagrasper forceps had failed to achieve hemostasis. Hemospray is applied in short bursts from the canister, with carbon dioxide propulsion, through a 10-Fr catheter (Cook Medical) to the active bleeding site. A burst on average contains 1 to 5 g of powder and lasts about 1 second. A maximum of 20 g (that is, four bursts) is applied. It is important to note that the distal end of the catheter should be placed 2 to 3 cm away from the bleeding in order to prevent sticking of the catheter in moisture.

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Table 1 Characteristics of 16 patients treated with Hemospray for upper and lower gastrointestinal bleeding.

Patient no.	Sex Age, y	ASA grade (I-IV)	Initial Hb, g/L	No. of red cell packs	Shock	Previous endoscopies: Number Treatment, if any	Cause of bleeding Location	Size, mm × mm Spurting/oozing (Forrest grade for ulcers)	PPI co-therapy	Surgery/Interventional angiography	Antithrombotic used	Additional, modalities used	Immediate hemostasis	7-day re-bleed, day
1	F 72	III	76	1	No	0 None	Ulcer Duodenum, part I, anterior wall	20×20 Ib	Intravenous	No	Enoxaparin	Epinephrine	Yes	No
2	M 79	III	85	1	No	0 None	Ulcer Duodenum, parts I/II, anterior wall	20×20 Ib	Intravenous	No	Xarelto + NSAID	Epinephrine	Yes	No
3	F 67	II	96	0	No	0 None	Sphincterotomy Papilla of Vater	5×5 Spurting	No	No	No	Epinephrine	Yes	No
4	M 83	III	63	4	No	0 None	Ulcer Duodenum, part I, anterior wall	30×20 Ib	Intravenous	No	No	Epinephrine	Yes	No
5	M 51	III	120	0	No	0 None	Mucosectomy (10 mm diameter) Esophagus (30 cm ab ore)	10 mm Oozing	Intravenous	No	No[1]	Epinephrine, Coagulation	Yes	No
6	M 61	III	65	5	No	0 None	Portal hypertensive gastropathy Cardia	7×5 Oozing	Intravenous	No	No[2]	No	Yes	No
7	F 73	III	69	5	Yes	Yes Epinephrine, endoclip	Gastroesopagheal anastomosis Distal esophagus	7×5 Oozing	Intravenous	No	Aspirin	Epinephrine	Yes	Yes (day 1)
8	M 69	III	74	1	No	0 None	Stomach, corpus	5×5 Oozing	Intravenous	No	Aspirin[3]	Epinephrine, fibrin glue[4]	Yes	Yes (day 1)
9	M 44	I	50	6	Yes	1 Epinephrine, endoclip	Dieulafoy lesion Jejunum (after total gastrectomy)	6×5 Oozing	Intravenous	Yes (surgery 3 days after Hemospray application and interventional coiling)	No	Epinephrine	Yes	Yes
10	M 85	III	84	2	No	1 None	Ischemic ulceration Duodenum, part I–II	40×30 Ib	Oral	No	No	Epinephrine, Heater probe[5]		No
11	M 67	IV	88	0	No	0 None	Melanoma metastasis Stomach, corpus	60×80 Oozing	Intravenous	No	No	No	Yes	No
12	M 50	III	74	10	Yes	5 Rubber band ligation	Suspected gastric variceal bleeding Stomach, fundus	10×10 Oozing	Intravenous	No	No	Histoacryl	Yes	No
13	M 40	IV	70	2	No	3 OTSC	Tumor ulceration anastomosis Jejunum	5×50 Oozing	Intravenous	No	No	Rubber band, Epinephrine, Heater probe	Yes	No

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Table 1 (Continuation)

Patient no.	Sex Age, y	ASA grade (I-IV)	Initial Hb, g/L	No. of red cell packs	Shock	Previous endoscopies: Number Treatment, if any	Cause of bleeding Location	Size, mm × mm Spurting/oozing (Forrest grade for ulcers)	PPI co-therapy	Surgery/Interventional angiography	Antithrombotic used	Additional, modalities used	Immediate hemostasis	7-day re-bleed, day
14	M 87	IV	73	6	Yes	0 None	Recurrent anal carcinoma Anus	60 × 40 Oozing	No	No (Angio, no embolization)	No	Surgical stiches	Yes	No
15	M 56	II	133	0	No	0 None	Sphincterotomy Papilla of Vater	5 × 5 Spurting	Intravenous	No	No	Heater probe, Coagrasper, Epinephrine, Stent fully covered	No	No
16	M 73	III	50	3	Yes	0 None	Buried bumper after incision Stomach, corpus	5 × 5 Spurting	Intravenous	No	No	Heater probe, Hemoclips	Yes	No

ASA, American Society of Anesthesiologists; Hb, hemoglobin; PPI, protein pump inhibitor; NSAID, nonsteroidal anti-inflammatory drug; PEG, percutaneous endoscopic gastrostomy; OTSC, over-the-scope clip.

