# Hemostatic powder spray: a new method for managing gastrointestinal bleeding

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***Abstract***

Gastrointestinal bleeding is a leading cause of morbidity and mortality in the United States. The management of gastrointestinal bleeding is often challenging, depending on its location and severity. To date, widely accepted hemostatic treatment options 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. These approaches, albeit effective in achieving hemostasis, are associated with a 5–10% rebleeding risk. New simple, effective, universal, and safe methods are needed to address some of the challenges posed by the current endoscopic hemostatic techniques. The use of a novel hemostatic powder spray appears to be effective and safe in controlling upper and lower gastrointestinal bleeding. Although initial reports of hemostatic powder spray as an innovative approach to manage gastrointestinal bleeding are promising, further studies are needed to support and confirm its efficacy and safety.

The aim of this study was to evaluate the technical feasibility, clinical efficacy, and safety of hemostatic powder spray (Hemospray, Cook Medical, Winston-Salem, North Carolina, USA) as a new method for managing gastrointestinal bleeding.

In this review article, we performed an extensive literature search summarizing case reports and case series of Hemospray for the management of gastrointestinal bleeding. Indications, features, technique, deployment, success rate, complications, and limitations are discussed.

The combined technical and clinical success rate of Hemospray was 88.5% (207/234) among the human subjects and 81.8% (9/11) among the porcine models studied. Rebleeding occurred within 72 hours post-treatment in 38 patients (38/234; 16.2%) and in three porcine models (3/11; 27.3%). No procedure-related adverse events were associated with the use of Hemospray.

Hemospray appears to be a safe and effective approach in the management of gastrointestinal bleeding.

***Keywords:*** gastrointestinal bleeding, Hemospray, hemostatic powder spray

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## Introduction

Gastrointestinal bleeding (GIB) is one of the leading causes of morbidity and mortality in the United States with an estimated 20,000 deaths per year [El-Tawil, 2012]. Currently, endoscopic hemostasis is accepted as a first-line treatment modality in the management of GIB and has been demonstrated to be effective in reducing the rate of rebleeding, the need for surgical intervention, and mortality [Pedroto *et al.* 2012].

Widely used treatment modalities for GIB include injection therapy, ablative therapies (contact and noncontact), and mechanical hemostasis [Babiuc

*et al.* 2013]. Injection of epinephrine induces vasospasm and thrombosis of the bleeding vessels [Kubba and Palmer, 1996] resulting in control of bleeding in approximately 80% of cases [Calvet *et al.* 2004]. It is relatively easy to perform and facilitates the subsequent use of more permanent ablative or mechanical treatment options [Cappell and Friedel, 2008]. Adverse events of mucosal injection of epinephrine are infrequent and include perforation or tissue ischemia [Kovacs, 2008; Chung *et al.* 1996]. Histoacryl tissue adhesive (2-N-butyl-cyanoacrylate) injection is mainly used for bleeding gastric varices with reported hemostatic success rates between 95% and 100% [Fry *et al.* 2008].

Thermal coagulation uses heat to coagulate tissue proteins, causes tissue edema and vasoconstriction, and activates the clotting cascade with subsequent cessation of bleeding [Jensen and Machicado, 2005]. Potential adverse events of thermal coagulation include immediate rebleeding due to tissue adherence to the probe upon removal [Cappell and Friedel, 2008] and, rarely, deep tissue injury [Jensen and Machicado, 2009].

Mechanical hemostasis with hemoclips controls GIB by interrupting the blood supply to the bleeding site [Cappell, 2010]. Endoscopists commonly prefer metallic hemoclips or endoclips, which have a 94% initial success rate for control of bleeding [Jensen and Machicado, 2009; Lin *et al.* 2007]. Other mechanical modalities include over-the-scope clips (OTSCs) and hemostatic forceps. OTSCs have reportedly been used to achieve hemostasis in upper and lower GIB including bleeding from gastric ulcers, difficult to reach posterior duodenal wall lesions, and gastric tumors [Mönkemüller *et al.* 2012; Chan *et al.* 2014]. OTSCs have variable success rates, ranging from 71% to 100% in the management of GIB [Singhal *et al.* 2013]. Hemostatic forceps have an estimated 96% success rate in the management of bleeding from gastric ulcers [Nagata *et al.* 2010]. Hemoclips can quickly, precisely, and securely control bleeding [Singhal *et al.* 2013]. However, the use of hemoclips is often technically challenging and requires expertise for accurate and precise deployment. Limitations and adverse events of hemoclips include occasional early spontaneous dislodgement (dislodgment rates vary with type of clip used), risk of perforation [Nagata *et al.* 2010], and relative difficulty of deployment in hard to reach areas such as the lesser curvature of the stomach, the posterior wall of the duodenal bulb, or the gastric cardia [Cho *et al.* 2009].

Endoscopic band ligation (EBL) is another type of mechanical hemostasis used in the management of bleeding esophageal varices [Garcia-Tsao *et al.* 2007]. Owing to its established efficacy and low rate of adverse events, EBL is preferred over sclerotherapy for esophageal variceal bleeding [Kravetz, 2007]. Drawbacks of EBL include dysphagia, post-banding mucosal ulcerations and esophageal strictures. Also there is relative technical difficulty of deployment in a retroflexed position [Liu *et al.* 2008].

