REVIEW

2026 March 3 [Epub ahead of print]
https://doi.org/10.5946/ce.2025.209
pISSN: 2234-2400 • eISSN: 2234-2443

Open Access

CLINICAL ENDOSCOPY

Precise and optimal delivery techniques of hemostatic powders in gastrointestinal bleeding

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Gastrointestinal (GI) bleeding is associated with a high risk of mortality. While conventional endoscopic hemostasis methods, including epinephrine injection, heater probe coagulation, hemostatic clips, and band ligation, achieve an overall hemostasis rate of 85%–90%, 10%–20% of patients do not respond to these treatments. Several novel powders have shown promise as effective hemostatic agents. In this review, we discuss the evolution of endoscopic hemostasis and explore the potential of innovative hemostatic powder treatments in managing GI bleeding. Relevant articles were identified by searching PubMed from 2010 to 2025 using the keywords' "hemostatic powder", "GI bleeding", and "endoscopic hemostasis". A review of recent PubMed articles on topical hemostatic powders used in endoscopy, including Hemospray, EndoClot, Ankaferd Blood Stopper, Nexpowder, and various drug-based powders, demonstrated that these agents offered high immediate hemostasis rates exceeding 90%. Topical hemostatic powders are valuable for managing active GI bleeding, especially when conventional endoscopic techniques are unsuccessful or technically challenging, such as refractory and tumor bleeding.

Keywords: Gastrointestinal bleeding; Gastrointestinal tumor bleeding; Hemostatic powder

INTRODUCTION

Gastrointestinal (GI) bleeding is a serious medical issue, referring to any bleeding that occurs within the digestive tract. GI bleeding is typically divided into upper and lower GI bleeding based on the location of the bleeding. Upper GI bleeding originates above the ligament of Treitz, with common sites including the esophagus, stomach, and duodenum. Upper GI bleeding occurs at a rate of 100 to 150 cases per 100,000 adults annually.[1,2] In contrast, lower GI bleeding occurs in the colon, rectum, or anus. Lower GI bleeding occurs at a rate of 20 to 30 cases per 100,000 adults annually.[3]

The clinical presentation of GI bleeding varies based on the location and severity of the bleed. Typically, hematemesis (vomiting blood) and melena (black, tarry stools) are indicative of upper GI bleeding, whereas hematochezia (passage of fresh blood) is more commonly associated with lower GI bleeding.[2] However, hematochezia may also be seen in cases of massive upper GI bleeding due to rapid transit of blood through the intestines. Systemic manifestations, such as fatigue, weakness, and shortness of breath, can occur secondary to blood loss and anemia. In cases of severe bleeding leading to hypovolemia, signs of shock, such as hypotension, tachycardia, and altered mental status, may also be present.[2]

Upper GI bleeding mainly arises from peptic ulcers, varices, erosions, tears, inflammation, and tumors of the upper digestive tract. Peptic ulcer bleeding is the most common cause of upper GI bleeding, involving ulcers in the stomach or duodenum that

Received: June 28, 2025 **Revised:** September 6, 2025
Accepted: October 1, 2025

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erode into blood vessels and are often related to *Helicobacter pylori* infection, the use of nonsteroidal anti-inflammatory drugs, or antiplatelet agents.[4] Following peptic ulcer bleeding, variceal bleeding is the second most common cause of bleeding from dilated veins in the upper GI tract due to portal hypertension.[4,5]

Common causes of lower GI bleeding include diverticular disease, angiodysplasia, colon polyps or tumors, inflammatory bowel disease, hemorrhoids, and anal fissures.[6] Diverticular bleeding is the most frequent cause, characterized by small bulging pouches in the colon wall that can bleed, especially when inflamed or infected, predominantly affecting older adults.[6,7] Angiodysplasia refers to abnormal, fragile, and dilated blood vessels in the colon's mucosal and submucosal layers, which can cause intermittent bleeding.[8] It is an acquired vascular lesion more common with advancing age, and is considered the second most common etiology for lower GI bleeding.[8]

