

N-butyl Cyanoacrylate Embolotherapy for Acute Gastroduodenal Ulcer Bleeding¹

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Purpose: Various embolic agents have been used for embolization of acute gastrointestinal (GI) arterial bleeding. N-butyl cyanoacrylate (NBCA) is not easy to handle, but it is a useful embolic agent. In this retrospective study, we describe our experience with NBCA embolization of acute gastroduodenal ulcer bleeding.

Materials and Methods: NBCA embolization was performed in seven patients with acute upper GI arterial bleeding; they had five gastric ulcers and two duodenal ulcers. NBCA embolization was done in the left gastric artery ($n = 3$), right gastric artery ($n = 2$), gastroduodenal artery ($n = 1$) and pancreaticoduodenal artery ($n = 1$). Coil was used along with NBCA in a gastric bleeding patient because of difficulty in selecting a feeding artery. NBCA was mixed with Lipiodol at the ratio of 1:1 to 1:2. The blood pressure and heart rate around the time of embolization, the serial hemoglobin and hematocrit levels and the transfusion requirements were reviewed to evaluate hemostasis and rebleeding.

Results: Technical success was achieved in all the cases. Two procedure-related complications happened; embolism of the NBCA mixture to the common hepatic artery occurred in a case with embolization of the left gastric artery, and reflux of the NBCA mixture occurred into the adjacent gastric tissue, but these did not cause any clinical problems. Four of seven patients did not present with rebleeding, but two had rebleeding 10 and 16 days, respectively, after embolization and they died of cardiac arrest at 2 months and 37 days, respectively. One other patient died of sepsis and respiratory failure within 24 hours without rebleeding.

Conclusion: NBCA embolization with or without other embolic agents could be safe and effective for treating acute gastroduodenal ulcer bleeding.

Index words : Gastrointestinal tract, hemorrhage
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Acute upper gastrointestinal (GI) arterial bleeding requires immediate treatment such as endoscopic sclerotherapy, endoscopic band ligation, endoscopic hemoclip application or surgery. It is not easy to find and ablate, ligate or clip bleeding foci in endoscopic fields that display massive hemorrhage or blood clot because endoscopic management requires patient cooperation and good visual fields. Surgery is perhaps the only the way to treat GI bleeding if there are no alternatives such as endoscopic management or radiological intervention, but surgery is too invasive. Radiological embolotherapy has recently been used for treating patients with GI bleeding because it allows us to treat them regardless of poor cooperation and massive hemorrhage or blood clot, and it is less invasive (1 - 3).

Various embolic agents such as coil, gelfoam, polyvinyl alcohol particle or n-butyl cyanoacrylate (NBCA; B. Braun, Melsungen, Germany) are used for treating GI bleeding (4 - 7). Liquid embolic agents that can quell bleeding foci might be more effective for upper GI arterial bleeding because the vascular system in the upper GI tract is the form of a network and this may permit adjacent collateral channels to feed bleeding foci even when a feeding artery is occluded. We used NBCA to treat acute gastroduodenal ulcer bleeding and we evaluated its clinical effectiveness in this retrospective study.

