

Efficacy and safety of TC-325 (Hemospray™) for non-variceal upper gastrointestinal bleeding at Middlemore Hospital: the early New Zealand experience

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ABSTRACT

AIMS: A case series to review early experiences with Hemospray™ for a variety of non-variceal upper gastrointestinal bleeding (UGIB) at Middlemore Hospital.

METHODS: Hemospray™ was administered therapeutically as first line or rescue at the discretion of the endoscopist. All cases of UGIB requiring Hemospray™ at Middlemore Hospital were identified to the investigator who undertook analysis of electronic and hard copy notes.

RESULTS: Between October 2013 and July 2016, 36 patients were treated endoscopically with Hemospray™. Source of bleeding was predominantly gastric in 17, 15 were duodenal and four oesophageal. The majority of lesions were peptic ulcer or post-intervention (78%), with others being Mallory Weiss tear (MWT), gastric mass, Dieulafoy lesion, portal hypertensive gastropathy and post-biopsy. Thirty-one were actively bleeding with mostly oozing haemorrhage (75%). Twenty-three patients were on antithrombotic therapy (ATT), two each on warfarin and low molecular weight heparin (LMWH) and 19 on antiplatelet agents. Hemospray™ was administered therapeutically in all cases, as first line or rescue. Acute haemostasis was achieved in all patients; four (11%) episodes of re-bleeding occurred within seven days, with average follow-up of 16 months. There were no instances of equipment malfunction or adverse events specific to use of Hemospray™.

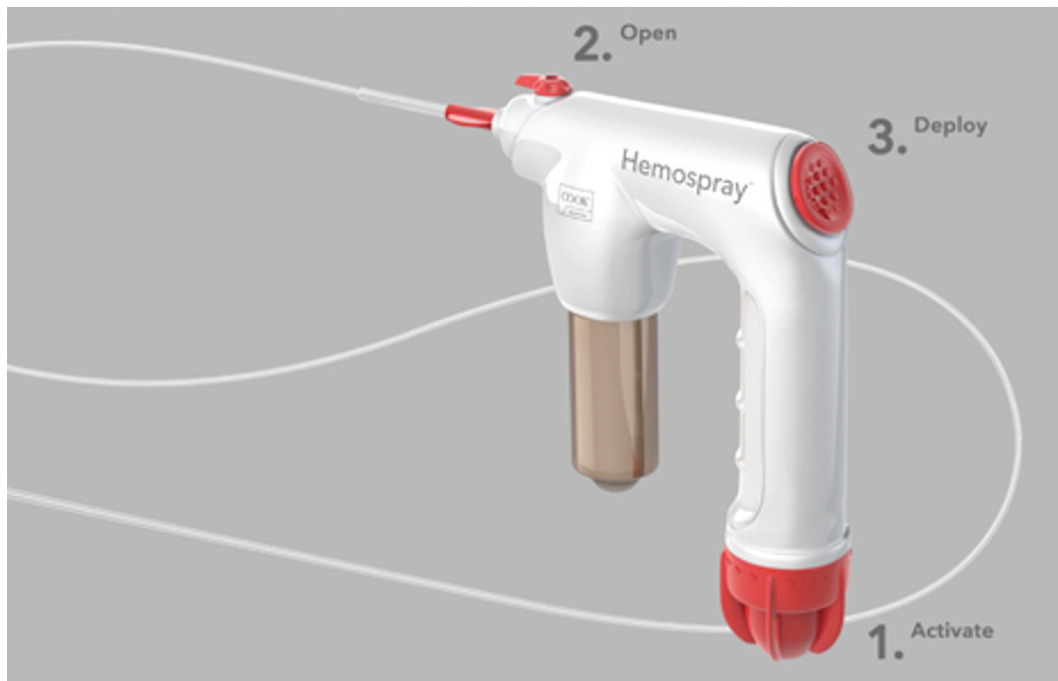
CONCLUSIONS: Our early experience with Hemospray™ is very promising and there is clear role for Hemospray™ as a rescue therapy when standard methods have failed to achieve haemostasis and possibly as first line in cases of diffuse bleeding not amenable to standard interventions. However, Hemospray™ is not recommended as a standalone therapy for spurting haemorrhage due to the increased frequency of re-bleeding.