Before endoscopic assessment and treatment, a systemic approach should be used to stabilize the patient.[9] Prompt assessment to evaluate the patient's airway, breathing, and circulation is always the priority. This involves ensuring adequate resuscitation to maintain systolic blood pressure over 100 mmHg and a pulse rate below 100 beats per min using intravenous crystalloid fluid.[2] Blood transfusion is indicated to maintain hemoglobin level higher than 7 g/dL, platelet counts over 50,000/mm3, and prothrombin time international normalized ratio less than 15 seconds.[4] If the patient is on anticoagulant therapy, reversal agents should be considered.

PHARMACOLOGICAL TREATMENT

In pharmacologic treatment, proton pump inhibitors (PPIs) play a significant role in managing GI bleeding, particularly in the upper GI tract.[10,11] Acid suppression to maintain an intragastric pH above 3 for over 20 hours daily is the cornerstone of peptic ulcer treatment.[12] PPIs achieve this by inhibiting gastric acid secretion through covalent binding to the sulfhydryl groups of cysteine residues on the H+/K+-ATPase enzyme in the parietal cells of the stomach.[13,14] This mechanism allows PPIs to reduce gastric acid secretion to promote healing of peptic ulcers, stabilize thrombi on the bleeding site, and decrease the GI bleeding severity before endoscopic treatment.[15]

Potassium-competitive acid blockers (P-CABs) inhibit the H+/K+-ATPase enzyme in gastric parietal cells by reversibly competing with luminal potassium ions.[16] Unlike PPIs, which are acid-labile prodrugs requiring activation in the acidic environment of the parietal cell canaliculi and typically need enteric coating to prevent degradation before absorption—P-CABs are active drugs upon absorption and are stable in gastric acid, eliminating the need for enteric coating.[17] This allows P-CABs to achieve near-maximal acid inhibition from the first dose and maintain effective acid suppression for up to 24 hours; in contrast, PPIs usually require 3 to 5 days to reach maximal acid inhibition due to their mechanism of action and pharmacokinetics.[18] These pharmacodynamic and pharmacokinetic properties give P-CABs potential advantages over PPIs, including stronger and more durable acid suppression, faster onset of action, and greater stability in acidic environments.[19] Some recent studies have already shown non-inferiority of P-CABs to PPIs in acute upper GI bleeding.[20,21] However, more evidence is needed to prove the efficacy of P-CABs to be the first-line therapy in acute upper GI bleeding.[22] In contrast to upper GI bleeding, there is no widely established specific pharmacological therapy for lower GI bleeding. Endoscopic interventions are generally the most common first-line treatments for lower GI bleeding.

ENDOSCOPIC TREATMENT

After the initial assessment, stabilization of vital signs, and pharmacological treatment, endoscopic intervention is the next critical step in the management of GI bleeding. Endoscopy is the cornerstone of both diagnosis and treatment, and should be performed within 24 hours for patients with GI bleeding. Endoscopic hemostasis can be performed after identifying the source of bleeding in the digestive tract. It aims to stop bleeding by physically or chemically closing the bleeding vessel or lesion, promoting clot formation, and minimizing tissue damage. Conventional endoscopic therapeutic techniques include injection, thermal coagulation, and mechanical therapy.[4]

The primary method of injection therapy involves using diluted epinephrine, typically mixed with normal saline at ratios of 1:10,000 or 1:20,000.[23] This solution is injected in volumes of 0.5 to 2.0 mL into four quadrants within 3 mm of the bleeding site. This mixture is selected because of its ability to induce local tamponade and vasoconstriction. Epinephrine injection is particularly beneficial for temporarily reducing bleeding during active hemorrhage in endoscopic procedures, which enhances visualization and facilitates subsequent endoscopic interventions.