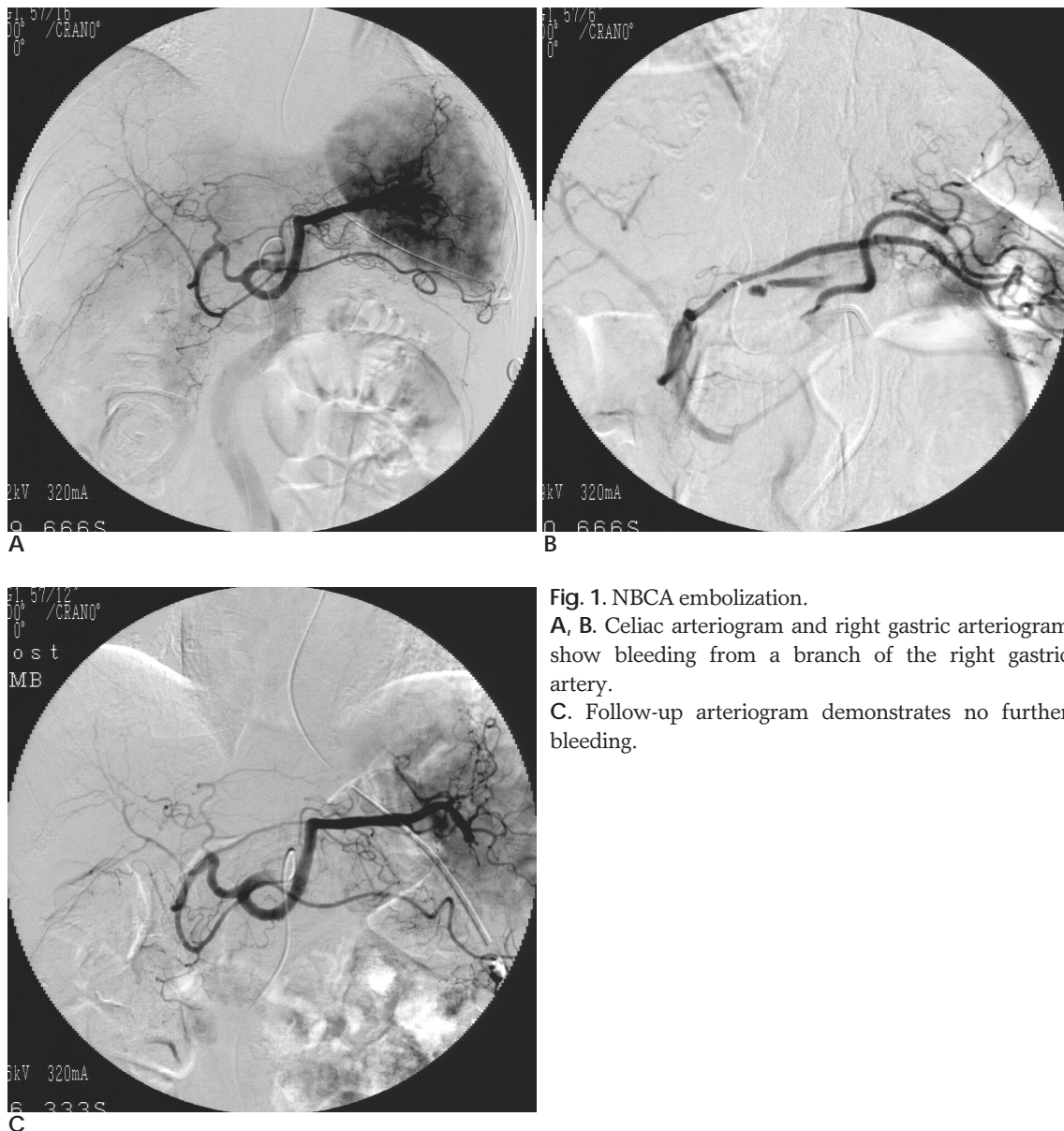


Fig. 1. NBCA embolization.

A, B. Celiac arteriogram and right gastric arteriogram show bleeding from a branch of the right gastric artery.

C. Follow-up arteriogram demonstrates no further bleeding.

Materials and Methods

Patient Population

NBCA embolization was performed in seven patients with acute upper GI arterial bleedings between December 2002 and September 2005 (Fig. 1). The patients ranged in age from 43 to 68 years and their mean age was 57 years. The patients included five men and two women. Embolization was performed in these 7 patients for five gastric ulcers and two duodenal ulcers

(Table 1). Coils were used along with NBCA in a patient with gastric ulcer bleeding because of the trouble with selecting the feeding artery (Fig. 2).

Embolization Techniques

Angiography with the digital subtraction technique was performed to detect bleeding foci. It included arteriography in the celiac trunk, superior mesenteric artery, right and left gastric artery, gastroduodenal artery or pancreaticoduodenal artery. A 5 Fr RH catheter (Cook, Bloomington, U.S.A.) was used to select the celiac trunk

