

## Cyanoacrylate spray as treatment in difficult-to-manage gastrointestinal bleeding

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rylate in spray had favorable results in uncommon indications. Cyanoacrylate used as a spray is a technique that can be used as an alternative method in emergent settings.

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**Key words:** Cyanoacrylate; Gastrointestinal bleeding; Hemostasis; Mexico; Spray

**Core tip:** Up to 5%-10% of patients with gastrointestinal bleeding may have persistent bleeding that does not respond to endoscopic measures. When failure of the initial management strategy is observed, new techniques can be used. Cyanoacrylate is a polymer that crystallizes upon contact with blood and, if used as a spray, can help achieve hemostasis with minimal or no risk to patients.

### Abstract

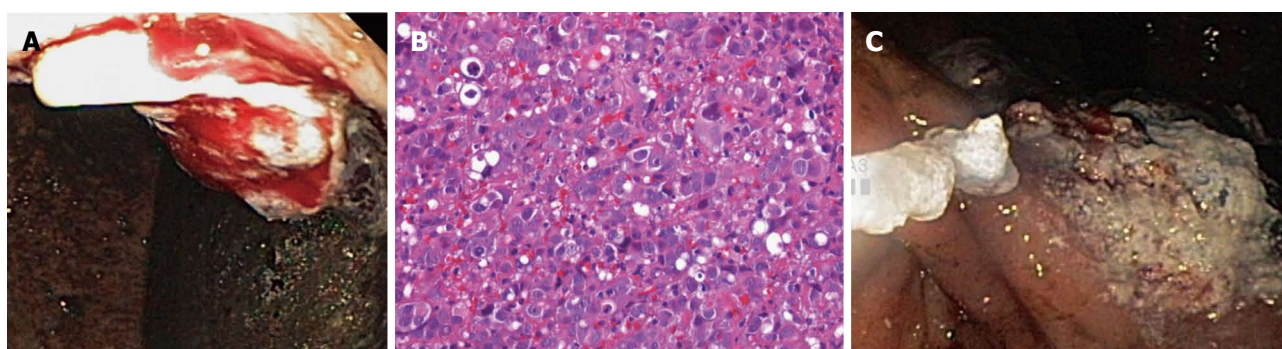
Gastrointestinal bleeding can be a life-threatening event that is managed with standard endoscopic therapy in the majority of cases. However, up to 5%-10% of patients may have persistent bleeding that does not respond to conventional measures. Several endoscopic treatment techniques have been proposed as strategies to control such cases, such as epinephrine injection, hemoclips or argon plasma coagulation, but there are certain clinical scenarios where it is difficult to achieve hemostasis even though adequate use of the available resources is made. Reasons for these failures can be associated with the lesion features, such as extent or location. The use of long-standing techniques in non-traditional scenarios, such as with cyanoacrylate for gastric varices sclerosis, has been reported with favorable results. Although new products such as TC-325 or Ankaferd Blood Stopper hemosprays may be useful, their formulations are not available worldwide. Here we present two clinical cases with very different scenarios of gastrointestinal bleeding, where the use of cyanoac-

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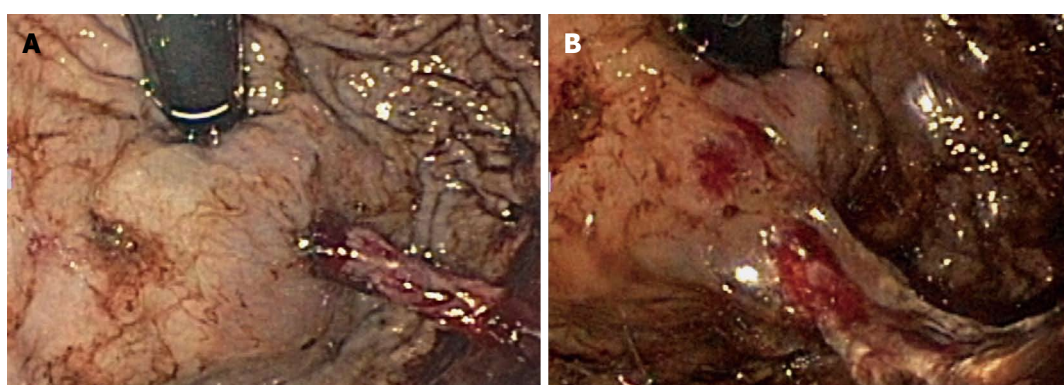
### INTRODUCTION

