ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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Hemostatic Powder TC-325

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G&H What therapeutic options have traditionally been available for endoscopic hemostasis of gastrointestinal bleeding?

AB A number of therapeutic options have been available for years. Their respective efficacies depend on, to a certain extent, the etiology of the bleeding, whether the bleeding is occurring in the upper or lower gastrointestinal tract, and whether the bleeding is malignant or nonmalignant. Even within nonmalignant bleeding, there exist various causes, including ulcers or nonulcer etiologies with varying natural histories.

One of the traditional options for delivering endoscopic hemostasis is thermal therapy, of which there are numerous types, including both contact and noncontact methods of delivery. There also exists injection therapy (usually injection of epinephrine mixed with saline). Finally, there are mechanical methods of hemostasis, which include endoscopic clips (likely the most widely applied mechanical measure currently being used), as well as ligation band devices in addition to other technologies.

G&H What limitations are associated with these modalities?

AB Despite having several hemostatic options, some causes of bleeding are still hard to manage. Endoscopists usually treat ulcer bleeding quite well, although there still remains subgroups of patients who exhibit refractory rebleeding. Patients with high-risk ulcer lesions, as well as those afflicted with malignant disease and chronic kidney disease, are at an increased risk of worse outcomes for both upper and/or lower gastrointestinal bleeding. In addition, the advent of new antiplatelet and anticoagulant agents has led to an increased risk of bleeding and rebleeding. For all of these reasons, new hemostatic methods are required.

G&H What is TC-325, and how does it achieve hemostasis?

AB TC-325 (Hemospray, Cook Medical) belongs to a family of products called hemostatic powders. This agent consists of small mineral granules that achieve hemostasis. TC-325 binds to actively bleeding sites, and the granules absorb all of the water from blood or secretions, and then swell and adhere to the bleeding sites, essentially acting like a bandage over the hemorrhagic lesion. This is the main mechanism by which TC-325 is thought to act, although much remains uncertain about additional roles of the powder.

G&H What are the main advantages and disadvantages of this agent?

AB One advantage is that TC-325 is sprayed onto the bleeding site so that no direct contact is required; any spray applied in the general area—if directly layered over the bleeding site—works well. Therefore, the administration of TC-325 is not very technically demanding with regard to endoscopic expertise.

However, there are a number of issues related to this product. The powder must be applied directly to the bleeding site, which is not always possible; moreover, the powder only adheres to actively bleeding lesions. A big problem is that as soon as the powder comes into contact with any type of moisture, it will amalgamate and may block the delivery catheter. Therefore, in order to deliver the product effectively, the endoscopist must limit the amount of contact that the product has with any type of moisture, including performing minimal aspiration into the accessory channel.

G&H How safe is this product?

AB TC-325 appears to be quite safe. It, or a derivative, has been used for decades in various medical applications, although only recently (over the past 3 years) has it been used for hemostatic purposes in the gastrointestinal tract, by being delivered through an endoscope. Endoscopists were initially concerned about intestinal obstruction and embolization through the vasculature into tissues, but none of these concerns have been noted, at least with the limited follow-up data currently available. The product is biologically inert and does not appear to have any tissue interaction. The product also appears to wash out very quickly, as early as 12 to 24 hours, so long-term exposure does not appear to be an issue.

G&H Can you discuss the animal model and clinical data conducted thus far on TC-325?

AB The results of several small animal model studies have been published, suggesting that the agent is quite safe. TC-325 was used in a laparoscopic model of bleeding in which the product was applied to a spurting vessel, and the animals were then sacrificed. There was no evidence of either tissue reaction or embolization.

The early landmark paper in clinical experience was published by Dr Joseph Sung and his group in Hong Kong. More recent data—which unfortunately tend to originate from small, uncontrolled, cohort studies—have suggested that TC-325 has a role to play in a number of upper and lower gastrointestinal bleeding settings.

However, due to the fact that this product washes out as early as 12 to 24 hours, TC-325 does not appear well adapted to deal with any lesion exhibiting a delayed risk of rebleeding, such as high-risk ulcer lesions, which generally carry a high risk of rebleeding over 72 hours. On the other hand, this agent is helpful in achieving initial hemostasis; it appears to be perfectly adapted to lesions that do not have a prolonged risk of rebleeding, and it may have a role to play in providing hemostasis of an actively bleeding lesion before transfer of a patient.

G&H What were the principal findings of your recent study in this area?

AB The study that my colleagues and I conducted aimed to provide information from a significant number of patients from a single institution, where there existed homogeneity in the way that the agent was applied. Thus, we reported on 60 patients who underwent a total of 67 treatments. Indications included both nonmalignant and malignant causes of bleeding from both the upper and lower gastrointestinal tract. Our study, first authored by Dr Yen-I Chen, confirmed that TC-325 is extremely effective in achieving immediate hemostasis: 98.5% of patients stopped bleeding immediately upon application of the powder.

