Endoscopic management of bleeding gastric varices with N-butyl, 2-cyanoacrylate glue injection in children with non-cirrhotic portal hypertension

Authors Ujjal Poddar, Vibhor Borkar, Surender Kumar Yachha, Anshu Srivastava

Institution Department of Pediatric Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

submitted 29. March 2016
accepted after revision 29. July 2016

Bibliography
DOI http://dx.doi.org/10.1055/s-0042-114981
Published online: 29.9.2016
Endoscopy International Open 2016; 04: E1063–E1067

E-ISSN 2196-9736

Corresponding author
Ujjal Poddar, MD, DNB, DM, Professor
Department of Pediatric Gastroenterology,
SGPGIMS, Lucknow
226014, Uttar Pradesh
India
Fax: +915222668017
ujjalpoddar@hotmail.com

Background and study aims: In view of the paucity of literature, we carried out this audit to evaluate the safety and efficacy of N- butyl, 2-cynoacrylate glue injection therapy in secondary prophylaxis of gastric varices in children.

Patients and methods: Consecutive children (≤18 years) with non-cirrhotic portal hypertension who presented with bleeding from gastric varices and who had undergone cyanoacrylate glue injection therapy were included. They were evaluated for safety, efficacy and complications. Their long-term outcomes and follow-up were recorded.

Results: Over 11 years, 28 children with median age 13 (range, 8 to 18) years (68 % boys), underwent cyanoacrylate glue injection for bleeding gastric varices. In 25 (89 %) cases, extrahepatic portal venous obstruction was the etiology and isolated gastric varices were the source of the bleeding. Primary and secondary gastric variceal bleeding was seen in 11 (39 %) and 17 (61 %) children, respectively. A total 36 sessions with median volume of 2 (range, 1 – 5) mL of glue injections were required (2 sessions in 8 children). Hemostasis was achieved in all and 57 % had gastric variceal obliteration. Two children had early (< 1 month) rebleeding and 2 children had late rebleeding. One child had gastric ulcer. Over a median follow-up of 24 (8 – 98) months, 14 children underwent surgery (12 porto-systemic shunt), 2 were lost to follow-up, 1 died and there was no recurrence of bleeding in the remaining 11.

Conclusions: Cyanoacrylate glue injection is highly effective mode of secondary prophylaxis of bleeding gastric varices in children with non-cirrhotic portal hypertension. Rebleeding occurred in 14 % but treatment-related complications were uncommon. However, a large controlled clinical trial is required to confirm our findings.

Introduction

Portal hypertension is a common cause of significant upper gastrointestinal bleeding in children. Although cirrhosis is the common cause of portal hypertension in children in the developed world [1], non-cirrhotic portal hypertension (NCPH), especially extrahepatic portal venous obstruction (EHPVO), is the most common cause in developing countries [2,3]. Most children with EHPVO present with variceal bleeding due to rupture of esophageal varices, which can be managed effectively with endotherapy using sclerotherapy (EST), band ligation (EVL) or a combination of both [4 – 8]. Primary gastric varices are not uncommon but most are a continuation of esophageal varices in the form of gastroesophageal varices and do not bleed often [9 – 11]. A significant proportion of primary gastric varices (gastroesophageal) disappear with the obliteration of esophageal varices [9,10]. On the contrary, the risk of bleeding is substantial with secondary gastric varices (new varices that appear after eradiation of esophageal varices) and with gastric varices that persist despite eradication of esophageal varices [9,11]. Secondary gastric varices mainly comprise isolated gastric varices and gastroesophageal varices along the greater curvature of the stomach (GOV2). The prevalence of isolated gastric varices is low at initial presentation but increases significantly with concomitant increased risk of bleeding after obliteration of esophageal varices [9,12,13].