TC-325 (Hemospray™, Cook Medical Inc, Winston-Salem, NC, US) is a synthetic haemostatic powder recently licensed for use in non-variceal upper gastrointestinal bleeding (UGIB) in New Zealand. Middlemore Hospital was the first centre in Australasia to use Hemospray™. Proposed mechanism is via formation of a mechanical barrier and concentration of clotting factors, which enhances activation of the clotting

cascade.¹ The in vitro effects of TC-325 on standardised coagulation and platelet function have been studied, showing that both prothrombin time and activated partial thromboplastin time are reduced in a dose-dependent manner in the presence of the powder.² These results suggest that Hemospray™ may facilitate local hemostasis.

There is a growing body of evidence supporting its safety and efficacy for peptic

Figure 1: Hemospray™ device.



ulcer-related haemorrhage,³⁻⁵ and to a lesser extent in malignancy related^{6,7} and other causes of UGIB such as portal hypertensive gastropathy⁸ and post-interventional bleeding.^{6,9} Results indicate high rates of success for oozing haemorrhage; 73–100% for initial haemostasis and 11–33% for re-bleeding.^{3,4} However, concern remains around spurting haemorrhage with variable success for initial haemostasis (0–100%)^{3,4,6} and higher rates of re-bleeding (35–50%),^{3,10} particularly when combined with the use of antithrombotic therapy.

Methods

The Hemospray™ package includes a delivering device with a powder syringe (20g each), two catheters (7 and 10 F, suitable for a working channel of 2.8 and 3.7 respectively) and a CO₂ cartridge (Figure 1). The latter is activated by turning a red knob placed at the base of the handle until it stops. Before inserting the catheter in the working channel of the endoscope, blood must be removed as much as possible and the bleeding site must be identified. Air is then flushed through the accessory channel and the catheter is slowly advanced until the catheter tip is visualised. Care must be taken to avoid direct contact between the catheter tip and blood or mucosa to avoid occlusion.

It is advisable to maintain a 1–2cm distance from the bleeding site during the procedure. Then, after turning the red valve, placed at the top of the delivery device to the open position, TC-325 is ready to be delivered by depressing the red trigger button in 1–2 second pulses. Following the manufacturer's instructions, no more than three devices (60g) should be applied per patient. However, in one case up to seven syringes were used with no adverse effects seen.⁴

Hemospray™ was used therapeutically as first line or rescue, at the discretion of the endoscopist. Between October 2013 and July 2016 all cases of UGIB requiring Hemospray™ at Middlemore Hospital were identified to the investigator who undertook analysis of electronic and hard copy notes. No more than one canister was used for any single application. All endoscopists had undertaken a training session with Hemospray™. This case series was approved by the institutional review board (#1848).

Results

A total of 36 patients (mean age of 68.6 years), 25 male (69%) were treated endoscopically with Hemospray™. Clinical presentation was haematemesis in 12, 20 with melaena, five with syncope, seven

Table 1: Endoscopic findings, management and outcomes.

Location	Lesions	Number	Stigmata	Hemospray™	Outcome
Gastric	Ulcer	9	4 Spurting	4 Rescue	1 Re-bleed
			3 Oozing	1 First line, 2 rescue	-
			1 Adherent clot	Rescue	-
			1 Clean base	First line	-
	Gastric polypectomy	3	3 Oozing	2 First line, 1 rescue	-
	Gastric mass	1	Oozing	First line	-
	Post ESD gastric lesion	1	Oozing	Rescue	-
	Gastric polyp	1	Oozing	Rescue	-
	Dieulafoy lesion	1	Visible vessel	Rescue	-
	Portal hypertensive gastropathy	1	Oozing	First line	-
Duodenal	Ulcer	15	1 Spurting	Rescue	-
			11 Oozing	1 First line, 10 rescue	2 Re-bleed
			1 Adherent clot	Rescue	1 Re-bleed
			1 Visible vessel	Rescue	-
			1 Clean base	First line	-
Oesophageal	Post biopsy	2	2 Oozing	2 Rescue	-
			Mallory Weiss tear	1	Oozing
	Ulcer	1	Oozing	Rescue	-

Hemospray was administered therapeutically as first line (n=9) (Figure 2), or rescue (n=27) (Figure 3). Other modalities used were adrenaline injection (n=21), thermal therapy (n=4) and mechanical (n=18).