Table 1. Clinical Findings in the Seven Patients who underwent NBCA embolization

Age/ Gender	Underlying condition	Bleeding foci	Embolic agents used	Ratio of NBCA and Lipiodol	Complications	Recurrent bleeding	Clinical follow-up
43/M	Chronic alcoholics, duodenal ulcer	Gastroduodenal artery branch	NBCA	1:1	No	No	1 day: death, sepsis/respiratory failure
65/F	Gastric ulcer	Right gastric artery branch	NBCA	1:1	No	No	2 months: outpatient visit
49/M	Chronic alcoholics, Tbc, gastric ulcer	Right gastric artery branch	NBCA	1:1	No	No	12 months: outpatient visit
47/M	Chronic alcoholics, gastric ulcer	Left gastric artery branch	NBCA	1:1	Reflux to right hepatic artery	No	9 months: outpatient visit
51/M	DM, duodenal ulcer	Pancreaticoduodenal artery branch	NBCA	1:1	No	Yes	2 months: death, cardiac arrest
76/M	ESRD, gastric ulcer	Left gastric artery branch	NBCA, coil	1:2	No	No	16 months: outpatient visit
68/F	Pseudomembranous colitis, gastric ulcer	Left gastric artery branch	NBCA	1:2	Overflow into adjacent tissue	Yes	37 days: death, cardiac arrest

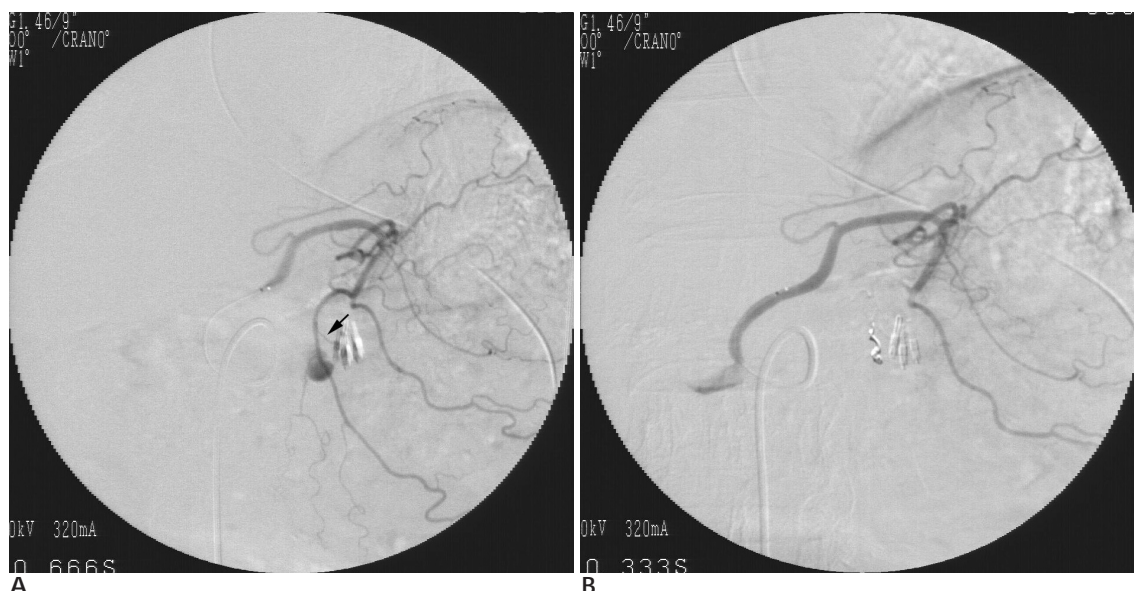


Fig. 2. NBCA embolization combined with coil.

A. Left gastric arteriogram demonstrates contrast extravasation.

B. Considering the difficulty in selecting a fine branch (arrow) from that extravasation and also because to the anticipated vasospasm due to several trial of selection, we embolized the mother vessel distal to the branch with coil, and we then injected the NBCA mixture into the mother vessel proximal to the branch. The post-embolization angiogram shows no further extravasation.

and superior mesenteric artery, and a Microferret catheter and wire (Cook, Bloomington, U.S.A.) or a Progreat catheter and 0.018 inch GT wire (Terumo, Tokyo, Japan) was employed to select the right and left gastric artery, gastroduodenal artery and pancreaticoduodenal artery. A very cautious approach to the bleeding foci was performed in a bid to avoid triggering vascular spasm that would make it impossible to inject the NBCA mixture or the spasm would delay procedures and so make the procedural time longer.