Endoscopic hemostasis for post-polypectomy bleeding can be achieved with the use of detachable snares or clips [Di Giorgio *et al.* 2004]. The use of an endoloop to ligate the stalk of a large polyp before snare polypectomy and therefore minimize the risk of post-polypectomy bleeding has been described [Katsinelos *et al.* 2006]. However, flat and indurated lesions may pose a significant challenge as the use of detachable snares or clips may not be effective in this setting [Cappell, 2010]. Another mechanical hemostatic modality is endoscopic ultrasound (EUS)-guided angiotherapy. Conventionally, EUS-guided angiotherapy is employed when other standard hemostatic approaches have failed. Reported cases of its use have included gastric variceal hemorrhage, refractory hemosuccus pancreaticus, Dieulafoy lesions, duodenal ulcers, and gastrointestinal stromal tumors [Levy *et al.* 2008; Levy and Song, 2013]. It is reported to have a 96% success rate in controlling GIB [Binmoeller *et al.* 2011]. Radiologic embolotherapy is considered to be a salvage therapy with reported technical success rates of 69–100% and rebleeding rates of 10–30% within 30 days of initial application [Luchtefeld *et al.* 2000; Weldon *et al.* 2008]. A major adverse event of embolotherapy is the increased risk of bowel ischemia or infarct after arterial embolization, which has been reported to range from 0% to 22% [Maleux *et al.* 2009].

Alternative modalities in the management of GIB are needed, as the current methods have varying limitations in efficacy, require expertise, and are occasionally associated with adverse events. A relatively simple, safe and effective method of endoscopic hemostasis is the use of hemostatic powders. Such powders were used in the battlefields to control external bleeding [Babiuc *et al.* 2013], however, only recently they have been

studied and successfully applied in the gastrointestinal tract in both animal and human subjects. To the best of the authors' knowledge, there are three hemostatic powders in use for control of GIB: the TC-325 (Hemospray, Cook Medical, Winston-Salem, NC, USA), the Ankaferd Blood Stopper (Ankaferd Ila Kozmetik A- Turkish Food and Drug Administration), and EndoClot (EndoClot Plus, Inc.) [Barkun *et al.* 2013; Barkun, 2013]. The most widely and recently studied hemostatic powder is the Hemospray, which is marketed in many countries; however, it has not yet been approved for use in the United States. This review article evaluates the technical feasibility, safety, efficacy, and adverse outcomes of Hemospray in the management of both upper and lower GIB in humans and animal models.

## Materials and methods

We conducted an extensive English literature search using Pubmed, Medline, Medscape, and Google to identify peer-reviewed original research and review articles using the keywords 'endoscopy techniques', 'endoscopic hemostasis', 'Hemospray', 'hemostatic powder', and 'treatment of gastrointestinal bleeding'. The search period included articles published until August 2014. We selected studies involving humans and animal models and manually searched the references to identify additional relevant studies. Inclusion criteria for evaluation were the technical success, feasibility, safety, efficacy, and adverse outcomes of Hemospray in the management of both upper and lower GIB at various locations and severity. In a recent article by Holster and colleagues, technical success was defined as continuous hemostasis observed after 3–5 minutes of Hemospray use [Holster *et al.* 2014]. Search results yielded case reports and case series. Hemospray to date is not licensed for use in the United States.

### *Mechanism of action*

Hemostatic powder is an inorganic powder that does not attach to nonbleeding surfaces and, thus, only affects areas of active bleeding [Barkun *et al.* 2013; Barkun, 2013]. The powder demonstrates adhesive properties and dehydrates tissue through absorption of water molecules, causing an increase in its volume [Barkun *et al.* 2013; Barkun, 2013]. It acts as a physical barrier upon contact with moisture and it concentrates clotting factors at the site of bleeding with subsequent clot formation [Babiuc *et al.* 2013]. Hemospray is neither taken up nor broken down by the mucosa and therefore does not appear to cause any local or systemic damage [Sung *et al.* 2011]. Hemospray is administered with a syringe, a 7-French or 10-French catheter inserted into the endoscope channel and an introducer handle with a built-in carbon dioxide canister, which ejects the powder out of the catheter and onto the bleeding site [Sung *et al.* 2011] (Figures 1–3).

## Results

A total of 19 original published articles were considered appropriate for inclusion in this review article. These were studies performed in the United Kingdom, United States, Japan, Italy, Hong Kong, Canada, France, Belgium, The Netherlands, Germany, Sweden, Spain, Switzerland, Denmark, and Egypt. Of the 19 studies, 6 were case reports [Fujita, 2012; Granata *et al.* 2013; Sargon and Laurie, 2013; Stanley *et al.* 2013; Paganelli *et al.* 2014; Moosavi *et al.* 2013] and 13 were case series. A total of 17 studies studied humans (234 cases) [Sung *et al.* 2011; Chen *et al.* 2012; Fujita *et al.* 2012; Granata *et al.* 2013; Leblanc *et al.* 2013; Ibrahim *et al.* 2013; Smith *et al.* 2013; Sargon and Laurie, 2013; Stanley *et al.* 2013; Soulellis *et al.* 2013; Yau *et al.* 2014; Smith *et al.* 2014; Holster *et al.* 2014; Sulz *et al.* 2014; Paganelli *et al.* 2014; Chen *et al.* 2014; Moosavi *et al.* 2013], while the remaining two performed in the United States involved porcine models (11 cases) [Giday *et al.* 2011, 2013]. The mean age of human subjects was 54.9 years. 69.2% (162/234) of the patients included in those studies were males and 29.9% (70/234) were females. Subject gender was not reported in two case reports [Granata *et al.* 2013; Moosavi *et al.* 2013]. All cases are summarized in Tables 1 and 2.