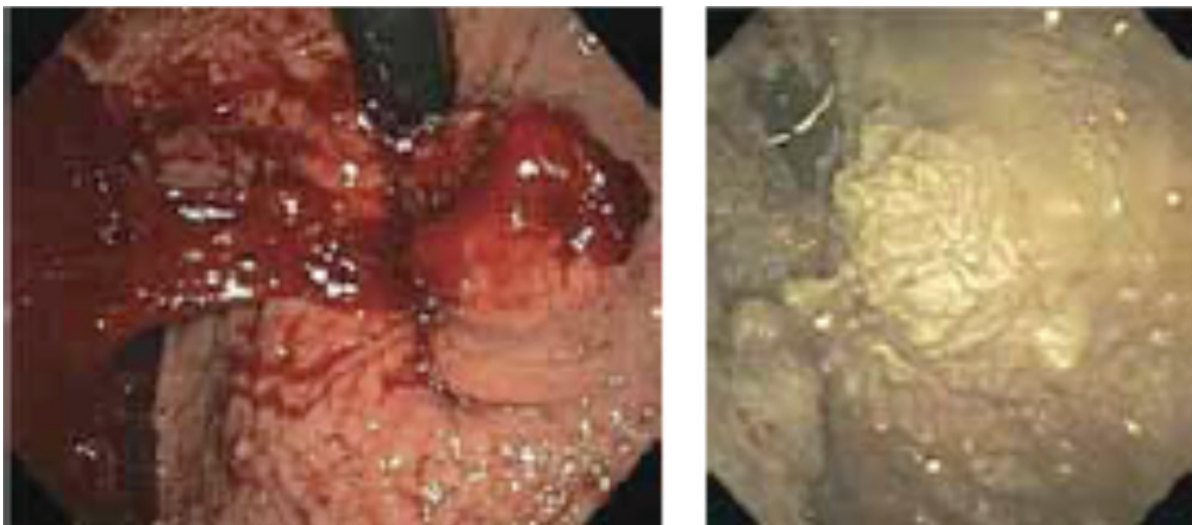
Figure 2: Bleeding gastric cardia mass, before (left) and after (right) Hemospray application.⁵

Figure 3: Gastric ulcer (arterial bleed), post clipping with ongoing ooze (left) and after Hemospray™ administration (right), hemostasis achieved.



with presyncope and one each with symptomatic anaemia and elective procedure. Rockall score ranged from 3–10, mean 5.9 with evidence of haemodynamic instability (heart rate >100 beats/min, systolic blood pressure <100 mmHg) in 13. Laboratory results showed a mean haemoglobin (Hb) nadir of 79.8 g/L (normal 135–170 g/L), thrombocytopenia (platelets <150x10⁹/L) in nine and eight with coagulopathy (international normalised ratio (INR) >1.2). Review of medications showed 19 patients on antiplatelet agents (64%) and four on anti-coagulation, two each with warfarin and LMWH. Nine (27%) patients were on proton pump inhibitors (PPI) at admission and 27 (75%) were on PPI at discharge.

Source of bleeding (Table 1) was most commonly gastric (n=17) or duodenal (n=15) with a small number of oesophageal (n=4). Bleeding was secondary to peptic ulcer (n=24), post polypectomy (n=3), gastric polyp (n=1), gastric mass (n=1), post endoscopic submucosal dissection (ESD) (n=1), portal hypertensive gastropathy (n=1), Dieulafoy lesion (n=1), Mallory Weiss tear (n=1), post oesophageal biopsy (n=2) and an oesophageal ulcer (n=1). Thirty-one lesions were actively bleeding; the majority demonstrated oozing haemorrhage (n=27) with five cases of spurting haemorrhage.

Acute haemostasis was achieved in 100% of patients, with four episodes of re-bleeding within seven days. Two of the patients who re-bleed were anti-coagulated, one with LMWH and one with dual anti-platelets, the latter of which was an arterial bleed. The remaining two were in a technically difficult position where clips were not able to be placed.

