

# Safety and Cost-Effectiveness of N-butyl-2-Cyanoacrylate without Lipiodol in Endoscopic Management of Gastric Varices

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<sup>1</sup> Conception of study

<sup>2,3</sup> Experimentation/Study conduction

<sup>2,3,4</sup> Analysis/Interpretation/Discussion

<sup>1,4</sup> Manuscript Writing

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## Abstract

**Introduction:** Gastric varices are frequently seen in patients with portal hypertension. The mainstay of treatment is variceal injection with a mixture of N-butyl-2-Cyanoacrylate and lipiodol. The use of N-butyl-2-Cyanoacrylate without lipiodol is not extensively studied and it can be a cost-effective approach. The objective of our study was to evaluate whether the use of N-butyl-2-Cyanoacrylate without lipiodol is a safe and effective endoscopic treatment for gastric varices.

**Material and Methods:** This prospective observational study was conducted between June 2016 and May 2017 at the Department of Gastroenterology, Gujranwala Medical College/ DHQ Teaching Hospital, Gujranwala. A total of 100 patients with gastric varices diagnosed on upper GI endoscopy were enrolled in the study. N-butyl-2-Cyanoacrylate without lipiodol was injected into the gastric varices of all the patients. All procedures were performed by experienced gastroenterologists. The patients underwent monthly follow-up endoscopies to determine the outcome and adverse events.

**Results:** Out of 100 patients, 40 patients (40 %) were men and 60 (60%) were women. The mean age was 53 years. The mean volume of N-butyl-2-Cyanoacrylate used per session was 1.5ml ± 0.5 ml (range 1-2ml). Obliteration of Gastric varices was achieved in 92 patients (92%) while in 04 patients (4%) varices did not obliterate over a mean follow-up of 12 months. No treatment-related immediate or late complications were observed in all patients. Four patients (4%) died of delayed rebleeding (after two weeks of intervention).

**Conclusion:** Injection therapy of gastric varices with N-butyl-2-Cyanoacrylate alone without lipiodol is a safe and cost-effective method for gastric varices.

**Keywords:** Cirrhosis, Gastric Varices, N-butyl-2-Cyanoacrylate, Outcome.

## Introduction

Liver cirrhosis is a global health problem. In patients with liver cirrhosis, the rate of varices formation is 5 to 15% per year, and 25% of patients with varices will develop variceal hemorrhage.<sup>1</sup> Despite the recent advancement in the management, variceal hemorrhage has a 6-week mortality rate of 10%-20%.<sup>2,3</sup> Though when compared with esophageal varices, the gastric varices bleed less frequently but they bleed with greater intensity.<sup>4</sup> The gold standard test to diagnose and classify these varices is upper GI endoscopy. Sarin et al classified esophageal varices according to their size and the gastric varices according to their location & concomitant presence of esophageal varices.<sup>4</sup> Different methods have been used for the management of gastric varices which include band ligation, sclerosis with ethanolamine oleate, and obturation with tissue glues like N-Butyl 2-cyanoacrylate and TIPS (transjugular intrahepatic portosystemic shunts). There is also a case report of using hemostatic nanopowder for bleeding gastric varices.<sup>5</sup> A study comparing conventional sclerotherapy with cyanoacrylate glue injection showed that cyanoacrylate glue injection is more effective than conventional sclerosis for controlling first variceal hemorrhage.<sup>6</sup> Other studies comparing the tissue glues with band ligation have also concluded that bleeding control was similar in both groups but rebleeding was more in-band ligation in long-term follow-up.<sup>7,8</sup> TIPS (transjugular intrahepatic portosystemic shunts) is an effective alternative to endoscopic intervention in patients with Child-Pugh class C (due to the high risk of treatment failure).<sup>9</sup> In 1986, Nib Sohendra et al, successfully obliterated gastroesophageal varices using N-butyl-2-Cyanoacrylate, which is now being practiced in different countries of Europe and Asia.<sup>10</sup> Cyanoacrylate injection has also been shown to prevent the first episode of bleed in patients with gastric varices when compared with beta-blockers.<sup>11</sup> Most common side effects seen with Cyanoacrylate injection therapy are re-bleeding due to glue cast extrusion, sepsis, distant embolism, and gastric ulcer formation.<sup>12</sup>

### Technical Consideration:

N-butyl-2 cyanoacrylate is a chemical substance that solidifies on contact with an aqueous medium, through a polymerization process. Lipiodol is a poppy seed oil that when mixed with N-butyl-2 cyanoacrylate delays the polymerization process by 20 seconds thus preventing the blockage of the injection needle. However, the use of lipiodol increases the overall cost

of the procedure to about more than 10 times, a serious concern in developing countries. When used with care and expertise, N-butyl-2 cyanoacrylate can be injected without mixing with it lipiodol, thus making it a cost-effective approach.

## Materials and Methods

This prospective observational study was conducted at the Department of Gastroenterology, Gujranwala Medical College/DHQ Teaching Hospital, Gujranwala from June 2016 to May 2017. A total of 100 patients with gastric varices diagnosed on upper GI endoscopy, were enrolled in the study. A sample size of 100 was calculated using a 95% confidence interval, a 5% margin of error, and taking an expected outcome of 93%. Informed written consent was taken from all study participants after the approval from the ethical board. Their demographic data, history, and clinical examinations were recorded.

