Hemospray® Data Summary

For more information on Hemospray visit: hemospray.cookmedical.com
Safety analysis of Hemospray in a porcine model of gastric bleeding

Study Design:
This study was conducted in accordance with Good Laboratory Practice guidelines and to investigate the local and systemic histopathologic effects of Hemospray in a porcine model of gastric bleeding.

Study Aim:
• To investigate the local and systemic histopathologic effects of Hemospray in a swine model of gastric bleeding.

Treatment Procedure:
• Nine animals underwent creation of a looped vascular bundle (the gastroepiploic artery and vein) which was placed into the stomach lumen. Six treatment animals then underwent endoscopic needle-knife puncture of the bundle to create Forrest grade 1A or 1B bleeding.
• The Hemospray delivery catheter was positioned past the endoscope tip and approximately 2 cm away from the stomach wall. Powder was sprayed onto the area of bleeding until hemostasis was obtained and witnessed for at least 10 consecutive minutes.

Methods:
• Nine female, juvenile domestic, pigs underwent laparotomy to allow gastrotomy and looping of a portion of the gastroepiploic artery and vein (i.e., a vascular bundle) through a 1 cm incision in the stomach wall. Six animals (the treatment group) then underwent endoscopic needle-knife puncture of the looped vascular bundle to create Forrest grade 1A (pulsatile hemorrhage) or 1B (oozing hemorrhage) bleeding. Three animals (the control group) did not undergo incision of the transferred vascular bundle and were not given Hemospray powder.
• The Hemospray delivery catheter was positioned past the endoscope tip and approximately 2 cm away from the stomach wall. Powder was sprayed onto the area of bleeding until hemostasis was obtained and witnessed for at least 10 consecutive minutes. The laparotomy site then underwent layered closure. All animals survived at least 8 days after the procedure.

“Animal studies have shown Hemospray to be a highly effective and safe single agent to achieve hemostasis.”

Sam Giday, MD
Center for Digestive Health, Orlando, Florida
Summary of Final Results:

Hemostatic Results:
Hemostasis was achieved in all animals (6/6) treated with Hemospray. Three animals had Forrest grade 1A hemorrhage and 3 animals had Forrest grade 1B hemorrhage. Pre-treatment, post-treatment, and follow-up PT, PTT, platelet counts, and hematocrit values did not vary substantially.

Histopathology Results:
No hemostatic powder was identified grossly in any stomach specimens. No hemostatic powder was identified histologically in any local or systemic tissue samples (including stomach, heart, liver, kidney, spleen, pancreas, lung, brain, and lymph nodes). Histopathologic findings showed inflammation and fibrosis around the gastrostomy site consistent with normal wound healing. While the gross examination of all looped vascular bundles was normal, histologic evaluation demonstrated that all specimens had denuded (i.e., ulcerated) vascular bundle surfaces. Surface ulceration resulting in arterial erosion and rupture is a consequence of this animal model.

Histologic Images:
A) This image demonstrates the vascular bundle (solid arrow) protruding into the gastric lumen. Gastric mucosa does not cover the surface of the vascular bundle. Ulcerations (U) gradually exposed one of the branches of the translocated gastroepiploic artery (dotted arrow) to the gastric lumen. Surface ulceration resulting in arterial erosion and rupture is a consequence of this animal model. H&E stain, low magnification scan, approximately 95 original magnification.

B) This image is a higher magnification of the artery denoted by the dotted arrow in A. The ulcerated (U) lumenal surface has breached the arterial (A) wall, resulting in late GI bleeding (arrow). H&E stain, 940 original magnification.

Representative photomicrograph collage of tissue stalk collected at follow-up from control group animals. Suture sites (S), inflammation (I), fat cells (F), and a small muscular vessel (V) are noted. Gross evaluation of all (treatment and control) looped vascular bundles were normal, but histologic evaluation showed that all vascular bundles had denuded surfaces consistent with exposure to stomach contents. This finding is related to the severe injury model, not to Hemospray treatment.

Conclusion:
Hemospray:
• Did not cause any systemic embolic effects
• Did not cause any bowel obstruction or unintended luminal effects
• Did not cause any local or regional particulate effects
• Did not cause any systemic coagulopathic effects
• Did not affect healing of the surgical site

Reference:
Early clinical experience of the safety and effectiveness of Hemospray in achieving hemostasis in patients with acute peptic ulcer bleeding

Study Aim:
Early clinical evaluation of the safety and efficacy of Hemostatic Powder in achieving hemostasis for active peptic ulcer bleeding.