Nine patients died. Four deaths were unrelated to bleeding, two from advanced haematological disease, one invasive pancreatic adenocarcinoma and one with sepsis on a background of end stage liver disease. Four were palliated on recurrence of bleeding due to comorbidities, mostly advanced malignancy and one elderly patient with advanced dementia. One patient died of progressive multi-organ failure despite cessation of bleeding. Three of the lesions were unable to have mechanical therapy due to the location. One, as previously mentioned was an arterial bleed on dual anti-platelets that re-bleed despite clips, adrenaline and Hemospray™.

Average follow-up was 16 months. There were no instances of equipment malfunction or adverse events attributable to Hemospray.

Discussion

Hemospray was used as first line in cases where other modalities would not have been suitable, such as a broad based MWT, oozing gastric mass, post polypectomy, portal hypertensive gastropathy and gastric erosions with multiple areas of ooze and one case with an unclear source of bleeding in a patient with significant thrombocytopenia (platelets 72x10⁹/L). Hemospray™ was also used successfully on a malignant gastric mass as a bridge to radiation; the patient subsequently received radiation and has been stable with no further bleeding for 10 months. Where Hemospray™ was used as the mode of choice due to appropriate lesions as described above, there were no episodes of re-bleeding.

Hemospray rescue was used after failure of standard modalities, predominantly when clips had been deployed onto a visible vessel and ongoing ooze was present. There were five cases of spurting haemorrhage, all required multimodal management with adrenaline, clips, Hemospray™ +/- heater probe. Four of these patients had successful primary therapy with no re-bleeding, none of whom were on ATT, however, the one patient who was on dual anti-platelets re-bled and did not survive.

Our experiences with Hemospray have thus far been very promising with no Hemospray failures or adverse events seen. The high rates of acute hemostasis and low rates of re-bleeding, despite significant comorbidities and severity of bleeding (associated with high rates of haemodynamic instability, thrombocytopenia and coagulopathy) and high use of ATT in our group, make it an appealing modality. The majority of deaths were due to advanced underlying malignancy or other life limiting comorbidities in patients who were nearing end of life and do not necessarily represent true failures of therapy.

From the literature and our own experiences, there is a role for Hemospray in cases of diffuse bleeding such large ulcers, post endoscopic mucosal resection, portal hypertensive gastropathy, gastric antral vascular ectasia, unclear source of bleeding, malignancy or technically difficult location where standard therapies would be ineffective or impossible.^{1,6-8,11} In addition, at smaller centres where expert endoscopists may not be available, this is a simple alternative.⁷ It is important however, to consider if this is definitive and should be used as bridging therapy if the underlying pathology is likely to cause recurrent bleeding.

There has been some concern around the risks of perforation, obstruction and systemic embolisation. Two studies have sited perforation as a complication.^{3,5} The largest study, with 82 patients, reported a large number of technical issues including blockage of application catheter (4),

blockage of endoscope working channel (1) and endoscope adherent to the mucosa (2).⁵ This suggests endoscopists were working in close proximity to the mucosa. The recommendation is no closer than 1–2cm. At which distance the pressure is very low and unlikely to cause adverse effects such as perforation.

There is concern around the theoretical risk of systemic embolisation in variceal bleeding due to lower pressure of varices. However, recent studies have also shown safety and efficacy of Hemospray for acute variceal haemorrhage.^{12,13}

Of genuine concern is the risk of biliary orifice obstruction. There are reported cases in the literature after use for post-sphincterotomy bleeding.¹⁴ Hence it should be used with caution for this indication.

Hemospray has more recently been trialled in small numbers of lower GI bleeding (LGIB) for a variety of causes and again has been shown to be safe and effective. However, as with UGIB Hemospray, failures were seen with re-bleeding in two cases on ATT with spurting haemorrhage.^{9,15,16}

Conclusions

Although further studies are required to compare Hemospray to standard modalities and assess its use for LGIB and variceal haemorrhage, there is already a role for Hemospray. We would suggest its use as first line for oozing haemorrhage in cases of diffuse bleeding, unclear source of bleeding or technically difficult location and as rescue therapy for any bleeding where other modalities have failed.

Its safety and efficacy in oozing haemorrhage has been demonstrated in numerous studies, however, several studies have shown that spurting haemorrhage especially in the context of ATT use has lower rates of hemostasis with higher rates of re-bleeding. In cases of spurting bleeding, Hemospray is not advisable to be used as monotherapy but could be used in combination with mechanical therapy.

Competing interests:

Nil.

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