### *Location of bleeding*

Bleeding in the upper gastrointestinal tract was reported in the majority of cases. A total of 66 cases included gastric bleeding (66/234; 28.2%) [Sung *et al.* 2011; Chen *et al.* 2012; Fujita, 2012; Leblanc *et al.* 2013; Smith *et al.* 2013, 2014; Stanley *et al.* 2013; Yau *et al.* 2014; Sulz *et al.* 2014; Giday *et al.* 2011, 2013] and 15 cases of esophageal bleeding (15/234; 6.4%) [Chen *et al.* 2012; Leblanc *et al.* 2013; Yau *et al.* 2014; Smith *et al.* 2014; Sulz *et al.* 2014; Paganelli *et al.* 2014]. A total of 62 cases (62/234; 26.5%) of duodenal bleeding were reported [Sung *et al.* 2011; Chen

**Table 1.** Summary of reports on the use of Hemospray for endoscopic hemostasis in humans.

| Study | Mean Age (yrs) | Sample size | Sex | Location of bleed | Lesion size (mm) | Source of bleeding | Forrest Classification | Prior treatment | Delivery device | Subsequent treatments | Number of applications | Successful hemostasis | Rebleeding | Mortality 30 days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sung *et al.* [2011], Hong Kong** | 60.2 | 20 | 18M 2F | Stomach (6/20) Duodenum (14/20) | NR | Arterial | 1a (1) 1b (19) | None | 21g of Hemospray catheter and introducer with $CO_2$ canister | None | 1=13/20 2=5/20 >2=2/20 | 19/20 [95%] | 1/20 | None |
| **Chen *et al.* [2012], Canada** | 74 | 1 | F | Gastric Antrum | Large | Gastric adenoCA | N/A | None | 20 g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| | 69 | 1 | M | Distal esophagus | Large | AdenoCA | | None | 15 g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| | 58 | 1 | F | Duodenal bulb | 58×36×39 | AdenoCA pancreatic head | | None | 20g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| | 49 | 1 | F | Duodenal flexure | NR | Breast CA | | None | 20g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| | 53 | 1 | F | Gastric cardia | NR | Non-small cell lung CA | | Epi and APC | 20g of Hemospray powder in canister | None | 2 | 1/1 [100%] | 0/1 | None |
| **Fujita [2012], Japan** | 79 | 1 | F | Gastric fundus | 8 | Gastric varices | N/A | Lipiodol injection | 10g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| **Granata *et al.* [2013], Italy** | 51 | 1 | NR | Cecum | 30 | NR | N/A | Fibrin glue injection | Hemospray powder in canister | None | 2 | 1/1 [100%] | 0/1 | None |
| **Leblanc *et al.* [2013], France** | 67 | 1 | M | Proximal esophagus | 12 | SCC | N/A | None | 20 g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| | 71 | 1 | M | Gastric cardia | 25 | Intestinal metaplasia with LGD and HGD | | None | 20 g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| | 59.7 | 3 | 2M 1F | Distal esophagus | 23 | AdenoCA, and Barrett's esophagus | | None | 20 g of Hemospray powder in canister | None | 1 | 3/3 [100%] | 0/3 | None |
| | 60.9 | 7 | 5M 2F | Duodenum | 38.1 | Tubulovillous adenoma with LGD | | None | 20 g of Hemospray powder in canister | None | 1 | 7/7 [100%] | 0/7 | None |
| **Ibrahim *et al.* [2013], Egypt** | 61.7 | 9 | 7M 2F | Esophagus and GE junction | NR | Esophageal varices | N/A | None | 21g of Hemospray powder in canister | None | 8/9 (1) 1/9 (2) | 9/9 [100%] | 0/9 | None |
| **Smith *et al.* [2013], UK** | 69.8 | 3 | 2M 1F | Antrum | NR | PHG | N/A | APC (1) | 20g of Hemospray powder in canister | None | 1 | 3/3[100%] | 0/3 | None |
| | 66 | 1 | F | Proximal stomach | NR | PHG | | None | 20g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| **Sargon and Laurie [2013], United States** | 13 | 1 | M | Duodenum | NR | Duodenal ulcer | 1b | Embolization therapy | 25 – 30 g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| **Stanley *et al.* [2013], UK** | 37 | 1 | M | Gastric | Large | Gastric varices | N/A | Histoacryl and Lipiodol injections | Hemospray powder in canister | TIPS | 1 | 1/1 [100%] | 0/1 | None |
| **Soulellis *et al.* [2013], Canada** | 79 | 1 | M | Cecum | 30 | Sessile polyp (post-snare cautery, clip) | N/A | Metal clips | 20 g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| | 56 | 1 | M | Recto sigmoid | 10 | Tubular adenoma; HGD | | Epi, thermal probe, clip | 30 g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| | 82 | 1 | M | Lower GI tract | 350 | Dieulafoy lesion | | 5 metal clips, Epi | 20 g of Hemospray in canister | None | 1 | 1/1 [100%] | 0/1 | None |
| | 69 | 1 | M | Rectum | 70 | Radiation proctitis | | APC | 20 g of Hemospray in canister | None | 1 | 1/1 [100%] | 0/1 | None |