An important issue that we tried to identify was the residency time of the product: for how long does the product remain on the bleeding lesion? Because a number of the studied patients underwent second-look endoscopy, particularly in the upper gastrointestinal tract, we were able to observe that, in fact, the product disappears quite quickly. In 4 patients, we performed a repeat endoscopy within 24 hours, and no product remained. Thus, our best guess is that TC-325 likely washes out approximately as early as 12 to 24 hours in most patients. That is important to realize, and one of the key take-home messages from the study.

G&H How is this agent specifically suited to controlling bleeding from malignant tumors?

AB It is important to keep in mind that the available treatment options for malignant bleeding of the gastrointestinal tract are very limited and do not work very well. With regard to endoscopic treatment, as soon as the endoscopist attempts to treat the tissue—which is tumor and thus friable, necrotic tissue—more bleeding occurs, regardless of the modality utilized (especially if a contact method is used), hindering the aim of adequate hemostasis.

The other treatment options include radiation treatment, percutaneous tissue embolization, and surgery. Embolization and surgical intervention carry risks in these patients, who often have quite advanced tumors and are receiving palliative therapy. Risks include worsened local ischemia and systemic complications, the use of intravenous dye, and so on. Radiation treatment often works, but unfortunately takes some time to achieve hemostasis (usually days).

In contrast, the noncontact, nondamaging delivery of TC-325 is associated with a good risk-benefit ratio in this setting and can theoretically be very effective, at least acutely, compared with other methods of hemostasis; unfortunately, comparative data are lacking. Although preliminary results in malignant bleeding suggest that TC-325 may have a role to play, controlled studies are required.

G&H Does this agent have a role in the evaluation of hemostasis related to bleeding esophageal varices?

AB The manufacturer does not recommend using this product in the context of variceal bleeding because of the theoretical risk of embolization in a lower-pressure system. Having said this, a number of publications have recently appeared, suggesting that TC-325 may have a role to play in patients with variceal bleeding, as there has been no evidence of systemic or portal system embolization. In fact, a large randomized trial is currently ongoing in the Middle East further assessing the role of TC-325 in such patients.

The potential advantage of TC-325 is that in many areas of the world variceal bleeding is quite prevalent, yet expertise in performing endoscopic variceal banding or glue injection is not available. In such a setting, TC-325 may help stabilize patients by arresting initial bleeding, and it may allow patients to be transferred to more expert endoscopic centers. However, further research is needed in this area.

G&H How widespread is the use of this agent in clinical practice?

AB TC-325 is not yet approved in the United States. However, this agent has been approved in Canada and Mexico, many countries in Europe, a few countries in Asia, and recently in some countries in South America. In the countries where it has been approved by regulatory agencies, its use is becoming more and more widespread. TC-325 is available in many of the endoscopy units in these countries, and its use is not restricted to specialized centers. Based on my own experiences with the product, I would feel uncomfortable managing bleeding patients without having this agent available as a therapeutic option. I think that it is the best agent for providing immediate hemostasis, and it has a role to play in stabilizing the patient for either transfer or further treatment in the same setting or a scheduled second-look endoscopy. It could be argued that endoscopists who do not have endoscopic expertise in managing gastrointestinal bleeding probably should be trained in applying TC-325 because they could use it to stabilize a bleeding patient who could then be transferred to a more experienced center.

G&H Is cost a barrier to the use of this agent?

AB TC-325 is a single-use product, so once it has been used, the carbon dioxide gas that is part of the delivery system must be discharged and any unused powder discarded. Thus, this agent is expensive, and cost is indeed an issue. My colleagues and I presented an abstract at this year's Digestive Disease Week that tried to identify clinical settings in which the use of TC-325 is most cost-effective; however, more research is needed. Every endoscopy unit must make its own decisions based on acquisition costs of the product and any available alternatives.

G&H What are the next steps in research in this area?

AB An important issue right now is the paucity of head-to-head, controlled studies between TC-325 and standard methods of hemostasis in terms of stopping bleeding, stabilizing a patient for transfer, and preventing possible rebleeding, depending on the nature of the bleeding lesion. In addition, because TC-325 washes away quickly, it is imperative that we obtain a better understanding of the clinical indications in which the product is truly helpful. For example, if the risk of rebleeding in a given lesion (such as high-risk ulcers) is 72 hours but we know that TC-325 washes off within as early as 12 hours, it may be best to use other hemostatic modalities alone or in conjunction with TC-325 to prevent delayed rebleeding. As previously mentioned, one area where this agent appears to be quite promising, due to limited alternatives, is malignant bleeding. My colleagues and I are currently completing a randomized feasibility trial, in view of hopefully launching a global trial.

Dr Barkun is a consultant for Cook Inc.

Suggested Reading

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