Study Design:
Prospective, open label, single-arm study with 20 patients at one center

Primary Outcomes:
Safety: Incidence of procedural and treatment-related serious adverse events (SAE)
Effectiveness: Rate of acute hemostasis and rate of recurrent bleeding within 72 hours of Hemostatic Powder application

Summary of Results:
This final analysis includes 20 patients (2 females and 18 males) enrolled in the completed study. The mean patient age was 61 years (range, 37 to 85 years). All patients presented with hematemesis and/or melena. At index endoscopy, 6 patients (30%) were found to have a peptic ulcer located in the stomach, and the remaining 14 patients (70%) were found to have a peptic ulcer located in the duodenum.

Acute hemostasis was achieved in 19 of 20 patients (95%) with no recurrent bleed in 17 of 19 patients (89.5%) at 72 hours. No procedural or device-related serious adverse events were reported. No mortality or serious adverse events were reported at the 30-day follow-up after treatment.

Conclusion:
Early clinical evidence suggest that the application of Hemostatic Powder is safe in this sample of 20 patients with acute peptic ulcer bleeding. This device was also effective in achieving acute hemostasis in (95%) of the cases and subacute hemostasis in 90% of the cases.

Reference:
Hemospray for Nonvariceal Upper Gastrointestinal Bleeding: Results of the Seal Dataset (Survey to Evaluate the Application of Hemospray in the Luminal Tract)*†

Study Design:
Information on Hemospray was prospectively collected as part of an early limited release multi-center cohort post market product registry. Eighty-nine Hemospray case experiences were captured from 15 centers throughout Canada and Europe.

Outcome Measures:
- Ease of use compared to other hemostatic modalities
- Location and type of bleeds treated
- Method for achieving acute hemostasis

Methods of Hemostasis
Acute Hemostasis with Hemospray was achieved in 100% (89/89) of cases.
Acute Hemostasis was achieved with Hemospray alone in 57% (51/89) of cases.
Hemospray was used as an adjunct to other modalities or as a rescue therapy in 43% (38/89) of cases.
- Hemospray was identified as the final hemostasis treatment in 63% (24/38) of cases where more than one modality was used.
In 9 cases the order of treatment methods was unclear, but did include one or multiple other hemostatic modalities.

Contributors SEAL post market evaluation:
University of Manitoba, Winnipeg MT, St. Pauls Hospital, Vancouver BC, St. Michaels Hospital, Toronto ON, McGill University, Montreal QC, University Hospital Mainz, Germany, Queen Elizabeth Hospital, Birmingham, UK, Lund University Hospital, Malmo Sweden, Institute University Parc Tauli, Sabadell, Spain, Hvidovre Hospital, Copenhagen, Denmark, Hospital Cochin, Paris, France, Glasgow Royal Infirmary, Glasgow, Scotland, Erasmus Medical Center, Rotterdam, Netherlands, Ospedale San Paolo, Italy, Amsterdam Medical Center, Amsterdam Netherlands

An ease of use comparison was made for 79 patients and Hemospray was determined to be comparable to or easier than administration of clips or other hemostasis treatment modalities.

Hemostasis was achieved in under 10 minutes in 77% of cases with Hemospray. Hemospray was thought to save time in 59% of cases.

Out of the 40 patients from the dataset with peptic ulcers 44% (16/40) of those were classified as Forest 1a (pulsatile) and 48% (19/40) as Forest 1b (oozing).

Acute Hemostasis was achieved with use of Hemospray alone in 44% (7/16) of the cases with 1a bleeds and 63% (12/19) of the ones with 1b bleeds.

*Poster presented at DDW 2012
Data on file at Cook Medical.
Use of Hemospray in cancer-related upper GI hemorrhage: Case Series