*(Continued)*

**Table 1.** (Continued)

| Study | Mean Age (yrs) | Sample size | Sex | Location of bleed | Lesion size (mm) | Source of bleeding | Forrest Classification | Prior treatment | Delivery device | Subsequent treatments | Number of applications | Successful hemostasis | Rebleeding | Mortality 30 days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Yau *et al.* [2014], Canada** | 67.6 | 19 | 14M 5F | Esophagus (1/19) Stomach (5/19) Duodenum (13/19) | NR | Peptic ulcer (12/19) Dieulafoy lesion (2/19) Mucosal erosion (1/19) Angiodysplasia (1/19) Ampullectomy (1/19) Polypectomy (1/19) Unidentified (1/19) | 1a (4) | Epi (16/19) Thermal probe (10/19) Clips, bands (9/19) Transarterial embolization (2/19) Surgical oversewing (1/19) | 20 g of Hemospray powder in canister | 1/19 | 1 | 18/19 [94.7%] | 7/18 [38.9%] | 5/19 [26.3%] |
| **Smith *et al.* [2013], UK SEAL survey** | 69 | 63 | 44M 19F | Esophagus, Stomach, Duodenum (63) | NR | Gastric ulcers (14/63) Duodenal ulcers (16/63) Post-EMR (7/63) Tumor (5/63) Esophageal ulcer (3/63) Dieulafoy (2/63) GAVE (2/63) Gastritis (2/63) Mallory Weiss (2/63) Sphincterotomy (1/63) Esophagitis (1/63) GIST (1/63) Ampullectomy (1/63) Duodenal diverticulum (1/63) Aortoduodenal fistula (1/63) Duodenal erosions (1/63) Post-HALO® (1/63) Duodenal polyp (1/63) Diffuse duodenal bleeding unknown cause (1/63) | 1a (11) 1b (16) | Monotherapy (55/63) Second-line therapy (8/63) | 20 g of Hemospray powder in canister | Angiographic embolization (1/8) Bipolar probe, epi (1/8) Clip, Epi, Surgery (1/8) Clip (1/8) Epi, heater probe (1/8) Heater probe, clip | 1 | 47/55 [85%] | 7/47 [15%] | 3/55 [5%] |
| **Holster *et al.* [2014], Spain and Netherlands** | 63 | 9 | 5M 4F | Cecum Ascending colon Transverse colon Rectum | NR | Colorectal anastomosis (1/9) Rectal ulcer 1/9) Colonic diverticulum (1/9) Cecal adenoCA (1/9) Proctitis (1/9) Polypectomy (4/9): rectum (2), transverse colon (1), ascending colon (1) | N/A | Monotherapy (6/9) Clips and/or Epi (3/9) | 20 g of Hemospray powder in canister, 10 Fr catheter | None | 1 | 7/9 [77.8%] | 2/9 [22.2%] | None |

*(Continued)*

**Table 1.** (Continued)

| Study | Mean Age (yrs) | Sample size | Sex | Location of bleed | Lesion size (mm) | Source of bleeding | Forrest Classification | Prior treatment | Delivery device | Subsequent treatments | Number of applications | Successful hemostasis | Rebleeding | Mortality 30 days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Sulz *et al.* [2014], Switzerland** | 67 | 16 | 13M<br>3F | Esophagus (2/16)<br>Stomach (5/16)<br>Duodenum(4/14)<br>Papilla of Vater (2/16)<br>Jejunum (2/16)<br>Anus (1/16) | NR | Duodenal ulcer<br>Sphincterotomy papilla of vater<br>Esophagus<br>PHG: cardia<br>Gastro-esophageal anastomosis<br>Jejunal Dieulafoy<br>Duodenal ulcer<br>Metastatic gastric melanoma<br>Gastric varices<br>Jejunal tumor ulceration<br>Recurrent anal carcinoma<br>Buried bumper after incision, stomach | 1b (4)<br>N/A (12) | Monotherapy (2/16)<br>Salvage therapy (14/16)<br>Injection<br>Clip<br>Heater probe<br>APC | 20 g of Hemospray powder in canister, 10 Fr catheter | Angiographic embolization<br>Surgery | 1 | 15/16 [93.8%]<br>Monotherapy 2/2 [100%]<br>Salvage therapy 13/14 [92.85%] | 2/16 [12.5%] | None |
| **Paganelli *et al.* [2014], Canada** | 0.91 | 1 | F | Esophagus | NR | Esophageal ulcer | N/A | Sclerosing agent injection | Hemospray | None | 1 | 1/1 [100%] | 0/1 | None |
| **Chen *et al.* [2014], Canada** | NR | 67 | 43 M<br>24 F | NVUGIB (21/67)<br>Malignant UGIB (19/67)<br>LGIB (11/67)<br>Intra-procedural bleeding (16/67) | NR | NR | 1a (3)<br>1b (10)<br>Remaining N/A | None | Hemospray | None | 1 | 20/21 [95.2%]<br>19/19 [100%]<br>11/11 [100%]<br>16/16 [100%] | 8/17 [47%]<br>6/19 [31.6%]<br>0/11<br>0/16 | None<br>4/19 [21.1%]<br>None<br>None |
| **Moosavi *et al.* [2013], Canada** | NR | 1 | NR | Duodenum | NR | Sphincterotomy | N/A | None | 5 g of Hemospray powder in canister | None | 1 | 1/1 [100%] | 0/1 | None |

AdenoCA, adenocarcinoma; APC, argon plasma coagulation; SCC, squamous cell carcinoma; LGD, low-grade dysplasia; HGD, high-grade dysplasia; N/A, not applicable; NR, not reported; EMR, endoscopic mucosal resection; Epi, epinephrine; TIPS, transjugular intrahepatic portosystemic shunt; GAVE, gastric antral vascular ectasia; NVUGIB, nonvariceal nonmalignant upper gastrointestinal bleeding; UGIB, Upper gastrointestinal bleeding; LGIB, lower gastrointestinal bleeding; PHG, portal hypertensive gastropathy.

**Table 2.** Summary of reports describing the use of Hemospray for endoscopic hemostasis in animal models.

| Study | Animal | Sample size | Location of bleed | Lesion Size (mm) | Source of bleeding | Forrest Classification | Prior treatment | Delivery device | Subsequent treatments | Number of applications | Successful hemostasis | Rebleeding | Mortality 30 days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Giday *et al.* [2011], United States** | Pigs | 5 | Gastric | NR | Gastroepiploic artery | 1a (5) | No | 20 g of Hemospray powder in canister | None | 1 | 5/5 [100%] | 1/5 [20%] | 5/5 |
| **Giday *et al.* [2013], United States** | Pigs | 6 | Gastric | NR | Gastroepiploic artery | Forest 1a (3) Forest 1b (3) | No | 20g of Hemospray powder in canister | None | 1 | 6/6 [100%] | 2/6 [33.3%] | None |

*et al.* 2012; Leblanc *et al.* 2013; Sargon and Laurie, 2013; Yau *et al.* 2014; Smith *et al.* 2014; Sulz *et al.* 2014; Moosavi *et al.* 2013]. Ibrahim and colleagues studied nine cases of bleeding at the gastroesophageal junction (9/234; 3.85%) [Ibrahim *et al.* 2013]. A total of 26 cases of bleeding in the lower gastrointestinal tract (26/234; 11%) were reported [Granata *et al.* 2013; Soulellis *et al.* 2013; Holster *et al.* 2014; Sulz *et al.* 2014; Chen *et al.* 2014].

