

Hemostasis with Powder – Experience with EndoClot™ in Difficult UGI Bleedings

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Bibliography

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Introduction

Gastrointestinal bleedings are associated with considerable lethality, and with an incidence of 50 -100/100,000 people it is a picture commonly seen in clinical practice. For upper gastrointestinal bleedings, lethality is indicated as being 5-11% [1] on average. In 60 - 80 % of cases the bleedings subside spontaneously, at least temporarily.

Anti-thrombotic therapy, i. e. the administration of antiplatelet inhibitors such as ASA or Clopidogrel or also oral anticoagulants such as phenprocoumon can trigger and/or extend bleeding from an existing mucosal lesion [5]. Patients undergoing this type of therapy have a higher risk of persistent bleeding and a significantly higher mortality and thus require in particular endoscopic intervention [6]. The significance of endoscopy lies in its considerable contribution to stabilising the acute situation and the further clinical course. Identifying and clarifying the source of bleeding and thus the cause of this complication is achieved in approximately 90% of the cases in upper [1] and in approximately 75% in lower gastrointestinal bleeding [4]. The goal of endoscopic intervention is to achieve definitive haemostasis or, if bleeding has occurred previously, to prevent it from recurring. For this purpose, the various procedures with different principles such as injection therapy with adrenalin, saline solution, Histoacryl, Aethoxysclerol, mechanical methods (endoclips, loop, rubber band ligation) or thermal methods (electrocoagulation, argon-plasma coagulation, laser)

have established themselves in clinical practice [2, 3]. A common characteristic of these procedures is the localised mechanism of action at the source of the bleeding, which presupposes knowledge of the precise location of the bleeding, followed by exact application. Treatment is aggravated by the often difficult conditions of endoscopy to identify the source of bleeding in a clinical emergency setting. If the source is not located or if the intervention is not successful, further endoscopic procedures, additional diagnostics or even surgical procedures become necessary if the active bleeding persists and continues to put the patient at risk. All established procedures are associated with mucosal contact or lesions which can render haemostasis impossible due to existing anticoagulation or diffuse tumour bleeding. In these cases, haemostasis with powder is advantageous and considered a very promising method for treating diffuse bleedings also in an emergency setting [Hoffmann], especially with regard to the increasing number of patients being treated with new oral anticoagulants.

EndoClot™ represents a new procedure for endoscopic haemostasis. It involves the use of a haemostatic powder. During endoscopy it is sprayed extensively onto the mucosae, thus covering it.

Material and methodology

EndoClot™ has been authorised since 2011 and is commercially available in Europe since

2012. The procedure can be used both in the upper and in the lower gastrointestinal tract, as monotherapy or as add-on therapy to the existing techniques.

The powder is made of individual particles of modified polysaccharides derived from plant starch without animal or human components. Contact with blood is necessary for the mechanism of action to unfold. The manufacturer-designated AMP[®] particles (absorbable modified polymers) withdraw water from the blood by forming a gel. This forms an adhesive clot on the source of the bleeding. At the same time, the concentration of coagulation factors is increased, accelerating physiological coagulation. The gel matrix is water soluble, can thus be rinsed away completely and is fully absorbable. The patient has to fast for 24 hours after the application. The application system consists of a catheter (230 cm x 5 mm) with a powder-gas mixing chamber to which the powder container and an indoor air compressor are connected. The catheter can be introduced through the working channel of any routine endoscope. In doing so, the highest level of the compressor should be chosen to prevent humidity from entering the catheter, as this may cause the gel to already form inside the device and block the catheter. When the source of bleeding is reached, the lower compressor level is selected. Gentle, even tapping of the powder container then provides a continuous powder jet which can be directed onto the desired location. Between October 2012 and July 2013 we applied this procedure in 22 patients in addition to conventional haemostasis methods or as monotherapy. The selection of patients was at the discretion of the examiner. The combination with other techniques of haemostasis and the sequence of the applications was also determined by the examiner based on the circumstances of the endoscopic situation. In 17 cases EndoClot™ was used as monotherapy, in four cases in combination with clips, and once in combination with Suprarenin injection.