<table>
<thead>
<tr>
<th>Case</th>
<th>Patient Summary</th>
<th>Treatment</th>
<th>Results/Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>74-year-old patient with inoperable metastatic gastric adenocarcinoma, hypotensive and tachycardic</td>
<td>Hemospray (20g) was applied to the tumor with successful hemostasis.</td>
<td>The patient remained hemodynamically stable without further signs of active bleeding. Two treatments of radiotherapy were given 5 days after endoscopy. No rebleeding occurred and the patient was discharged 20 days later.</td>
</tr>
<tr>
<td>2</td>
<td>69-year-old patient with history of chronic obstructive lung disease, hematemesis, intermittent vomiting and melena, EGD revealed a large distal esophageal firm mass suspicious for malignancy; which bled on contact and developed constant oozing after biopsies</td>
<td>Approximately 15 g of Hemospray was applied with good hemostasis. Oral pantoprazole was started after the procedure patient remained stable without clinical signs of ongoing hemorrhage.</td>
<td>No recurrent bleeding was noted 13 days after Hemospray therapy.</td>
</tr>
<tr>
<td>3</td>
<td>58-year-old patient with diabetes and hypertension, hematemesis, and tachycardic, EGD revealed an ulcerated mass in the duodenal bulb that was actively oozing.</td>
<td>Approximately 20 g of Hemospray was administered with good results.</td>
<td>No rebleeding occurred at 41 days post Hemospray use.</td>
</tr>
<tr>
<td>4</td>
<td>53-year-old patient with stage IIIA non-small cell lung cancer, tachycardic, large ulcerated necrotic mass involving the gastric cardia, recurrent melena with hemodynamic instability. Repeat gastroscopy showed active oozing from the previously observed friable mass.</td>
<td>Hemospray application with good results.</td>
<td>Five days later, the patient’s haemoglobin and platelet count dropped. After appropriate resuscitation, a third EGD was performed showing the same large lesion that was actively bleeding managed with diffuse reapplication of Hemospray (20 g) with immediate hemostasis. Radiation therapy was initiated the same day; however, 6 days later, hemorrhage recurred and a decision was made with the patient’s family for palliative management. The patient died 12 days after the third Hemospray treatment.</td>
</tr>
<tr>
<td>5</td>
<td>A 49-year-old patient with stage IV breast cancer, recurrent melena. EGD revealed severe infiltrating disease of the duodenal flexure from the known periduodenal metastatic lymphadenopathy with active oozing.</td>
<td>A total of 20 g of Hemospray was applied, and hemostasis was achieved.</td>
<td>No rebleeding occurred as of 14 days after Hemospray application.</td>
</tr>
</tbody>
</table>

Conclusion:
Hemospray may become the method of choice in neoplastic bleeding given its noncontact application, malleable nature, and ability to cover large and multiple areas of bleeding. Initial hemostasis was achieved in all subjects with only 1 case of rebleeding; the technology may thus be useful both acutely and as a bridge to further adjuvant therapy. Complications such as embolism or bowel obstruction were not observed.

Reference:
Early experience with Hemospray used to treat upper GI bleeding related to malignancies or after therapeutic interventions

Study Design:
Seventeen patients who either experienced bleeding after completion of an endoscopic intervention or who had malignancy-related bleeding (which required repeat blood transfusions) observed during diagnostic endoscopy were candidates for inclusion in this single-arm study.

Outcome measures:
Primary: Immediate hemostasis
Secondary: Recurrent bleeding at 7 and 30 days after Hemospray application, mortality at 7 and 30 days after Hemospray application, and adverse events possibly related to Hemospray application.

Methods and Results:

<table>
<thead>
<tr>
<th>Therapeutic intervention resulting in upper GI bleeding</th>
<th>No. Patients</th>
<th>Hemospray as first hemostatic treatment</th>
<th>Immediate hemostasis achieved, no. (%)</th>
<th>Recurrent bleeding</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal EMR</td>
<td>5</td>
<td>5 (100)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Duodenal EMR</td>
<td>4</td>
<td>4 (100)</td>
<td>0</td>
<td>1*</td>
<td>0</td>
</tr>
<tr>
<td>Ampullary resection</td>
<td>2</td>
<td>2 (100)</td>
<td>0</td>
<td>1*</td>
<td>0</td>
</tr>
<tr>
<td>Biliary sphincterotomy</td>
<td>1</td>
<td>1 (100)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hemostatic outcomes in the malignancy group</th>
<th>Recurrent bleeding</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Malignancy</td>
<td>No. Patients</td>
<td>Hemospray as first hemostatic treatment</td>
</tr>
<tr>
<td>Esophageal</td>
<td>2</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Gastric</td>
<td>2</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>1</td>
<td>1 (100)</td>
</tr>
</tbody>
</table>

*No active bleeding identified.

“Overall, Hemospray appears to be an effective hemostatic therapy for nonvariceal upper GI bleeding related to endoscopic therapeutic interventions and malignancies.”

Prof. Fredric Prat
Cochin Hospital, Paris, France

Reference:
Customer Service

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