### *Size of bleeding source*

The mean size of bleeding source was 37.4 mm, with a range from 8 to 350 mm [Chen *et al.* 2012; Fujita, 2012; Granata *et al.* 2013; Leblanc *et al.* 2013; Soulellis *et al.* 2013; Yau *et al.* 2014]. Several cases did not report the size of bleeding source [Sung *et al.* 2011; Chen *et al.* 2012; Ibrahim *et al.* 2013; Smith *et al.* 2013, 2014; Sargon and Laurie, 2013; Holster *et al.* 2014; Sulz *et al.* 2014; Paganelli *et al.* 2014; Chen *et al.* 2014; Moosavi *et al.* 2013; Giday *et al.* 2011, 2013] and two characterized the bleeding as 'large' [Chen *et al.* 2012; Stanley *et al.* 2013].

### *Source of bleeding*

Seven studies reported cases of arterial bleeding secondary to acute peptic ulcers and the gastroepiploic artery [Sung *et al.* 2011; Yau *et al.* 2014; Smith *et al.* 2014; Chen *et al.* 2014; Moosavi *et al.* 2013; Giday *et al.* 2011, 2013]. There were 12 reported cases of Hemospray use in variceal bleeding [Fujita, 2012; Ibrahim *et al.* 2013; Stanley *et al.* 2013; Sulz *et al.* 2014], 4 in bleeding due to portal hypertensive gastropathy in cirrhotic patients [Smith *et al.* 2013; Sulz *et al.* 2014] and 44 cases reported bleeding from malignant tumors such as gastric, pancreatic and anal adenocarcinomas, metastatic rhabdomyosarcoma, melanoma, breast, and non-small cell lung cancers [Chen *et al.* 2012; Leblanc *et al.* 2013; Sargon and Laurie, 2013; Holster *et al.* 2014; Sulz *et al.* 2014; Paganelli *et al.* 2014]. Leblanc and colleagues and Smith and coworkers used hemostatic powder to control bleeding after completion of endoscopic mucosal resection (EMR) [Leblanc *et al.* 2013; Smith *et al.* 2014]. A total of five of the studies reported successfully treated cases of post-polypectomy bleeding from a clipped sessile polyp in the cecum, rectum, transverse and ascending colon, a high-grade tubular adenoma in the rectum, Dieulafoy lesions, and radiation proctitis [Soulellis *et al.* 2013; Yau *et al.* 2014;

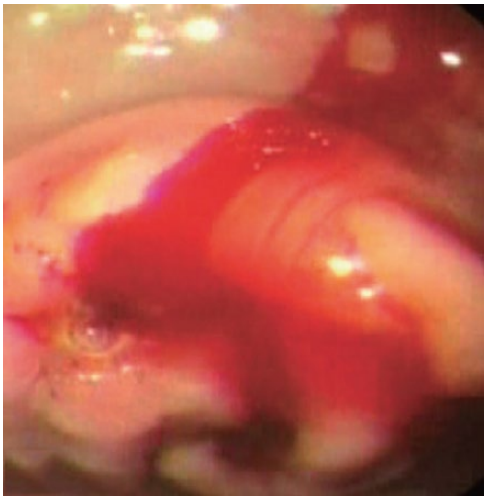

**Figure 1.** Endoscopic view of actively bleeding gastric ulcer.
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classified as Forrest 1a and 27.3% (3/11) as Forrest 1b (see Tables 1 and 2).

### *Primary method of treatment*

Hemospray was used as the primary and sole treatment modality of endoscopic hemostasis in 83% (194/234) of the cases (see Tables 1 and 2). The remaining 17% (40/234) of the cases were treated with a different hemostatic method (metallic clips, argon plasma coagulation, and epinephrine, lipiodol, fibrin injections, and surgery) prior to application of the hemostatic powder [Chen *et al*. 2012; Fujita, 2012; Leblanc *et al*. 2013; Smith *et al*. 2013; Sargon and Laurie, 2013; Soulellis *et al*. 2013; Yau *et al*. 2014; Smith *et al*. 2014; Sulz *et al*. 2014].

### *Technical and clinical success rates*

The combined success rate of Hemospray in achieving hemostasis was 88.5% (207/234)

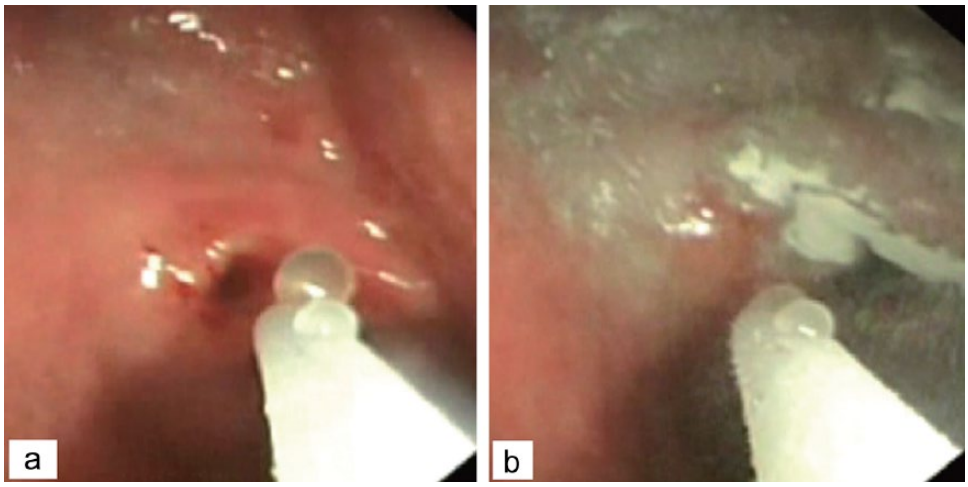


**Figure 2.** Application of Hemospray on bleeding ulcer.
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Smith *et al*. 2014; Holster *et al*. 2014; Sulz *et al*. 2014]. Hemospray efficacy in achieving hemostasis was demonstrated in gastric antral vascular ectasias (GAVE) and in post-sphincterotomy bleeding [Smith *et al*. 2014; Sulz *et al*. 2014; Moosavi *et al*. 2013]