Thermal coagulation was the first endoscopic treatment developed.[24] When the tissue temperature reaches 60 °C, proteins

coagulate, leading to thermal contraction of the bleeding vessels and surrounding tissue, effectively controlling hemorrhage.[25] Thermal therapies are classified into contact and non-contact modalities.[25] Contact devices—such as heater probes, bipolar electrocoagulation, and soft monopolar electrocoagulation—apply pressure directly to the bleeding site with the probe tip, delivering heat and electrical energy to achieve hemostasis.[26] In contrast, argon plasma coagulation (APC) is a non-contact thermal technique that delivers a jet of ionized argon gas to the bleeding lesion.[27] Argon gas is emitted from the probe and ionized by a high-frequency electrical current, which conducts energy to the tissue, causing superficial coagulation and stopping the bleeding without direct contact. APC is especially effective for treating superficial vascular lesions such as angiodysplasia and gastric antral vascular ectasia.[28] However, while the non-contact nature of APC is advantageous for small, superficial vessels, it may be less effective for controlling bleeding from larger vessels because of its limited depth of coagulation.[29]

Mechanical therapies, including band ligation and clipping techniques, manage GI bleeding by providing a direct and effective local tamponade to achieve hemostasis.[30] Band ligation is a widely used mechanical method that is particularly effective in controlling variceal bleeding.[4,31] The elastic band constricts the tissue and underlying blood vessels, effectively compressing the vessel lumen and blood flow. This constriction leads to thrombosis and eventual necrosis of the ligated tissue, preventing further bleeding. Clipping is another essential mechanical therapy that involves the application of metal clips to bleeding sites for hemostasis.[32] Through-the-scope clips (TTSC) are small, metal clips that can be delivered through the working channel of a standard endoscope without the need to withdraw the scope.[33] The clip is opened and positioned directly over the bleeding vessel. Once at the target location, the clip is closed to compress the tissue and seal the bleeding vessels. Over-the-scope clips (OTSC) are larger, more robust clips mounted on a cap fitted over the endoscope tip.[34] Different to TTSCs, the endoscope must be withdrawn to mount the OTSC device before reintroduction. OTSCs offer greater closure force and tissue capture compared to TTSCs, making them highly effective for larger, fibrotic, or refractory bleeding lesions.[35,36]

INTRODUCTION OF HEMOSTATIC POWDER THERAPY

Despite advances in conventional endoscopic therapies, only a few patients with GI bleeding experience refractory or recurrent bleeding. These cases present significant clinical challenges and are associated with high morbidity and mortality rates. Hemostatic powder spray, introduced in clinical practice in 2011, is a novel endoscopic technique for managing active GI bleeding, especially peptic ulcer bleeding.[37] The hemostatic powder is delivered through a spraying system under endoscopic visualization. When applied to the bleeding site, the hemostatic powder absorbs water and swells to create an adhesive barrier that covers the lesion and promotes hemostasis.[37] This non-contact, nonthermal approach can avoid thermal injury. Furthermore, hemostatic powder does not require precise targeting or direct manipulation of the bleeding vessel, making it particularly useful for endoscopy trainees working in difficult-to-approach sites.[38]

Hemostatic powders used in endoscopy control GI bleeding through several mechanisms, including mechanical tamponade, concentration of coagulation components, and activation of platelets and coagulation. When applied to a bleeding site, hemostatic powders rapidly absorb water and form an adhesive layer that covers the tissue, thereby physically sealing the bleeding site. This acts as a mechanical barrier and provides immediate hemostasis. By absorbing local moisture, these powders concentrate platelets and coagulation proteins at the bleeding site, enhancing natural clot formation and accelerating the clotting cascade.

METHODS OF REVIEWING HEMOSTATIC POWDER THERAPY

TC-325 (Hemospray, Cook Medical), EndoClot (EndoClot Plus Inc), ABS (Ankaferd İlaç Kozmetik A.Ş.), and UI-EWD (Nexpowder, Next Biomedical Co., Ltd.) are commercially available hemostatic powders.[39] We reviewed relevant articles identified through a PubMed search from 2010 to 2025 using the keywords: "hemostatic powder", "GI bleeding", and "endoscopic hemostasis".

