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Gastroenterology

Safety and Efficacy of the Use of Hemospray™ in Patient with Non Variceal Upper Gastrointestinal Bleeding

*Dr. Sinan W, Jasim
**Dr.Raghad J. Al-Akayshee

ABSTRACT

Background:The gastrointestinal bleeding, is a major cause of morbidity and mortality. Hemospray is one of the new introduced agents for control of gastrointestinal bleeding. Method:The study was carried out in Gastroenterology and Hepatology Teaching Hospital in prospective manner on a sample of Iraqi patients from the period from July 2014 to July 2015 who required endoscopic evaluation for suspected UGIB and were treated with Hemospray. Results: A total of 14 patients were treated with Hemospray during the study period. Their mean age was 60.6 y (ranging 30 to 77 year). Clinical presentation included hematemesis in 12 patients (85.3%), melena in 14 patients (100%), and presyncope in 6 patients (42.8%). Physical examination revealed hypotension (systolic blood pressure ? 90 mmHg) in all patients and tachycardia (heart rate >100 beats/min) in six (42.8%). Hemospray was administered as a primary modality (71.4%) and as a rescue modality (28.6%) with a rate of acute hemostasis (primary end point) in 100% and rebleeding in 7% of patients. All the patient has secured hemostasis observed for at least three minutes following Hemospray application. Recurrent bleeding occurred in one patient within 24 hours (one of the patient with severe erosive esophagitis) in whom secure hemostasis was achieved after another attempt of Hemospray.No recorded complications other than technical complication of catheter blockage which had occurred in two patients. No serious adverse effects, morbidity or mortality was observed in the follow up period.Conclusion: Hemospray™ appears to allow safe control of acute bleeding and may be used to stop upper gastrointestinal bleeding as a temporary measure or a bridge toward more definitive therapy.

Introduction:

Upper gastrointestinal bleeding (UGIB) is defined as bleeding derived from a source proximal to the ligament of Treitz.Upper gastrointestinal bleeding UGIB is major health problem in the world. Many modalities are used for endoscopic intervention to stop various causes of UGIB.Hemospray™ is a novel therapy for management of certain conditions of UGIB.

Patients and method:

This prospective study was carried out in Gastroenterology and Hepatology Teaching Hospital on a sample of Iraqi patients from the period from July 2014 to July 2015.Hemospray™ (Cook Medical Inc., Winston-Salem, NC) was the technique used to endoscopically control UGIB in 14 patients with variable causes. Each patient was admitted, resuscitated, history was taken (Past medical history of PU, Chronic liver disease, tumor, NSAIDs and anticoagulant use. Physical examin ation done and vital signs were recorded, sent for investigation (mainly Hemoglobin (Hb), Prothrombin Time (PT) and International normalization ratio (INR) were included).

The selection of patients was for the possible indication of:

1- UGI Bleeding from within endoscopic reach of Upper GI tumor.

2- Difficulty in achieving hemostasis by another modalities (either because they might be difficult technically or ineffective or non - available).

The exclusion criteria were:

1- Variceal UGIB.
2- Non active bleeding.
3- Refusal to participate.
4- Pregnant women or lactating women.

The endoscopy was carried out by an expert endoscopist using Olympus Lucera CV-260 or Pentax APK-5000-i upper endoscopy systems with the patient under no sedation. The cases that were amenable to be treated by other endoscopic modalities were excluded and only difficult cases to be managed by usual methods were included.

The aim of the procedure was having secure hemostasis for at least three minutes after spraying the powder (the primary end point) and observation for no recurrence of the bleeding for the next three days (i.e. the period of hospital admission)(the secondary end point).

* FICMS(Int.Medicine),CAB GIT&Hepatology FIICMS GIT & Hepatology/Gastroenterology and Hepatology Teaching Hospital - Medical City, Baghdad
**(CABM, FICMS GE & H)/Gastroenterology and Hepatology Teaching Hospital - Medical City, Baghdad

This was modified from " Hemospray Versus the Combined Conventional Technique for Endoscopic Hemostasis of Bleeding Peptic Ulcers : A Pilot Study"which is still ongoing trial by Andrew Kwek Boon Eu, Changi General Hospital who decide to have at least 5 minutes of secure hemostasis after propulsion of hemospray.