### Instruments & Technique:

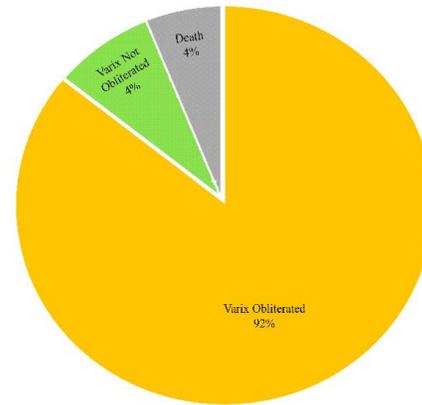
All the patients received standard medical treatment of upper GI bleeding. Gastroscopy was performed to define the type of gastric varices according to Sarin classification. A standard sclerotherapy injection needle of 21G was used in all patients. Distilled water was instilled into the catheter to fill the dead space within it. Cyanoacrylate was filled in a 5cc syringe. After puncturing gastric varix, N-butyl-2 cyanoacrylate (1 to 2ml mL) was rapidly injected into varix by an expert endoscopy technician, followed by a rapid push of distilled water (quantity pre-calculated according to the dead space). Monthly follow-up endoscopy was performed in all the patients to assess the treatment success i.e varix obliteration and further need of sessions.

## Results

100 patients received injection treatment with N-butyl-2 cyanoacrylate glue for the gastric varices. The mean age was 53 years (range 28-60 years), 40 patients (40 %) were men and 60 (60%) were women. All the patients had liver cirrhosis (Child A cirrhosis in 40 patients, Child B cirrhosis in 50, and Child C cirrhosis in 10 patients). Concomitant esophageal varices were present in 62 patients (GOV2) and 38 patients had isolated gastric varices (IGV1).

**Table 1: Characteristics of Patients**

	Number	Percentage (%)
<b>No. of Patients (Male/Female)</b>	100 (40/60)	(40%/60%)
<b>Mean Age (Range) year</b>	53 (28-60)	
<b>Child Class (A/B/C)</b>	40/50/10	
<b>Type of Varix</b>		
• GOV2	62	62%
• IGV1	38	38%
<b>Varix Bleeding Status</b>		
• Active	10	10%
• Recent	86	86%
• Never	04	4%



**Figure 1: Varix Obliteration Results**

**Table 2: Results of Cyanoacrylate Glue Treatment**

	Value	Percentage %
<b>Mean Cyanoacrylate per session (Range)</b>	1.5 ml (1-2ml)	
<b>No. of Sessions per patient 1/2/3/4</b>	6/36/40/10	
<b>Rebleeding</b>		
<b>Treatment Success</b>	92	92%
<b>Treatment Failure</b>	04	4%
<b>Deaths</b>	04	4%

The mean volume of N-butyl-2-Cyanoacrylate used per session was 1.5ml ± 0.5 ml (range 1-2ml). Initial hemostasis was achieved in all 10 patients who presented with active variceal bleeding. The mean follow-up time was 12 months. Complete obliteration of gastric varices was achieved in 92 patients (92%). This required a single session in 06, two sessions in 36, and three sessions in 40 patients, and four sessions in 10 patients. Two patients (2%) had early re-bleeding (within 24 hours) and five patients (05%) had late rebleeding (after 24 hours) that were successfully managed with another session of glue injection. Treatment failure (failure to obliterate gastric varix after four sessions) was noted in four patients (04%). Four patients (4%) died due to delayed bleeding (after 2 weeks of therapy).

## Discussion

The most common cause of upper GI bleed is Peptic ulcer disease<sup>13</sup> but in patients with cirrhosis, variceal hemorrhage is the major cause.<sup>14</sup> The prevalence of esophageal varices in compensated cirrhosis is about 30% and in decompensated cirrhosis is about 60%.<sup>15</sup> Treatment options for patients with bleeding from gastric varices are octreotide, terlipressin, and TIPS. Endoscopic therapy with cyanoacrylate glue is another viable option not only in cases where TIPS is not feasible or available but also as a sole therapy. The glue typically is combined with lipiodol solution. Our study showed that endoscopic injection of gastric varices with cyanoacrylate without using lipiodol is a cost-effective approach in all patients whether they present with active bleeding or the treatment is given for prophylaxis. A randomized controlled trial, comparing the effectiveness of cyanoacrylate glue injection, b-blockers, and no treatment also showed that primary hemorrhagic from gastric varices was less frequent in those treated with cyanoacrylate glue injection compared with those who were treated with beta-blockers or no treatment.<sup>16</sup> Mixing of lipiodol with cyanoacrylate delay the polymerization process but it tremendously increases the overall cost of the procedure. So, when used with care and expertise, the cyanoacrylate glue can be injected successfully into varix without using lipiodol. A similar study was published in 2014 in which undiluted cyanoacrylate and methacryloxysulfolane (NBCM) was used to obturate the gastric varices in twenty patients without mixing it with lipiodol and eradication of gastric varices was noted in all patients over a median follow-up of 31 months. 13 patients required only one session & the rest seven required two sessions. The maximum

volume of NBCM injected was 2ml. No complications were observed in all patients except mild epigastric pain in two patients.<sup>17</sup>

## Conclusion

Injection therapy of gastric varices with N-butyl-2-Cyanoacrylate alone without the use of lipiodol is a safe and cost-effective method in the endoscopic management of gastric varices.

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