NBCA was carefully prepared without contact with ionic fluid or blood, which would make the liquid NBCA to become polymerized and solid. It was mixed with iodized oil (Lipiodol; Laboratoire Guerbet, Roissy, France) at a ratio of 1:1 to 1:2 to achieve radio-opacity under fluoroscopy. A lower ratio (more Lipiodol) prolongs the time for NBCA to solidify and this is useful to embolize bleeding foci that are not easy to approach and that are far from a microcatheter's tip.

The NBCA mixture was injected into the bleeding foci after several test injections of liquid contrast agent to correctly set the injection rate and prevent reflux to a proximal feeding artery or embolism to non-target organs. These test injections were useful if the viscosities of the contrast agent and NBCA mixture are a little different and there might be a gap between adequate injection power for the contrast agent and that for the NBCA mixture. Microcatheters were flushed with 5% or 10% glucose fluid before injecting the NBCA mixture.

The microcatheters were removed out of a body 1 to 2 seconds after injection of the NBCA mixture to prevent casts of the NBCA mixture at the bleeding foci from attaching to the tips of the microcatheters. Follow-up angiography was performed after embolization.

Study Endpoints

This study was performed retrospectively with reviewing the charts and telephoning the patients. This study received institutional review board approval. An informed consent was obtained from all the patients and the patients' families before embolization. The gastrointestinal endoscopy done before embolization was reviewed to determine the underlying diseases and whether there were arterial bleeding foci and where these foci were. The endoscopy after embolization was reviewed to see whether the bleeding foci had healed and whether there was rebleeding from the foci.

The blood pressure and heart rate at the time of embolization, the serial hemoglobin and hematocrit levels

and the transfusion requirements were reviewed to evaluate hemostasis and rebleeding. The sudden stoppage of bleeding caused a change in blood pressure and heart rate, which was an indicator of sorts to let us know whether the embolization was effective.

Results

Technical success of using NBCA for upper GI arterial bleeding was achieved in all seven patients even though coil was added along with NBCA for one patient. Hemostasis was verified via the angiography performed immediately after embolization in all the patients, and there was rise of blood pressure and a reduced heart rate around the time of embolization for four of seven patients. Two procedure-related complications occurred: one was embolism of the NBCA mixture to the common hepatic artery in the case of embolizing at the left gastric artery. Follow-up angiography showed a partial filling defect without flow disturbance. The other was reflux of the NBCA mixture into the adjacent gastric vessels, and endoscopy 10 days after the embolization showed no complication such as tissue ischemia or infarct.

The bleeding foci were in the left gastric artery (3 patients), right gastric artery (2 patients), gastroduodenal artery (1 patient) and pancreaticoduodenal artery (1 patient), which were all confirmed on angiography. The underlying diseases are listed in Table. There were gastric ulcers (5 patients) or duodenal ulcers (2 patients). One gastric ulcer patient, who initially underwent endoscopic alcohol injection and hemoclip application, did not achieve hemostasis, and the patient was referred to us for embolization.

The patients were followed up for 1 day to 16 months and the mean duration was 6 months. One of seven patients died the day after gastroduodenal artery branch embolization due to sepsis and respiratory failure, but there were no signs or symptoms of rebleeding. Another two patients had rebleeding 10 days and 16 days after embolization, respectively, and one of the two died of cardiac arrest 2 months after their embolization even though the rebleeding was controlled with medical treatment. The other one underwent subtotal gastrectomy due to recurrent bleedings 23 days after embolization and that patient died of cardiac arrest two weeks after the surgery.

The other four patients had no signs and symptoms of rebleeding and they have been followed up via outpa-

tient visits.

Discussions

The common way to manage patients with such GI bleedings as hematemesis, hematochezia or melena is endoscopy. This methodology can find the bleeding foci and achieve hemostasis through band ligation, application of hemoclips or injection sclerotherapy. Yet there are some limitations in controlling active GI arterial bleeding. It is not easy to get a clear vision via endoscopy due to massive hemorrhage and the patient's irritability. Moreover, it is difficult to approach the gastric fundus or small bowel distal to the third portion of the duodenum.