TC-325 (HEMOSPRAY)

Hemospray, which is composed of bentonite, a naturally occurring inert mineral powder (aluminum phyllosilicate clay), is the first and most widely used hemostatic powder globally for endoscopic management of GI bleeding.[40] When applied to a bleeding site, Hemospray absorbs water from the blood, swells,

and forms an adhesive gel-like barrier over the lesion. This physical barrier achieves hemostasis by providing a mechanical tamponade and concentrating clotting factors to promote coagulation. The powder is delivered via a catheter inserted through the endoscope's working channel and propelled by compressed CO_2 directly to the bleeding area.[41]

Hemospray was first used in peptic ulcer bleeding, which can be used either as a primary therapy or a salvage treatment.[42] Multicenter prospective studies show that Hemospray achieves immediate hemostasis in around 95% of patients with bleeding peptic ulcers when used as monotherapy or in combination with conventional endoscopic treatments.[41,43] For portal hypertension-related bleeding, Hemospray showed efficacy in controlling portal hypertensive gastropathy, enteropathy, and colopathy bleeding.[44] Multiple studies have also demonstrated that Hemospray achieves rapid hemostasis in acute esophageal and gastric variceal bleeding.[45,46] Furthermore, Hemospray achieved a high successful hemostasis rate (>90%) in lower GI bleeding, including postpolypectomy wound bleeding, ulcer bleeding, diverticulum bleeding, ischemic colitis, and diffuse mucosal oozing.[47-50] Recent evidence also proved promising efficacy for initial hemostasis, around 80% in GI tumor bleeding.[51]

Hemospray was approved by the Food and Drug Administration (FDA) in 2018 to facilitate endoscopic hemostasis and reduce recurrent non-variceal GI bleeding. Hemospray has demonstrated a high procedural success rate exceeding 95% and a hemostatic rate greater than 90% involving both upper and lower GI bleeding.[52] In comparison to conventional endoscopic therapy, Hemospray had a similar hemostatic effect in non-variceal bleeding.[53] The hemostasis rate in GI tumor bleeding seems to be higher when using Hemospray than conventional endoscopic treatment.[54,55] However, the recurrent bleeding rate and the need for further endoscopic treatment during the second-look endoscopy were higher when using monotherapy of Hemospray.[56] In this situation, current guidelines suggest Hemospray as an additional therapy or a salvage therapy after conventional endoscopic treatments in GI bleeding.[4,57]

Hemospray is generally considered safe. Serious complications, such as thromboembolism, bowel obstruction, and coagulopathy, have not been reported in clinical practice. However, there have been some case reports of Hemospray-related GI perforation and transient bile duct obstruction.[58-60] Among older patients with advanced malignancies and friable tissue, Hemospray should be used cautiously.

ENDOCLOT

The EndoClot Polysaccharide Hemostatic System is an FDA-approved hemostatic powder used to control non-variceal GI bleeding. Composed of plant-derived starch-based material, it forms a mechanical barrier at bleeding sites to promote rapid hemostasis.[61] Additionally, EndoClot particles rapidly absorb water from blood, concentrating platelets, red blood cells, and coagulation proteins to accelerate the patient's natural clotting cascade.[61,62] The retention time of EndoClot hemostatic powders is reported to be within 24 h, leading to a risk of early rebleeding following treatment.

Similar to Hemospray, EndoClot achieves a high rate of immediate hemostasis in non-variceal upper GI bleeding, generally over 90%, and has comparable rebleeding rate of <20% within 30 days.[62,63] EndoClot can be applied as a monotherapy or in combination with conventional endoscopic therapy, which is most effective in diffuse or extensive bleeding activity or in cases where the approach to the bleeding vessel is difficult.[64] EndoClot is also effective in controlling lower GI bleeding, including postpolypectomy bleeding, colonic tumors, and diverticular bleeding.[65] It has also been shown to achieve immediate hemostasis for GI tumor bleeding, with a rebleeding rate of around 20% within 30 days.[66] Similar to Hemospray, EndoClot is effective as monotherapy and rescue therapy in GI bleeding, while bleeding related to malignancy may be the best field of application.[67]

