Topical Endoscopic Hemostasis in Gastrointestinal Bleeding

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Overview

Endoscopic hemostasis is key in treatment of bleeding for acute gastrointestinal bleeding (GIB) and more advanced interventional procedures (i.e. endoscopic submucosal dissection).[1,2] Injection therapy, mechanical therapy, and thermal therapy have been the mainstay tor endoscopic hemostasis.[1,2]

Doppler endoscopic probes, over the scope clips, and hemostatic powders/sprays have emerged as newer technologies in the treatment of GIB.[1-3] Hemostatic powders and sprays, initially used in the military for combat-related bleeding, provide a mechanical barrier when exposed to fluid.[2,3] A tamponade is formed through absorption of the fluid, resulting in the initiation of a clotting cascade.[4] The clot eventually sloughs off after 24-72 hours leaving no residue, according to studies.[5] Common clinical applications for hemostatic powders include: tumor-related bleeding, bridge to definitive therapy, diffuse or refractory bleeding, and as an adjunct/bridge therapy for variceal bleed.[2]

The following are topical endoscopic hemostatic agents currently approved by the Food and Drug Administration (FDA) for use in the United States:

- **Hemospray** (Cook Medical) is an inert, bentonite powder (TC-325) indicated for hemostasis of non-variceal bleeds in the gastrointestinal tract.[6] The delivery system is powered by carbon dioxide through a catheter inserted into the working channel of an endoscope.[6]
- **Nexpowder** (Medtronic) is intended to be used for hemostasis of non-variceal, upper GIB.[7] An inert powder is delivered through a catheter inserted into an endoscope.[7] The delivery system is battery powered. The powder consists primarily of E-poly-L-lysine and aldehydrated dextran.[7]
- **PuraStat-GI** (3-D Matrix) is a sterile gel made of a synthetic peptide and sterile water for injection which is provided in a prefilled syringe delivered via an endoscopic catheter.[8] It is intended for hemostasis of mild and moderate bleeding post endoscopic submucosal dissection (ESD) or endoscopic mucosal resection (EMR) as an adjunct, bridge, prophylactic, or rescue therapy for intraprocedural venous bleeding or prophylactic therapy to prevent post procedure bleeding.[8]
- **EndoClot PHS** (Olympus) is intended for hemostasis of nonvariceal GIB with the exclusion of Forrest Ia classification of bleeding.[9] It is composed of absorbable modified polymer particles delivered via a gas source through a catheter inserted into an endoscope.[9]

Clinical Guidelines/Society Reviews

Guidelines form the International Consensus Group published in the Annals of Internal Medicine in 2019 address the use of TC-325 as follows[14]:

- Statement B11a In patients with actively bleeding ulcers, we suggest using TC-325 as a temporizing therapy to stop bleeding when conventional endoscopic therapies are not available or fail. (GRADE: conditional recommendation, very low quality evidence)
- Statement B11b In patients with actively bleeding ulcers, we suggest against using TC-325 as a single therapeutic strategy versus conventional endoscopic therapy (clips alone, thermocoagulation alone, or combination therapy). GRADE: conditional recommendation, very low quality evidence).[14]

The American Society for Gastrointestinal Endoscopy (ASGE) offered a technology assessment of devices used in endoscopic hemostasis of nonvariceal GIB in 2019. Hemospray for control of lower GIB, early anastomotic bleeding, and post sphincterotomy bleeding was thought to have promise.[15]

The ASGE concluded the following[15]:

> Other than injection therapy, which should not be used as a monotherapy, there are few compelling data that strongly favor any one device over another. For endoscopists, the choice of a hemostatic device should depend on the type and location of the bleeding lesion, the availability of equipment and expertise, and the cost of the device.[15]

Physician Advisor Insight

A panel of General Surgeons within our HealthTrust Physician Advisor Network offered the following insight with regard to topical hemostatic agents in endoscopy:[16:]

- Electrocautery, epinephrine injections, and clips continue to be the mainstay of endoscopy primarily due to cost of the topical agents. Patient circumstances drives selection of hemostatic modality.
- Topical agents are most effective for tumor bleeding or diffuse gastritis with less utility in cases of focal, severe hemorrhage. As a result hemostatic agents do not replace coagulation, clips, or injection.
- There are no known significant differences in efficacy across topical agents. They are thought to be interchangeable and selection of product is based on what is stocked by the organization.
- The mode of delivery for hemostatic agents drives the need for training, which can be done by a fellow gastroenterologist or the supplier.
- Conversion would be facilitated with data on the new hemostatic agent and understanding of financial implications.