Surgery was one of first-line treatment modalities for GI bleeding, but nowadays, it may be the last choice that's performed after medical treatment, endoscopy or intravascular embolization because it is much too invasive compared to the other treatments.

Intravascular embolization has recently been attracting attention because it is less invasive (1 - 3). It has some other strong points, especially for active arterial bleeding, because of the ease of detecting bleeding foci on angiography, in spite of massive hemorrhage, and it is possible to perform angiography and embolization regardless of the irritability of patients.

A variety of embolic agents have been used to block GI arterial bleeding and different embolic agents are used according to the bowel level (4 - 10). The large bowel and small bowel, except the duodenum, have a vascular system that's different from the stomach and duodenum. The former has a vascular system with a form of end arteries and the latter has the form of a network. A network allows embolization with complete vascular block because it has extensive collateral circulation and the possibility of tissue ischemia or infarct around the bleeding foci is low, so liquid agents or small particulate agents are favored for embolization. On the contrary, the use of metallic coils or large particulate agents may result in incomplete embolization because there can be collateral flows to the bleeding foci, which prevent hemostasis. The end artery type of vascular system has poor collateral circulation; embolization with complete vascular block may cause tissue ischemia or infarct around the bleeding foci. Metallic coils or large particulate agents are favored when performing embolization for this type of vessel.

NBCA is one of the liquid embolic agents, and poly-

merization happens if it is exposed to ionic materials (11). It was first used to embolize brain AVMs, and there have since been various applications of NBCA, including craniofacial AVMs and extremity AVMs, hemangiomas in the mandible, arteriovenous fistula with a long fistula tract, hypervascular tumor, varicocele, gastric varices, the portal vein before partial hepatectomy, intractable epistaxis and acute arterial hemorrhage (12 - 20). Kish et al (4) reported that NBCA embolization was feasible and effective for controlling acute arterial hemorrhage that was due various etiologies and at various anatomic sites. In this study, we investigated the feasibility of performing NBCA embolization in acute upper GI arterial bleeding.

In our study, the microcatheters were removed out of the body 1 to 2 seconds after injecting the NBCA mixture to prevent the NBCA casts in the bleeding foci from being attached to the tips of the microcatheters. There can be some fragments of polymerized NBCA that stick to the tips of angiocatheters that overly the microcatheters and they can become emboli during the procedure. However, in our case, when the angiocatheters and RH catheters were removed after post-embolization angiography, we could not find any polymerized NBCA fragments at the tips of them.

The risk of an embolism to non-target organs or for reflux to the surrounding tissues always exists when performing NBCA embolization and they can cause ischemia or infarct of non-target organs or the surrounding tissues (21 - 24). Reflux to tissues around the bleeding foci in the stomach or duodenum is not fatal because these organs have a vascular network that provides rich collateral circulation.

In fact, the amount of NBCA that was infused into bleeding foci in this study was so small that the risk of embolism to distant organs was not high; the amount of NBCA was less than 0.5 mL. We usually mixed 0.5 mL NBCA and 0.5 to 1 mL Lipiodol and we used a 1 mL syringe for injection. The injected amount was 0.5 to 0.8 mL and we injected 0.2 to 0.5 mL of the mixture into bleeding foci, considering that the amount used to fill a microcatheter lumen is about 0.3 mL. The real amount of NBCA was 0.07 to 0.25 mL when taking the mixing ratio into account; therefore, any side effects or complication of NBCA itself may be minimal enough to disregard.

Combination of NBCA and other embolic agents such as coil or gelfoam can be very useful in controlling GI or other arterial bleeds. Yamakado (25) et al reported that a

combination of coil and NBCA was useful in a ruptured pseudoaneurysm that was difficult to embolize with coil alone. One patient in our study underwent embolization with coil and NBCA due to difficulty in superselecting a bleeding focus.

NBCA is not easy to handle and it takes some experience to use it without complications. Therefore, achieving technical success for NBCA embolization might be determined by the expertise of the operators, which could be a limitation of this study. There were also some other limitations of this study; it was a retrospective study and there was a small number of patients.

In summary, NBCA embolization could be safe and effective for the treatment of acute gastroduodenal ulcer bleeding and it sometimes needs the combined use of other embolic agents for achieving better embolization.

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