ANKAFERD BLOOD STOPPER

ABS is a herbal-based topical hemostatic agent used for the management of GI bleeding, particularly in cases resistant to conventional treatments. ABS is a standardized mixture of five herbal extracts, including *Thymus vulgaris*, *Glycyrrhiza glabra*, *Vitis vinifera*, *Alpinia officinarum*, and *Urtica dioica*.[68] ABS works by rapidly forming an encapsulated protein network that promotes clot formation, angiogenesis, cellular proliferation, and wound healing.[68]

Clinical trials showed a primary hemostasis rate of around 90% in upper non-variceal GI bleeding treated by ABS.[69] ABS also showed hemostatic efficacy in variceal bleeding.[70,71] Similar to other hemostatic powders, ABS has been successfully applied endoscopically to control lower GI bleeding from various benign lesions and neoplastic sources without significant complications.[72,73]

In contrast to other hemostatic powders, the complex mixture of herbal extracts in ABS demonstrated antibacterial effects against *H. pylori*. A previous study showed that ABS significantly reduces the viability of various *H. pylori* strains, expanding its therapeutic potential by controlling bleeding and potentially reducing the bacterial load.[74]

UI-EWD

Nexpowder contains aldehyde dextran and ε-poly amino acid at a 4:1 ratio, which react with moisture at the bleeding site to form a strong adhesive hydrogel, enhancing its ability to remain in the bleeding site and control bleeding.[75] For upper GI bleeding, Nexpowder demonstrated a success rate of approximately 94% to 96% for immediate hemostasis, even among patients who had failed to achieve hemostasis with conventional endoscopic treatments.[76,77] For upper GI tumor bleeding, Nexpowder achieved immediate hemostasis at 97.5%, while the rebleeding rate within 28 days was only 22.5%.[78]

Nexpowder also had a high success rate in hemostasis for lower GI bleeding, including diverticular bleeding, radiation proctitis, angiodysplasia, procedure-related bleeding, tumor bleeding, and ulcer bleeding.[79] More importantly, Nexpowder had a significantly lower rebleeding rate (5.5%) compared with conventional treatment within 28 days.[79] Notably, a previous study reported the ability of Nexpowder to manage refractory lower GI bleeding where conventional therapy failed. In a study of 59 patients with refractory lower GI bleeding, initial hemostasis was achieved at 100% using Nexpowder, and the rebleeding rate within 30 days was only 8.5%.[80]

HEMOSTATIC DRUG POWDER

The integration of a powder spray system with hemostatic drugs offers an alternative approach for managing difficult GI bleeding. Using an air-driven spray mechanism, specific drugs with hemostatic effects can be efficiently delivered directly to the bleeding site, thereby enhancing local hemostasis. Tranexamic acid (TXA) is an antifibrinolytic agent that inhibits fibrin degradation by binding to plasminogen, thereby preventing the breakdown of blood clots and reducing bleeding.[81,82] Numerous studies have shown that TXA is effective in decreasing blood loss and transfusion needs in surgical settings.[83-85] While the systemic use of TXA in GI bleeding remains debated,[86,87] the endoscopic application of topical TXA in addition to conventional endoscopic hemostasis has been shown to significantly reduce early treatment failure in patients with bleeding peptic ulcers.[88]

Sucralfate, a basic aluminum salt of sucrose octasulfate, enhances mucus secretion, increases mucosal blood flow, and stimulates local prostaglandin production.[89,90] When exposed to acid, sucralfate dissolves into aluminum salts and sucrose sulfate, which bind to exposed proteins on damaged cells, forming a protective barrier that shields the GI mucosa.[91,92] Sucralfate also binds to growth factors, promoting angiogenesis and facilitating mucosal healing.[92] A recent randomized controlled trial demonstrated that colonoscopic spraying of 3 g sucralfate powder on polypectomy wounds significantly reduced the risk of delayed postpolypectomy bleeding.[93] Through the precise drug powder spray, the drug dosage can be minimized to avoid possible adverse events. However, the idea of drug powder delivery for GI bleeding requires further validation.