### *Forrest classification*

Of the 81 bleeding peptic ulcer cases in the human subjects, 38.3% (31/81) were classified as Forrest 1a and 61.7% (50/81) as Forrest 1b. Among the porcine model study group, 72.7% (8/11) were

among the human subjects and 81.8% (9/11) among the porcine models. Rebleeding occurred within 72 hours post-treatment in 16.2% (38/234) of patients [Sung *et al*. 2011; Yau *et al*. 2014; Smith *et al*. 2014; Holster *et al*. 2014; Sulz *et al*. 2014; Chen *et al*. 2014] and in 27.3% (3/11) of animal models [Giday *et al*. 2011, 2013]. The patients who did not respond to Hemospray were eventually treated with one or more of the following modalities: electrocautery, hemoclips, epinephrine injection, transarterial embolization, or surgery [Sung *et al*. 2011; Yau *et al*. 2014; Sulz *et al*. 2014; Chen *et al*. 2014].

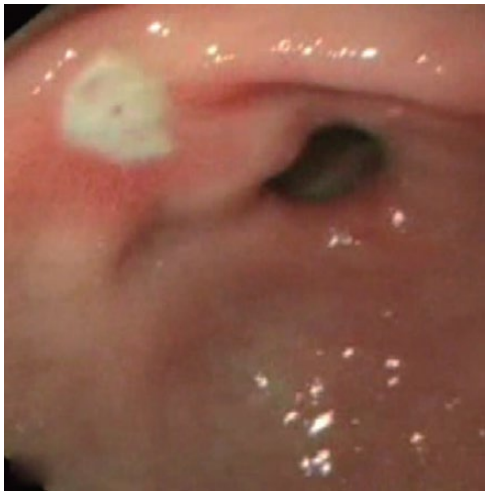

**Figure 3.** Successful achievement of hemostasis after Hemospray application.
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### *Adverse events and limitations*

No procedure-related adverse events were associated with the use of Hemospray. Rare adverse events of Hemospray may include embolism, intestinal obstruction, and allergic reaction to its components. However, given the relatively low-pressure system used in the canister during deployment of the powder, the risk of embolism is minuscule [Babiuc *et al.* 2013]. Reports of hemostatic powder dislodgement from the gastrointestinal mucosa approximately 48 hours after its use may theoretically cause intestinal obstruction [Sung *et al.* 2011]. However, review of the literature did not reveal any of these potential adverse events.

Although the Hemospray is technically easy to apply, the endoscopist should avoid deployment with the endoscope too close to the mucosa, because the powder may obstruct the view or clog the delivery catheter. It is suggested that proper time should be allowed for the powder to settle before any aspiration attempt, as this may block the operating channel or the delivery catheter. Also, using the hemostatic powder before other hemostatic modalities, may lead to loss of landmarks and prohibit any alternative hemostatic approach [Barkun *et al.* 2013; Barkun, 2013]. Endoscopists should heed the theoretical risk of perforation due to carbon dioxide pressure used for the Hemospray application. Pressures may reach as high as 55 mmHg and may tear the colonic wall if the catheter is placed too close or in contact with a lesion in thin areas such as the cecum or into a diverticulum [Soulellis *et al.* 2013].

## Summary and future directions

The reported findings on the use of Hemospray are promising. Hemospray is a novel treatment modality and a therapeutic alternative for difficult cases of GIB and appears relatively easy to use in everyday gastroenterology practice. It may be an alternative or a complement to the current hemostatic techniques in areas that may be technically difficult to access, such as the lesser curvature of the stomach, posterior wall of the duodenal bulb, and gastric cardia, and in large bleeding areas due to ulcers, tumors, GAVE or post-EMR. We identified potential limitations in the cases reviewed. Although the literature on Hemospray use is quickly expanding, the number of subjects studied thus far is small. Large randomized, prospective studies are needed to further characterize the safety and efficacy of Hemospray in treating various types of GIB. As noted by Babiuc and colleagues, most of these cases involved treatment of relatively mild bleeding in human subjects (61.7% Forrest 1b bleeding lesions) [Babiuc *et al.* 2013]. Also, the number of female participants in these studies was disproportionally low (70/232; 30.2%). Further studies are needed to investigate the efficacy of Hemospray in colonic bleeding. Hemospray to date is not licensed for use in the United States. Overall, Hemospray has a potential role in endoscopic hemostasis or may serve as an adjunct to other established non endoscopic therapies such as surgery, embolization, or transjugular intrahepatic portosystemic shunt (TIPS) for the management of GIB.

## Conflict of interest statement

None of the authors have any conflicts of interest or financial relationships with the company that produces or distributes the treatment modality described in the review article.

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## References

Babiuc, R., Purcarea, M., Sadagurshi, R. and Negreanu, L. (2013) Use of Hemospray in the treatment of patient with acute UGIB – short review. *J Med Life* 6: 117–119.

Barkun, A. (2013) New topical hemostatic powders in endoscopy. *Gastroenterol Hepatol* 9: 744–746.