Patient characteristics

15 male and seven female patients with a mean age of 72 years (44-85) were treated. The cases involved the upper gastrointestinal

tract, with a clear majority of cases affecting the stomach. Twice the source of bleeding was located in the oesophagus with grade D reflux oesophagitis with an ulcer, four times in the duodenum or jejunum, of which one case involved bleeding of the papilla after replacement of a stent due to malignant stenosis of the common bile duct, and fifteen times in the stomach, where in addition to peptic ulcers the patients suffered in particular from tumour bleeding within the context of advanced carcinoma, in one case involving a metal stent in the pyloric orifice. In altogether eight cases the bleeding originated from a malignant lesion.

More than two thirds, namely 15 of 22 patients, suffered from impaired coagulation: in the majority of patients (13) this impairment was purely iatrogenic due to anti-thrombotic medication, partly in double or triple combination, and in three patients coagulation was impaired due to a disease, e. g. due to thrombocytopenia or liver cirrhosis.

The exact data is shown in **Table 1**. Successful haemostasis was defined as a stable Hb value and the absence of clinical bleeding stigmata. Retrogastroscopy to control the bleeding site was not performed routinely.

Results

In 21 of 22 (95.45%) patients, the intervention achieved sufficient haemostasis. In one patient, this was not achieved. This was an 83-year-old patient with a Forrest Ib bleeding from a very large peptic ulcer under therapeutic medication with Clexane which could not be paused due to cardiological reasons. In this case, permanent haemostasis was only achieved in the third gastroscopy after 5 clips and Suprarenin injections.

The application of the powder lasted about 2 - 10 minutes, excluding the preparation time of the endoscopic assistance (fetching and assembling the catheter application system).

Altogether, EndoClot was used selectively 17 times for primary haemostasis and five times as add-on to other procedures. In four cases, clips had initially been used for haemostasis but were not successful; in three of these four

patients coagulation was significantly impaired. Sufficient haemostasis was finally achieved by using the EndoClot system. (Fig. 1a-e)

One patient initially received a Suprarenin injection due to bleeding of an ulcer, after which EndoClot was applied as add-on.

In 14 of 15 patients receiving anticoagulant medication or other coagulation impairment, sufficient haemostasis was achieved with the powder.

In seven of 22 cases more than one EndoClot set was used: in four cases occlusion of the catheter occurred during the procedure, most probably due to humidity, so that another set was needed, in three cases haemostasis had not been achieved definitively after the application, so that another or second application was carried out during the same endoscopic procedure, which was successful. Complications such as aspiration, mucosal lesions, additional bleeding, perforation or allergic reactions did not occur.

Fig. 1

- a** Ulcer in the pre-pyloric antrum with Forrest Ib seeping haemorrhage under Plavix and Marcumar
- b** Persistent seeping haemorrhage after application of four clips
- c** Start of EndoClot™ therapy
- d** Ulcer and immediate surrounding continuously and extensively covered with first layer
- e** Image before withdrawal: Dense and extensive coating, about centrally: exact bleeding location marked: dark blood-powder gel matrix without progression.

Case no.ID	Gender	Age	Bleeding source	Anticoagulation	Additive/selective	Successful for 48 h
1	f	48	Grade D reflux oesophagitis with ulcer	Decomp. liver cirrhosis	selective	yes
2	m	78	Granulation polyp in the antrum	Xarelto, thrombocytopenia	selective	yes
3	m	62	Papilla bleeding with stent due to malignant DHC stenosis	none	selective	yes
4	m	81	Initially diagnosed stomach cancer, sampling site	Plavix	selective	yes
5	m	83	Large ulcer in the antrum, Forrest Ib	Clexane, therapeutically	selective	no
6	f	82	Sarcoma in the duodenum, Forrest Ib	ASA	selective	yes
7	m	76	Tumour bleeding in the SEMS in the pyloric orifice	ASA	selective	yes
8	m	76	Peptic ulcers, Forrest Ib	ASA, Plavix, Xarelto	Additive to 2 clips	yes
9	f	72	Peptic ulcers, Forrest Ib	ASA, Clexane therapeutically	selective	yes
10	m	85	Tumour bleeding cardia cancer	ASA, Plavix	selective	yes
11	m	84	Peptic ulcers, Forrest Ib	Plavix, Marcumar	Additive to 4 clips	yes
12	f	71	Jejunal ulcer	none	selective	yes
13	m	80	Sampling site corpus	ASA	Additive to 2 clips	yes
14	m	44	Peptic ulcers, Forrest Ib	Thrombocytopenia and Quick of 43 %	Additive to 2 clips	yes
15	m	81	Tumour bleeding in stomach cancer	none	Additive to Supra-injection	yes
16	f	75	Deep ulcer in the pylorus, Forest III	none	selective	yes
17	f	78	Ulcer in curvature fold, Forrest III	ASA	selective	yes
18	m	44	Grade D reflux oesophagitis with ulcer	none	selective	yes
19	m	63	Tumour bleeding cardia cancer	none	selective	yes
20	f	84	Erosion in the duodenum, Forrest Ib	Dabigatran	selective	yes
21	m	80	Duodenal ulcers, Forrest Ib	ASA	selective	yes
22	m	65	Tumour bleeding in cardia cancer	none	selective	yes