Upper gastrointestinal (GI) bleeding is a common disease, with approximately 48% of cases related to peptic ulcer disease<sup>[1]</sup>. Although endoscopy is highly effective in the control of active bleeding, up to 5%-10% of patients may have persistent bleeding that does not respond to conventional measures, or have recurrent bleeding that is common in conditions in which the underlying disease is not cured (e.g., varices, tumors)<sup>[2]</sup>. In this scenario, recurrent bleeding can be considered an independent risk factor potentially leading to mortality<sup>[1]</sup>.

An ideal method of endoscopic hemostasis would



**Figure 1** Patient with ulcerated adenocarcinoma of the lower third of the esophagus. A: Ulcerative lesion at the minor curvature with oozing; B: Diffuse adenocarcinoma (poorly differentiated). Neoplastic cells alternate with polymorphonuclear cells; C: Ulcerative lesion after cyanoacrylate spray.



**Figure 2** Gastric varices with active bleeding after sclerotherapy with 2-octyl cyanoacrylate. A: Bleeding fundic varices; B: Control of bleeding after placement of cyanoacrylate spray.

immediately stop active bleeding and prevent recurrent bleeding in both the short- and long-term for all types of lesions, be easy to apply to focal and diffuse areas in all locations in the GI tract, cause no significant tissue injury, be safe for the patient, endoscopist, and endoscope, have no limitation regarding the amount of therapy that can be applied, work in patients with decreased thrombotic function, and be inexpensive<sup>[3]</sup>. Currently, no endoscopic therapy achieves all of these characteristics, so new techniques or products must be proposed. Therapeutic measures using cyanoacrylate spray or new formulations, such as dust Hemospray (Cook Medical, Bloomington, IN, United States) have been proposed to achieve hemostasis<sup>[4]</sup>, but the latter is not available worldwide.

We report two clinical cases and their follow-ups demonstrating the usefulness of cyanoacrylate as a spray for GI bleeding.

## CASE REPORT

Patients were seen between October 2013 and January 2014 because of GI bleeding and failure of conventional endoscopic techniques. The clinical courses before and after endoscopies were reviewed. Hemostasis was defined as no oozing or spurting at the conclusion of endoscopy. All patients signed a consent form before the procedures.

## Spray technique

Using a 23-gauge injection needle catheter positioned 1 cm outside the tip of the endoscope, a total of 0.5-2.0 mL of a mixture of *N*-butyl-2-cyanoacrylate (Histoacryl; B. Braun Medical, Bethlehem, PA, United States) with lipiodol (0.5 mL:0.6 cc) was sprayed directly over the bleeding site, followed by a rapid 5-mL normal saline solution flush. After the spray, the needle was withdrawn inside the catheter, and the entire endoscope was removed, with the tip of the catheter sheath projecting outside the endoscope. The tip of the catheter was cleaned externally and removed.

## Case 1

A 62-year-old male patient with a history of ulcerated adenocarcinoma of the lower third of the esophagus received preoperative chemotherapy and a partial gastrectomy and esophagectomy (with resection of the middle and lower third). After surgery, radiochemotherapy was administered and he remained under surveillance.

After three years of follow-up, the patient showed disease recurrence and presented with melena and epigastric and midgut pain. Upper endoscopy was performed, and a malignant ulcer was seen in the lesser curvature, starting from the anastomosis until the pre-pyloric area, and the pathology report indicated an adenocarcinoma