Clinical Evidence

- A randomized controlled trial (RCT) investigated the use of TC-325 therapy in treatment of upper GIB (n=28) comparted to clinical management (n=31).[10] Hemostasis was achieved successfully in all TC-325 cases and additional treatment was required in both groups equally (TC-325-42.9% vs control - 58.1%, p=0.243). The TC-325 group and control group were similar in 30-day mortality (28.6% vs. 19.4%, p=0.406), 30-day re-bleed (32.1% vs 19.4%), required blood cell transfusions (71.4% vs. 80.6%, p=0.41), and hospital length of stay (17.74±17.7 days vs 12.8±14.1 days, p=0.227). The researchers concluded that while hemostasis was effectively achieved in malignant GIB, there was no reduction in 30-day mortality, 30-day re-bleeding, blood transfusions, or length of stay. Limitations of the study include that it was a single-center study including patients with advanced disease which may result in selection bias. The study size was smaller than planned.[10]
- A multicenter prospective study was completed to evaluate outcomes with the use of TC325 in upper GIB following elective endoscopic therapy.[4] The evaluation included use of TC-325 post endoscopy therapy a monotherapy, dual therapy with standard hemostatic techniques, or rescue therapy post failure of standard methods (n=73). Hemostasis was achieved in 100% of patients and 4% (n=2) experienced re-bleed within 30 days. Limitations of the study include that it was not a RCT, potential selection bias due to the decision to use TC-325 at the discretion of the surgeon, and variable interpretation of immediate hemostasis post TC-325 application among observers.[4]

- One multicenter, noninferiority, randomized trial of 244 patients with nonvariceal upper GIB compared the use of TC-325 with standard endoscopic treatments.[11] Bleeding control within 30 days was 90.1% in the TC-325 group (n-111) and 81.4% in the standard treatment group (n=113). Failure of hemostasis during the index endoscopy was lower in the TC-325 arm (2.7% vs 9.7%). Thirty-day bleeding recurrence and incidence of further endoscopy did not differ between the two groups. The researchers concluded that TC-325 is not inferior to standard treatment. The fact that the clinicians were not blinded was a limitation to this study.[11]
- Fifty studies (1445 patients) were included in a systematic review and meta-analysis to determine the safety and efficacy of TC-325 in treating upper GIB.[12] Pooled results evaluating initial hemostasis (90.7%, range 88.75-92.3%) was similar to treatment with epinephrine injection (95.1%), thermocoagulation (94.5%), and hemoclip placement (98.5%). Rebleeding rate was (26.5% range 23.7-29.0%)) which was higher compared to epinephrine (injection (19.6%), thermocoagulation (13.3%), and hemoclip placement (9.5%). There were limitations to this study. The authors reported that the literature available was low quality with a lack of controlled and comparative studies. Most of the studies included were conference abstracts with many case series. The samples were heterogenous patient samples and information was incomplete in some of the studies. Inconsistency in the timing of follow-up ranging from 12 hours to 3 months.[12]
- A meta-analysis of 16 studies covering 2742 endoscopic submucosal dissections (ESD) found that tissue shielding using polyglycolic acid (PGA) resulted in reduced incidence of delayed bleeding by 2/3 over traditional methods in high-risk patients.[13] Hemostatic spray systems demonstrated a 9-fold reduction in delayed bleeding in low risk patients when compared to traditional methods. There were limitations to this study. No research included in the analysis directly compared different endoscopic approaches, studies included were of small sample size and small number of studies, and questions remain regarding the utility and feasibility of PGA use this limiting the impact of such data.[13]

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