Barkun, A., Moosavi, S. and Martel, M. (2013) Topical hemostatic agents: a systematic review with particular emphasis on endoscopic application in GI bleeding. *Gastrointest Endosc* 77: 692–700.

Binmoeller, K., Weilert, F., Shah, N. and Kim, J. (2011) EUS-guided transesophageal treatment of gastric fundal varices with combined coiling and cyanoacrylate glue injection (with videos). *Gastrointest Endosc* 74: 10019–10025.

Calvet, X., Vergara, M., Brullet, E., Gisbert, J. and Campo, R. (2004) Addition of a second endoscopic treatment following epinephrine injection improves outcome in high-risk bleeding ulcers. *Gastroenterology* 126: 441–450.

Cappell, M. (2010) Therapeutic endoscopy for acute upper gastrointestinal bleeding (UGIB): techniques of therapeutic endoscopy. Available at: http://www.medscape.org/viewarticle/717727 (accessed 3 March 2014).

Cappell, M. and Friedel, D. (2008) Acute nonvariceal upper gastrointestinal bleeding: endoscopic diagnosis and therapy. *Med Clin North Am* 92: 511–550.

Chan, S., Chiu, P., Teoh, A. and Lau, J. (2014) Use of the Over-The-Scope Clip for treatment of refractory upper gastrointestinal bleeding: a case series. *Endoscopy* 46: 428–431.

Chen, Y., Barkun, A. and Nolan, S. (2014) Hemostatic powder TC-325 in the management of upper and lower gastrointestinal bleeding: a two-year experience at a single institution. *Endoscopy*. DOI: 10.1055/s-0034–1378098

Chen, Y., Barkun, A., Soulellis, C., Mayrand, S. and Ghali, P. (2012) Use of the endoscopically applied hemostatic powder TC-325 in cancer-related upper GI hemorrhage: preliminary experience. *Gastrointest Endosc* 75: 1278–1281.

Cho, I., Gaslightwala, I., Jensen, D. and Cohen, J. (2009) Endoclip therapy in the gastrointestinal tract: bleeding lesions and beyond. Available at: http://www.uptodate.com/contents/endoclip-therapy-in-the-gastrointestinal-tract-bleeding-lesions-and-beyond (accessed 3 March 2014).

Chung, S., Leong, H., Chan, A., Lau, J., Yung, M., Leung, J. *et al.* (1996) Epinephrine or epinephrine plus alcohol for injection of bleeding ulcer: a prospective randomized trial. *Gastrointest Endosc* 43: 591–595.

Di Giorgio, P., De Luca, L., Calcagno, G., Rivellini, G., Mandato, M., De Luca, B. *et al.* (2004) Detachable snare versus epinephrine injection in the prevention of postpolypectomy bleeding: a randomized and controlled study. *Endoscopy* 36: 860–863.

El-Tawil, A. (2012) Trends on gastrointestinal bleeding and mortality: Where are we standing? *World J Gastroenterol* 18: 1154–1158.

Fry, L., Neumann, H., Olano, C., Malfertheiner, P. and Mönkemüller, K. (2008) Efficacy, complications and clinical outcomes of endoscopic sclerotherapy with N-butyl-2-cyanoacrylate for bleeding gastric varices. *Dig Dis* 26: 300–303.

Fujita, T. (2012) Controlling gastric variceal bleeding with endoscopically applied hemostatic powder (Hemospray). *J Hepatology* 57: 1397–1398.

Garcia-Tsao, G., Sanyal, A., Grace, N. and Carey, W. (2007) Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology* 46: 922–938.

Giday, S., Kim, Y., Krishnamurty, D., Ducharme, R., Liang, D., Shin, E. *et al.* (2011) Long-term randomized controlled trial of novel nanopowder hemostatic agent (TC-325) for control of severe arterial upper gastrointestinal bleeding in a porcine model. *Endoscopy* 43: 296–299.

Giday, S., Van Alstine, W., Van Vleet, J., Ducharme, R., Brandner, E., Florea, M. *et al.* (2013) Safety analysis of a hemostatic powder in a porcine model of acute severe gastric bleeding. *Dig Dis Sci* 58: 3422–3428.

Granata, A., Curcio, G., Azzopardi, N., Barresi, L., Tarantino, I. and Traina, M. (2013) Hemostatic powder as rescue therapy in a patient with H1N1 influenza with uncontrolled colon bleeding. *Gastrointest Endosc* 78: 451.

Holster, I., Brullet, E., Kuipers, E., Campo, R., Fernández-Atutxa, A. and Tjwa, E. (2014) Hemospray treatment is effective for lower gastrointestinal bleeding. *Endoscopy* 46: 75–78.

Ibrahim, M., El-Mikkawy, A., Mostafa, I. and Deviere, J. (2013) Endoscopic treatment of acute variceal hemorrhage by using hemostatic powder TC-325: a prospective pilot study. *Gastrointest Endosc* 78: 769–773.

Jensen, D. and Machicado, G. (2005) Endoscopic hemostasis of ulcer hemorrhage with injection, thermal, and combination methods. *Tech Gastrointest Endosc* 7: 124–131.

Jensen, D. and Machicado, G. (2009) Contact thermal devices, endoscopic hemoclips, and epinephrine injection for ulcer hemorrhage. Available at: http://www.uptodate.com/contents/contact-thermal-devices-for-the-treatment-of-bleeding-peptic-ulcers (accessed 3 March 2014).

Katsinelos, P., Kountouras, J., Paroutoglou, G., Beltsis, A., Chatzi-mavroudis, G., Zavos, C. *et al.* (2006) Endoloop-assisted polypectomy for large pedunculated colorectal polyps. *Surg Endosc* 20: 1257–1261.

Kovacs, T. (2008) Management of upper gastrointestinal bleeding. *Curr Gastroenterol Rep* 10: 535–542.