CURRENT ROLE OF HEMOSTATIC POWDERS IN GI BLEEDING

Several new hemostatic powder devices have been introduced in recent years, including Hemospray, EndoClot, ABS, and Nexpowder. The hemostatic effects of hemostatic powders have been demonstrated and emphasized in refractory GI and tumor bleeding. Hemostatic powders are generally indicated for the management of active GI bleeding in cases where conventional endoscopic methods are difficult or fail. We summarize common scenarios for hemostatic powder use: (1) bleeding from neoplastic GI lesions; (2) lesions that are difficult to access endoscopically, including those at the posterior wall of the duodenum; (3) recurrent or refractory bleeding after conventional endoscopic hemostasis; (4) friable or fragile mucosa with diffuse bleeding; and (5) postprocedural bleeding, such as polypectomy bleeding, delayed bleeding after endoscopic mucosal resection or endoscopic submucosal dissection.

TIPS FOR HEMOSTATIC POWDERS IN GI BLEEDING

Although hemostatic powder is straightforward to use, several important tips should be followed to prevent spray malfunction and ensure optimal performance. Before powder application, the bleeding site should be thoroughly cleared of blood and fluids by suction to optimize adhesion and visibility. Subsequently,

air is to be flushed through the working channel of the endoscope to avoid clogging of the delivery catheter. The delivery catheter should then be passed through the working channel of the endoscope, before applying the hemostatic powder smoothly at a distance of about 1 to 2 cm from the bleeding site (Fig. 1). After powder delivery, the operator should avoid prolonged direct contact between the powder and the endoscope tip to prevent powder adherence to the endoscope. In the event of clogging, an alternative catheter that fits the delivery device should be used. Figure 2 illustrates a checklist to ensure smooth powder application.

LIMITATIONS FOR HEMOSTATIC POWDERS

Although hemostatic powders can be used as primary, adjunctive, or salvage therapy, there are concerns that limit their use as first-line therapy.[67] The high purchase cost of hemostatic powders compared to conventional endoscopic therapies is one such concern and may limit their widespread adoption. Besides the economic cost, hemostatic powders can obscure the endoscopic field and the bleeding source, complicating subsequent rescue interventions.[94] Technical challenges, such as catheter occlusion, may also arise during application, especially when the working channel is moist. In this situation, hemostatic powder sprays are typically reserved as the final step in endoscopic management. Recent consensus guidelines recommend their use as a temporary measure when conventional endoscopic treatments are unsuccessful or not feasible, which is particularly beneficial for malignant and refractory bleeding.[4,57]

HEMOSTATIC GEL

In addition to the novel hemostatic powder, hemostatic gel emulsion may represent an additional rescue option for uncontrollable peptic ulcer bleeding.[95] For instance, PuraStat, a novel transparent gel composed of self-assembling peptides, was developed to treat hemorrhages originating from small vessels in the GI tract.[96] It contains three types of amino acids that form matrix fibers that adhere to and seal blood vessels to create a mechanical barrier.[96]

Checklist for hemostatic powder application

- ☐ Clear the bleeding site by suctioning blood and fluids.
- ☐ Pre-flush the delivery catheter and accessory channel with air to prevent clogging.
- ☐ Maintain a 1–2 cm distance between the catheter tip and bleeding site during powder application.
- ☐ Avoid prolonged contact of the powder or catheter with the endoscope tip to prevent adherence.
- ☐ Monitor for catheter clogging; flush with air or switch to a backup catheter if needed.
- ☐ Use CO_2 propellant release to avoid excessive pressure and perforation risk.
- ☐ Allow the powder to settle before any suction or aspiration to prevent clogging of the catheter or working channel.