In this study we the time was decreased, firstly to ensure more efficacy and secondly to spare the time for our patient since they undergo the endoscopy without sedation. The hemospray was the primary monotherapy in the tumor cases and the second modality (after failure of the primary modality) in all cases of UGIB from esophageal site. In the remaining cases it was used either because of unviability of better modality (the case of bleeding from EST site and in which hemoclips or APC is mentioned is a reasonable choices especially after the use of tamponade pressure after injection and the case of gastric bleeding from gastric antral vascular ectasia (GAVE) or after failure of injection as in the rest of cases from bleeding from variable ulcer sites duodenal or gastric and after failure of the and unavailability of hemoclips.

The Hemospray™ package (figure 3) includes a delivering device with a powder syringe (20 g each), two catheters (7 and 10 F, suitable for a working channel of 2.8 and 3.7 respectively) and a CO2 cartridge. 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. Then, air is flushed through the accessory channel and the catheter is slowly advanced through it until the catheter tip is visualized. Care must be taken in not placing the catheter directly in contact with blood or the mucosa to avoid occlusion. It is advisable to maintain a 1-2 cm 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 s pulses (figure 2). Following the manufacturerrs instructions, no more than 3 devices (60 g) should be applied per patient. (23).in this study no more than half - one canister was used for single patient.

Results:

A total of 14 patients were treated with hemospray during the study period. Their mean age was 60.6 y (ranging 30 to 77 year).Clinical presentation included hematemesis in 12 patient (85.3%), melena in 14 patients (100%), and presyncope in 6 patients (42.8%).Physical examination revealed hypotension (systolic blood pressure ? 90 mmHg) in all patients and tachycardia (heart rate >100 beats/min) in six (42.8%). Laboratory investigations showed a mean hemoglobin nadir of 93.0 g/L (normal 135 g/L to 170 g/L), thrombocytopenia (platelets <150Ч10 /L) in six (42.8%) patients and coagulopathy (international normalized ratio >1.2) in one patient (7.1%). Medication review revealed that five of them were on antiplatelet (35.7%) and only one patient was on anticoagulant (warfarin) (7.1%) due to prosthetic metallic aortic valve. (Table 3)A bleeding from the esophagus was noted in five patients (35.7%) three of them having ulceration, one of them had esophageal tumor and the other had esophageal tear. Bleeding from the stomach was seen in six patients (42.8%), four of them had gastric tumor, one had gastric ulceration and the other one had GAVE. Duodenal bleeding was noted in three patients (21.4%), two of them had ulceration and the third on had bleeding from the ampulla post ERCP- EST. All the patients had active bleeding, eleven (78.5%) of them had oozing hemorrhage from bleeding site while the rest three (21.5%) of them had spurting hemorrhage. (Table 4)

Our study examined the use of Hemospray in UGIB (n=14), which originated from the previously mentioned causes. Hemospray was administered as a primary modality (71.4%) and as a rescue modality (28.6%) with a rate of acute hemostasis (primary end point) in 100% and rebleeding in 7% of patients. All the patient has secured hemostasis observed for at least three minutes following hemospray application. Recurrent bleeding occurred in one patient within 24 (one of the patient with severe erosive esophagitis) in whom secure hemostasis was achieved after another attempt of hemospray. (Table 5)No recorded complication apart from technical complication other than catheter blockage which had occurred in two patients, was not noticed.No serious effects, morbidity or mortality was observed in the follow up period.Our study examined the use of Hemospray in UGIB (n=14), which originated from different causes.Hemospray was administered as a primary modality (71.4%) and as a rescue modality (28.6%) with a rate of acute hemostasis (primary end point) in 100% and rebleeding in 7% of patients.

One patient (7.2%) of them had rebleeding occurred within 24 hour. He had severe erosive esophagitis at the distal third of the esophagus, underwent ERCP followed by development of hematemesis and melena. He was the first patient to use Hemospray for in our hospital (the endoscopist may not have been well oriented on using it that time), needed another session and hemostasis achieved successfully after that.