[1] Patient #5: clopidogrel stopped 7 days before mucosectomy

[2] Patient #6: very low platelets (7 G/L) because of osteomyelofibrosis

[3] Patient #8: aspirin and low platelets because of splenomegaly and liver cirrhosis

[4] Fibrin glue: Beriplast (CSL Behring AG, Berne, Switzerland)

[5] Size of the heater probe: 10 Fr

surgery as salvage therapy (**Table 1**). No deaths occurred within 7 days after Hemospray application, nor was any carbon dioxide-associated barotrauma observed.

Discussion

In this patient series, the outcomes are presented for 16 consecutive patients with active upper and lower GIB who were treated with Hemospray at two high volume tertiary centers in Switzerland. Our patient collection represents a typical distribution of causes of bleeding in the daily routine of gastroenterologists who are on call for emergencies [7]. In expert hands, Hemospray is very effective in achieving initial hemostasis. Our series emphasizes the possible range of application of Hemospray in upper and lower GIB in everyday clinical practice. Some case reports and small case series have also shown the high efficacy of Hemospray in achieving initial hemostasis of nonvariceal upper GIB [1, 2]. So far, only one small clinical prospective study has been published that analyzed the hemostatic effectiveness of Hemospray in actively bleeding ulcers (20 patients) [1]. Rebleeding appeared in 11 % of 19 patients with oozing bleeding. Very recently, the first European prospective nonrandomized multicenter survey analyzing nonvariceal upper GIB has been published (SEAL; Survey to Evaluate the Application of Hemospray in the Luminal tract), and includes 63 patients. In this survey of 63 patients [5], the majority (55; 87 %) were treated with Hemospray as monotherapy with a primary hemostasis rate of 85 % and a rebleeding rate at 7 days of 15 % [5]; 13 % were treated with Hemospray as salvage therapy with a hemostasis rate of 100 % [5]. In our case series, except in two cases, Hemospray was used as a salvage modality in the absence of immediate success of conventional hemostatic methods. In this particular setting this new tool in the endoscopist's armamentarium fulfills its purpose. Whether Hemospray may be the ideal first choice hemostatic tool and in which patients needs to be defined.

In Europe, Hemospray is not licensed for use in the lower gastrointestinal tract and therefore current use in the lower gastrointestinal tract is "off-label." The feasibility of Hemospray for colonic application was demonstrated recently by Soulellis et al. [3] (case series with 5 patients) and Holster et al. [7] (case series with 9 patients). The preliminary experience reported in the literature shows that Hemospray is a highly effective endoscopic hemostatic alternative in lower GIB [3, 7]. In our series, one patient had bled from the lower gastrointestinal tract, the cause being a relapsing anal carcinoma; Hemospray was applied in addition to a surgical suture. So far no other reports in literature have mentioned this indication for Hemospray.

There are only preliminary data based on case reports regarding the "off-label" use of Hemospray for variceal bleeding [8, 9]. Holster et al. [8] reported the first case of variceal bleeding refractory to standard endoscopic therapy, successfully treated with Hemospray, as a bridge towards a transjugular intrahepatic portosystemic shunt procedure. So far, no potential complications (e. g. embolization of the powder) after the use of Hemospray in variceal bleeding have been reported in the literature. In our series one patient with gastric varices was treated successfully with Hemospray after Histoacryl injection.

Bleeding after sphincterotomy seems to be a promising indication. In one of the two patients with this cause of bleeding in our series, hemostasis of a spurting bleeding from a sphincterotomy was difficult; finally success was achieved after combined

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Table 2 Use of Hemospray in 16 patients with gastrointestinal bleeding: Summarized demographic, clinical, and outcome data.