Kravetz, D. (2007) Prevention of recurrent esophageal variceal hemorrhage: review and current recommendations. *J Clin Gastroenterol* 41(Suppl. 3): 318–322.

Kubba, A. and Palmer, K. (1996) Role of endoscopic injection therapy in the treatment of bleeding peptic ulcer. *Br J Surg* 83: 461–468.

Leblanc, S., Vienne, A., Dhooge, M., Coriat, R., Chaussade, S. and Prat, F. (2013) Early experience with a novel hemostatic powder used to treat upper GI bleeding related to malignancies or after therapeutic interventions. *Gastrointest Endosc* 78: 169–175.

Leung Ki, E. and Lau, J. (2012) New endoscopic hemostasis methods. *Clin Endosc* 45: 224–229. DOI: 10.5946/ce.2012.45.3.224.

Levy, M. and Song, L. (2013) EUS-guided angiotherapy for gastric varices: coil, glue, and sticky issues. *Gastrointest Endosc* 78: 722–725.

Levy, M., Song, L., Farnell, M., Misra, S., Sarr, M. and Gostout, C. (2008) Endoscopic ultrasound (EUS)-guided angiotherapy of refractory gastrointestinal bleeding. *Am J Gastroenterol* 103: 352–359.

Lin, H., Lo, W., Cheng, Y. and Perng, C. (2007) Endoscopic hemoclip versus triclip placement in patients with high-risk peptic ulcer bleeding. *Am J Gastroenterol* 102: 539–543.

Liu, J., Petersen, B., Tierney, W., Chuttani, R., DiSario, J., Coffie, J. *et al.* (2008) Endoscopic banding devices. *Gastrointest Endosc* 68: 217–221.

Luchtefeld, M., Senagore, A., Szomstein, M., Fedeson, B., Van Erp, J. and Rupp, S. (2000) Evaluation of transarterial embolization for lower gastrointestinal bleeding. *Dis Colon Rectum* 43: 532–534.

Maleux, G., Roeflaer, F., Heye, S., Vandersmissen, J., Vliegen, A., Demedts, I. *et al.* (2009) Long-term outcome of transcatheter embolotherapy for acute lower gastrointestinal hemorrhage. *Am J Gastroenterol* 104: 2042–2046.

Mönkemüller, K., Toshniwal, J., Zabielski, M., Vormbrock, K. and Neumann, H. (2012) Utility of the "bear claw", or over-the-scope clip (OTSC) system, to provide endoscopic hemostasis for bleeding posterior duodenal ulcers. *Endoscopy* 44(Suppl. 2): E412–413.

Moosavi, S., Chen, Y. and Barkun, A. (2013) TC-325 application leading to transient obstruction of a post-sphincterotomy biliary orifice. *Endoscopy* 45(Suppl. 2): E130.

Nagata, S., Kimura, S., Ogoshi, H. and Hidaka, T. (2010) Endoscopic hemostasis of gastric ulcer bleeding by hemostatic forceps coagulation. *Dig Endosc* 22(Suppl. 1): 22–25.

Paganelli, M., Alvarez, F. and Halac, U. (2014) Use of Hemospray for non-variceal esophageal bleeding in an infant. *J Hepatology* 61: 712–713.

Pedroto, I., Dinis-Ribeiro, M. and Ponchon, T. (2012) Is timely endoscopy the answer for cost-effective management of acute upper gastrointestinal bleeding? *Endoscopy* 44: 721–772.

Sargon, P. and Laurie, T. (2013) Hemospray for life-threatening ulcer bleeding: first case report in the United States. *ACG Case Rep J* 1(1): 7–9.

Singhal, S., Changela, K., Papafragkakis, H., Anand, S., Krishnaiah, M. and Duddempudi, S. (2013) Over the scope clip: technique and expanding clinical applications. *J Clin Gastroenterol* 47: 749–756.

Smith, L., Morris, A. and Stanley, A. (2013) The use of Hemospray in portal hypertensive bleeding; a case series. *J Hepatology* 60: 457–460.

Smith, L., Stanley, A., Bergman, J., Kiesslich, R., Hoffman, A., Tjwa, E. *et al.* (2014) Hemospray application in nonvariceal upper gastrointestinal bleeding: results of the survey to evaluate the application of Hemospray in the luminal tract. *J Clin Gastroenterol* 48(10): e89–e92.

Soulellis, C., Carpentier, S., Chen, Y., Fallone, C. and Barkun, A. (2013) Lower GI hemorrhage controlled with endoscopically applied TC-325 (with videos). *Gastrointest Endosc* 77: 504–507.

Stanley, A., Smith, L. and Morris, A. (2013) Use of hemostatic powder (Hemospray) in the management of refractory gastric variceal hemorrhage. *Endoscopy* 45: E86–E87

Sulz, M., Frei, R., Meyenberger, C., Bauerfeind, P., Semadeni, G. and Gubler, C. (2014) Routine use of Hemospray for gastrointestinal bleeding: prospective two-center experience in Switzerland. *Endoscopy* 46: 619–624.

Sung, J., Luo, D., Wu, J., Ching, J., Chan, F, Lau, J. *et al.* (2011) Early clinical experience of the safety and effectiveness of Hemospray in achieving hemostasis in patients with acute peptic ulcer bleeding. *Endoscopy* 43: 291–295.

Weldon, D., Burke, S., Sun, S., Mimura, H. and Golzarian, J. (2008) Review: Interventional management of lower gastrointestinal bleeding. *Eur Radiol* 18: 857–867.

Yau, A., Ou, G., Galorport, C., Amar, J., Bressler, B., Donnellan, F. *et al.* (2014) Safety and efficacy of Hemospray in upper gastrointestinal bleeding. *Can J Gastroenterol Hepatol* 28 (2):72–76.