Table 1 Patients included in previous reports on cyanoacrylate spray use

Ref.	Sex/age (yr)	Cause of bleeding	Prior therapy	Glue mixture	Glue volume	Treatment (n)	Outcome	Follow-up
Walia <i>et al</i> <sup>[6]</sup>	F, 89	2 cm ulcer in duodenal bulb	20 mL of epinephrine solution (1:10000) + bipolar cautery and hemoclips	n-butyl-2-cyanoacrylate/normal saline	4 mL	1	Successful hemostasis	No rebleeding
	M, 40	3 cm posterior duodenal bulb ulcer with arterial spurting	Epinephrine injection and hemoclip	n-butyl-2-cyanoacrylate/normal saline	0.5 mL	1	Hemodynamic parameters stabilized	Prophylactic angiographic embolization
	M, 55	2 cm duodenal bulb ulcer with arterial spurting	4 mL of epinephrine injection and bipolar cautery	n-butyl-2-cyanoacrylate/normal saline	1 mL	1	Recurrent hematochezia 2 d after procedure	Died 31 d later due to uncontrolled sepsis
	M, 69	Oozing gastric vascular ectasia along the lesser curvature	Argon plasma coagulation and hemoclips	n-butyl-2-cyanoacrylate/normal saline	1 mL	1	Hemostasis	Recurrent gastrointestinal bleeding 18 d later from vascular ectasia in a different location
	M, 59	Active oozing underneath hemoclip applied after hot snare polypectomy of 1.5 cm rectal polyp	hemoclips	n-butyl-2-cyanoacrylate/normal saline	0.5 mL	1	Hemostasis achieved	No rebleeding
Prachayakul <i>et al</i> <sup>[6]</sup>	M, 84	5 cm gastric cancer at lesser curvature with oozing	Epinephrine injection (1:20000)	En/Lip 0.5:0.8 + sterile water	3.0 mL	1	Hemostasis achieved	No rebleeding at 9 wk
	F, 76	5 cm sessile polyp in the ascending colon with oozing	Epinephrine injection (1:20000)	En/Lip 0.5:0.8 + sterile water	2.0 mL	1	Hemostasis achieved	No rebleeding at 5 wk, patient died
	M, 15	Metastasizing germinoma with duodenal invasion	Epinephrine injection (1:20000)	En/Lip 0.5:0.8 + sterile water	1.0 mL	1	Rebleeding at 48 h, and required angio-embolization	Continues to bleed, patient alive
	M, 56	Pancreatic cancer with gastric invasion (6 cm ulcerating mass with oozing in the upper part of the lesser curvature)	Metallic clip	En/Lip 0.5:0.8 + sterile water	1.0 mL	1	Hemostasis achieved	No rebleeding at 6 wk
	F, 62	Ampullary carcinoma with invasion to the second portion of duodenum	Epinephrine injection (1:20000)	En/Lip 0.5:0.8 + sterile water	1.5 mL	1	Hemostasis achieved	No rebleeding at 9 wk, patient died
Shida <i>et al</i> <sup>[7]</sup>	-	Pancreatic cancer with invasion into intestinal wall	Argon plasma Failed embolization	n-butyl-2-cyanoacrylate/normal saline	0.5 mL	No data	Hemostasis achieved	No data
	-	Gall bladder cancer with invasion into intestinal wall	No data	n-butyl-2-cyanoacrylate/normal saline	0.5 mL	No data	Hemostasis achieved	No data
	-	Mucosal resection in sigmoid colon	No data	n-butyl-2-cyanoacrylate/normal saline	0.5 mL	No data	Hemostasis achieved	No data
	-	Duodenal ulcer	No data	n-butyl-2-cyanoacrylate/normal saline	0.5 mL	No data	Hemostasis achieved	No data

En/Lip: Enbucrilate/lipidol.



(Figure 1A and B). Further studies confirmed the diagnosis of stage IV esophageal adenocarcinoma. Fifteen days later, the patient returned due to two episodes of melena, associated with epigastric and mesogastric pain with hemoglobin 10.1 g/dL. In the upper endoscopy, no specific source was detected and oozing was observed in the entire ulcerated area of the lesser curvature. Histoacryl with lipidol (1 mL total) was sprayed on the surface of the tumor through a 23-G catheter until hemostasis was achieved (Figure 1C). The patient was discharged after 72 h with no evidence of rebleeding. After six weeks of follow-up, the patient was alive with no evidence of recurrence of bleeding.