Discussion

Haemostasis with EndoClot was successful in more than 95% of the cases in our patient collective, irrespective of the location of the bleeding, the cause of the bleeding or the coagulation situation. The principle of extensive action seemed to be particularly favoura-

ble in diffuse bleedings, e. g. in the region of the tumours. This is further complemented by the lack of mucosal invasiveness, thus preventing additional mucosal lesions, which is particularly important when it comes to vulnerable tumour surfaces, but also contributes generally to the safety of the procedure. In all eight cases of bleeding with a malignant back-

ground haemostasis was successfully achieved with EndoClot™, Suprarenin was additionally used in one case. In four cases, the patients suffered from impaired coagulation. Even the application of the powder through the mesh of a self-expanding metal stent in the pyloric orifice within the context of tumour bleeding was uncomplicated (Fig. 2), as was the application via duodenoscopy onto the papilla (Fig. 3).

An approximate location of the source of bleeding was, in fact, sufficient. The powder can be applied generously in multiple layers. The content of one powder container was usually sufficient. Guiding of the endoscope does not require the same level of precision as when placing a clip or in injection therapy. In addition, the exact mucosal exit site of an active bleeding inside the white powder area becomes very clearly delimited, which can be used diagnostically and enables exact clipping (if necessary) depending on the endoscopic situation. The combination with the established methods of haemostasis in any random sequence can be classified as advantageous without reserve.

Up to now, only case reports and publications about the Hemospray from COOK Medical exist. While these already show good efficacy of haemostasis with powder [7-9], the inorganic composition of Hemospray remains unclear; moreover, the application based on a cartridge principle differs significantly from that of EndoClot. The Micro-Tech product can

be applied more gradually and with more precise dosing. EndoClot is not authorised for Forrest Ia or varicose bleeding. This also distinguishes it from Hemospray. The good efficacy in spite of anticoagulant therapy, which has already been described in isolated cases for Hemospray, is very promising [10]. The use of new oral anticoagulants, sometimes used in triple combination in cardiological situations, has led to an increased in the number of GI bleedings. In view of the lack of an effective antidote, EndoClot can be used to bridge the therapeutic gap until coagulation has stabilised.

Clouding of the optical instrument on multiple occasions due to scattered powder particles, which necessitated repeated rinsing of the optical instrument, was problematic. In the event of contact of the catheters with humidity, there is a risk of clotting with irreversible obturation of the lumen, necessitating a change of the system. Potential risks include contact of the mucosae with the catheter, immersion in blood or rinsing fluid which should perhaps be aspirated beforehand, or also the low compression level when introducing the catheters. A fine, precisely dosed powder jet is only achieved when tapping of the powder container is done correctly. This requires experience and expertise. However, the primary notion that haemostasis in an emergency setting through application of the powder can be achieved at any time even by an inexperienced endoscopist does not appear to have been achieved yet.

Fig. 2 Tumour bleeding in the stent, continuous powder coating through the mesh.

Fig. 3 Powder coating of the papilla during ERCP.

Conclusion and outlook

For the first time, the introduction of a haemostatic powder provides a relatively simple and extensive principle of haemostasis, also in an emergency situation. This method should preferably be used in combination with the

conventional procedures. Any available additive effect should be used, especially against the backdrop of the frequently impaired coagulation caused by anti-thrombotic therapy. The actual potency of the technique and the envisaged indications still have to be demonstrated in further widespread application of

this method and in corresponding controlled studies with a statistically reliable number of cases.

Its use as monotherapy appears to be suitable in diffuse bleedings such as tumour bleedings and in particular in-stent bleedings.

A pre-installed system less susceptible to humidity and/or with individually packaged powder chambers to prevent replacement of the entire system in the event of malfunction is desirable.

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