Recurrent bleeding may be explained by the fact the hemostatic powder does not directly induce healing of the underlying lesion and is sloughed off from the mucosal wall within two to three days, leaving behind a clean remnant. (24)

In the largest four case series performed by Sung et al ([n=20]) (23), Smith et al ([n=82]) (25), Holster et al ([n=16]) (26) and Leblanc et al ((27)[n=17]), Hemospray was used as monotherapy in 50% to 95%, first modality in0% to 19% and rescue modality in 0% to 33% of patients, with an overallrate of acute hemostasis in 81% to 100%, and recurrent bleeding in11%to 31%. (23) (16) (27) (28).Our finding that spurting hemorrhage was present in the one patient in whom acute hemostasis was achieved with Hemospray is consistent with the experience of Leblanc et al (27) who reported effective control of pulsatile bleeding with Hemospray.The low rate of recurrent bleeding and Hemospray use as a rescue modality in our study could be due to selection bias in the tertiary care setting, with less encounters of thrombocytopenia in six (42.8%) patients, coagulopathy in one patient (7.1%) andfiveof them were on antiplatelet (35.7%).

The high rates of acute hemostasis suggest that Hemospray can be a good choice for control NVUGIB by experienced hand for short term with close follow up.No adverse events were noted during our follow up period and no mortality was occurred neither from hemospray use nor from UGIB or any other cause during the follow up period.

One patient received Hemospray for bleeding from sphincterotomy site with no complications. The use of hemospray in treatment of post ERCP-sphincterotomy bleeding is controversial. A case have been reported to have transient biliary obstruction following successful use of Hemospray in post-sphincterotomy hemorrhage Biliary patency was quickly restored with vigorous water irrigation and prodding open of the papillotomy orifice with a sphincterotome tip(29).

Another study report it safe and no obstruction occurred (30).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.(31)Technical complication other than catheter blockage which had occurred in two patients, was not noticed .In a large trial, 7 of 63 patients (11%) treated with Hemospray suffered technical-related complications (28).There were 3 blockages of the application catheter, 2 cases of the endoscope transiently adhering to the esophageal mucosa after use with the endoscope in retroflexion, 1 occlusion of the working channel of the endoscope and 1 malfunction of the CO2 cartridge. In spite of this, most of the examiners felt that Hemospray was easier to use than conventional hemostatic methods(28).

Special indications suppose some technical challenges. Powder application is feasible with a duodenoscope, but caution must be taken with the use of the elevator to prevent plication of the catheter (21) (32).

Till now there is no reported clinically significant adverse events bur specific concerns have been raised for some indications. For instance, when treating bleeding from esophageal or gastric varices, thromboembolism may be an issue because particles might enter the vascular system. In fact, its use in this setting is contraindicated by the manufacturer. However, the Hemospray™ outflow pressure is less than the intravariceal pressure of a bleeding varix when applied from a distance of 1-2 cm and no embolism has been shown in this indication (33) (34)(35).In vitro coagulation time modifications caused by TC-325 do not seem to pose any clinical problem in cirrhotic patients (33), however Hemospray is contraindicated in variceal bleeding with low venous pressure and numerous collateral shunts due to the risk of thromboembolism (33).

The application of a pressure spray on the resection area after EMR could theoretically cause a perforation. However, no perforation was detected in a small series (27).Only one case of bowel perforation after treatment of a severe portal hypertensive gastropathy with TC-325 has been reported (36) but it was not clear if the perforation was related to the procedure. Following the manufacturerrs instructions, Hemospray™ use is contraindicated in patients with suspected GI perforation or those at high risk of perforation during the endoscopic procedure (information provided by the manufacturer). Despite the progressive evolution in discovering different types of modalities to control UGIB endoscopically, the better facilities of blood transfusion and the ease of access for surgical intervention, the mortality rate from UGIB is still ranging between 6-8% in the past 30 years (3), so it is necessary to search for another methods of endoscopic hemostasis.Hemospray will be a good addition to the list of different choices for controlling NVUGIB giving his high advantages.

First, the ease of application without the need for advanced technical skills is desirable in emergency situations in which expert endoscopist are unavailable (27). Second, accurate localization and precise targeting are not necessary, making it useful in challenging anatomy compounded by endoscope angulation (37). Third, direct mucosal contact does not occur, reducing the risk of further tissue damage that could worsen bleeding an even result in perforation (24) (27).Fourth, its ability to cover large areas with multiple bleeding points makes it a suitable choice for hemorrhagic gastritis, gastric antral vascular ectasia, radiation-induced mucosal

injury and malignancy-related bleeding (23).
Finally Hemospray can be used prophylactically or therapeutically and either alone or in combination with conventional endoscopic therapies depending on the risk of recurrent bleeding (38).

Conclusion:

Hemospray appears to allow safe control of acute bleeding and may be used to stop upper gastrointestinal bleeding as a temporary measure or a bridge toward more definitive therap

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