## Case 2

A 48-year-old male patient with a history of type 2 diabetes mellitus, hypertension, Evans Syndrome, chronic renal failure, heart failure (American Heart Association/New York Heart Association class II–III), and decompensated liver cirrhosis due to hepatitis C virus infection (ascites and recurrent variceal bleeding) was admitted for upper endoscopy. Large esophageal varices were observed along with gastric varices (GOV1). Sclerotherapy of gastric varices was performed with 2-octyl cyanoacrylate, but hemostasis was not achieved, with the presence of persistent bleeding after puncture (Figure 2A). Therefore, Histoacryl with lipidol was sprayed on the surface through a 23-G catheter until hemostasis was achieved (Figure 2B). In the follow-up, no recurrent bleeding was documented and the patient was discharged after 72 h. After three months of follow-up, no recurrence of bleeding or adverse effects were reported.

## DISCUSSION

We demonstrate favorable results with cyanoacrylate spray application in two different cases of difficult-to-treat GI bleeding. Cyanoacrylate has been intensively studied and has been clinically applied as a tissue adhesive in ear surgery, bone grafts, repair of fistulas and skin closures<sup>[5]</sup>. Cyanoacrylate is from a class of synthetic rubbers that are used as monomers and polymerize in an exothermic reaction after coming into contact with a weak base such as blood<sup>[5]</sup>. There are two forms used in endoscopy. Enbucrilate (*N*-butyl 2-cyanoacrylate; Histoacryl) is formed of an alkyl group of four carbons, whereas acrylate (2-octyl cyanoacrylate) has an alkyl group of eight carbons (Dermabond; Johnson and Johnson, New Brunswick, NJ, United States)<sup>[5]</sup>. Histoacryl has been widely used for digestive bleeding due to gastric varices, and is currently medically approved by the United States Food and Drug Administration. It has several advantageous properties, among which the polymerization upon contact with blood enables its effective use. It is thought that the fluid used to clean the injection needle can influence the polymerization time. For the present cases, a saline solution was used for cleaning the needle at the end of the procedure as it triggers polymerization of

the rubber, which does not occur with distilled water. We achieved similar favorable results with this combination as with a previous report by Prachayakul *et al*<sup>[6]</sup>.

The use of cyanoacrylate in a spray is not a standard modality for endoscopic treatment of GI bleeding. Table 1 describes the 14 cases that have been reported. Most of the cases used the technique with only saline reported by Shida *et al*<sup>[7]</sup>, which was used as a rescue therapy in lesions where hemostasis had been difficult to achieve by conventional methods with argon plasma, epinephrine or hemoclips<sup>[7]</sup>. In these cases, hemostasis was achieved, but there were no data on the follow-up of the patients. Prachayakul *et al*<sup>[6]</sup> reported the successful use of cyanoacrylate and lipidol in a 0.5:0.8 ratio with sterile water with no adverse effects for treating tumoral lesions<sup>[6]</sup>. Only one of their patients showed rebleeding during the nine-week follow-up period. In the data presented by Walia *et al*<sup>[8]</sup>, three patients experienced rebleeding in a median follow-up of 42 d (range: 30–120 d)<sup>[8]</sup>. In our two cases, neither of the patients presented recurrence of bleeding on follow-up.

The importance of this technique is the ease of use and the absence of special equipment required, making it accessible to different institutions and clinical settings. We report the use of this technique in two different clinical settings of GI bleeding with favorable results. There has been concern about the possibility of embolism with intravenous application, but this would not occur with the spray technique. There are reports of new products, such as Hemospray and Ankaferd Blood Stopper (Ankaferd Health Products Ltd., Istanbul, Turkey)<sup>[9]</sup>, but these products are not available worldwide.

In conclusion, cyanoacrylate used as a spray is a technique that can be used as an alternative method in emergent settings for uncontrollable GI bleeding.

## COMMENTS

### Case characteristics

Two patients with persistent gastrointestinal (GI) bleeding that did not respond to conventional measures of endoscopic treatment.

### Clinical diagnosis

One patient with gastric varices and another with ulcerated adenocarcinoma of the lower third of the esophagus.

### Treatment

Endoscopic treatment with Histoacryl sprayed directly over the bleeding site was used with good results.

### Related reports

Scarce information about cyanoacrylate in spray is reported.

### Experiences and lessons

Cyanoacrylate used as a spray is a technique that can be used as an alternative method in emergent settings for uncontrollable GI bleeding.

### Peer review

The authors describe the technique of using cyanoacrylate spray for GI bleeding and two successful cases are reported. The article provides a technique that is useful in a clinical background.

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