Demograhic data	
Sex, male : female, n	13 : 3
Age, median (range), years	67 (40 – 87)
Clinical data	
ASA classification III/IV, n (%)	
III	10 (62.5 %)
IV	3 (18.75 %)
Shock present, n (%)	5 (31.25 %)
Number of red cell packs, median (range)	1 (0 – 10)
Clinical situation, n (%)	
Ulcer	4 (25 %)
Tumor bleeding	3 (18.75 %)
Post-sphincterotomy	2 (12.5 %)
Other (e. g. anastomosis, mucosectomy, PEG tube insertion, buried bumper incision)	7 (43.75 %)
Location, n (%)	
Esophagus	2 (12.50 %)
Stomach	5 (31.25 %)
Duodenum	6 (37.50 %)
Jejunum	2 (12.50 %)
Anus	1 (6.25 %)
Bleeding activity, n (%)	
Spurting	3 (18.75 %)
Oozing	13 (81.25 %)
Previously treated site, n (%)	4 (25 %) (2 epinephrine/ endoclip 1 rubber band ligation 1 OTSC)
PPI used, n (%)	14 (87.5 %)
Antithrombotics used, n (%)	4 (25 %)
Outcome data	
Immediate hemostasis after Hemospray, n (%)	
Total	15 (93.75 %)
As salvage therapy	13 (92.85 %)
As monotherapy)	2 (100 %)
Re-bleed within 7 days, n (%)	2 (12.50 %)
Surgery needed, n (%)	1 (6.25 %)
Mortality within 7 days, n (%)	0

ASA, American Society of Anesthesiologists; PEG, percutaneous endoscopic gastrostomy; PPI, protein pump inhibitor; OTSC, over-the-scope clip

use of a heater probe, the Coagrasper, epinephrine injection, Hemospray, and insertion of a fully covered metal stent. Moosavi et al. [10] reported a case of transient obstruction of a post-sphincterotomy biliary orifice after Hemospray application. Technically, application of Hemospray for bleeding in and around the papilla of Vater is challenging; maneuvers with the endoscope in the narrow lumen as bleeding continues may inadvertently bring the application catheter into contact with moisture, clogging up the distal end of the catheter and making spraying impossible.

Some limitations need to be mentioned. First, our series is limited by the small number of patients and also the diversity of indications for therapy. Second, patients treated in a tertiary endoscopy center are usually not comparable with patients in district hospitals. Thus there is a selection bias. Third, the decision to apply Hemospray or not was at the discretion of the endoscopist and therefore subjective and not reproducible. Exact criteria for when Hemospray should or should not be used as the first-line agent were not defined before this study was started. In any case the endoscopists, all experienced and trained in endoscopic hemostasis, never used Hemospray in standard situations as the first-line attempt.

In this context it needs to be mentioned that the over-the-scope clip (OTSC; Ovesco, Tübingen, Germany) system is also recognized as a new endoscopic hemostatic tool. We are still somewhat reluctant to apply the OTSC in bleeding situations because it is an implant material that usually stays in place for an indefinite time. In our study many endoscopists used Hemospray with a good success rate. Application of Hemospray can be learned easily and quickly without a long learning curve which is certainly a strength of this new hemostatic tool. For these reasons we prefer Hemospray over the OTSC. In addition, an OTSC could be applied subsequently if Hemospray fails. However, to date there are no data available that compare Hemospray with OTSC.

A fourth limitation is that the use of antithrombotics in our patient set appears relatively low with regard to the included population (mean age 67 years). We speculate that one reason could be that our patients had many co-morbidities (American Society of Anesthesiologists [ASA] classifications III and IV, 10 [62.5 %] and 3 [18.75 %] patients, respectively). At the time of bleeding, the majority of patients had already been hospitalized for at least some days, and the treating medical team had stopped aspirin or clopidogrel medication beforehand because of the life-threatening bleeding situation. The initially healthy patients (ASA I and II) had no antithrombotics.

In conclusion, Hemospray is a promising tool in the management of upper and also lower GIB. Hemospray is a welcome hemostatic modality that can be used not only instead of the current treatment modalities, but also as salvage therapy after failure of more usual modalities. The noncontact nature of Hemospray makes it desirable in situations involving larger areas of mucosa that would not otherwise be amenable to standard targeted therapies, particularly in patients on antithrombotic treatment. One can speculate, that direct use of Hemospray without prior use of established methods such as the use of heater probes, clips etc. might be cost-effective in particular clinical settings. Future multicenter randomized prospective trials are needed to increase the generalizability of case series findings.

Competing interests: None

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