Fig. 2. Checklist for powder application.

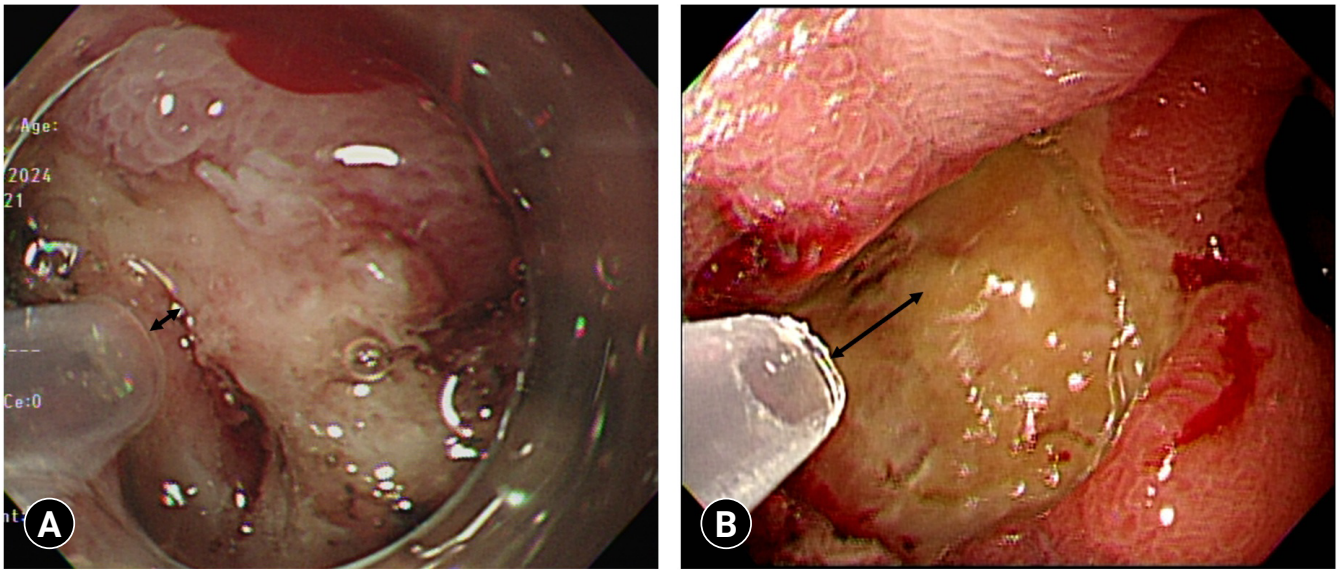

Fig. 1. Endoscopic view comparing (A) suboptimal powder application and (B) optimal powder application. (A) The catheter was too close to the lesion, so the moistness intruded the catheter and caused clogging. (B) To avoid catheter clogging, clear blood and fluids by suction and keep a distance of about 1 to 2 cm from the bleeding site. The arrow indicate the distance between the catheter and the powder target.

PuraStat has demonstrated a high success rate of approximately 90% when used as a rescue therapy following conventional treatments.[97] Moreover, clinical trials have demonstrated that PuraStat can reduce delayed bleeding and promote wound healing after endoscopic resection of the GI tract.[98] Compared with hemostatic powders, PuraStat is transparent, which enhances visualization and allows for more effective subsequent endoscopic interventions.[99]

CONCLUSIONS

With advances in medications and endoscopic techniques, the immediate hemostasis rate for GI bleeding has now exceeded 90%, whereas the 30-day rebleeding rate has declined to approximately 8% to 10%. Despite these improvements, the optimal management of refractory and tumor bleeding remains an ongoing challenge. Hemostatic powder sprays are emerging as promising adjuncts in difficult cases.

Conflicts of Interest

The authors have no potential conflicts of interest.

Funding

None.

Author Contributions

Conceptualization: all authors; Resources: XZL; Supervision: XZL; Visualization: HCC; Writing–original draft: HCC; Writing–review & editing: all authors.

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