Although gastric varices bleed in significantly fewer patients, they bleed more severely than do esophageal varices [11]. Upper gastrointestinal bleeding from gastric varices is difficult to treat because of high rates of mortality and morbidity, and rebleeding risks. The therapeutic options for gastric variceal bleeding are cyanoacrylate glue injection, transjugular intrahepatic portosystemic shunt (TIPS), balloon-occluded retrograde transvenous obliteration (B-RTO) and surgical porto-systemic shunt. As per Baveno-VI recommenda-

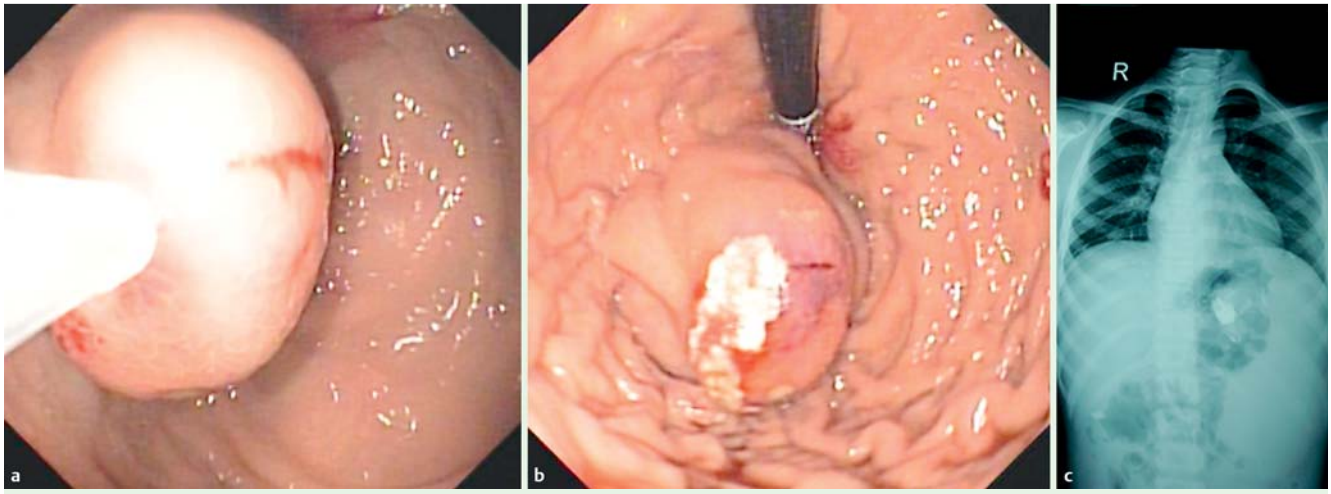

Fig. 1 **a** Endoscopic picture of F3 isolated gastric varix in 12-year-old boy (before glue injection). **b** Endoscopic picture of F3 isolated gastric varix in 12-year-old boy (after glue injection). **c** X-ray of the abdomen of the same patient showing glue-cast in the gastric varix.

tions [14] cyanoacrylate glue injection is first-line treatment for gastric variceal bleeding. Endoscopic intravascular injection with the tissue adhesive N-butyl 2-cyanoacrylate was originally proposed by Soehendra et al. [15] in 1986 as a therapeutic option for bleeding esophago-gastric varices. Subsequent studies have suggested that this method may achieve gastric variceal obliteration [16,17]. Experience with treating gastric varices with glue injection in children is limited to only a few case series [18–20]. Therefore, we analyzed our experience with use of cyanoacrylate glue in treating bleeding gastric varices in children with portal hypertension.

Patients and methods

We performed a retrospective audit of our experience using glue injection to treat bleeding from gastric varices in patients with portal hypertension after receiving approval from our institution's ethics committee. The study was conducted in the Pediatric Gastroenterology service of Sanjay Gandhi Postgraduate Institute of Medical Science, Lucknow, India from October 2003 to December 2015. Consecutive children (up to 18 years of age) who were diagnosed with acute upper gastrointestinal bleeding resulting from rupture of GV during the study period were included in this research. We included only non-cirrhotic portal hypertension (NCPH) including EHPVO, non-cirrhotic portal fibrosis (NCPF), and segmental portal hypertension due to splenic vein thrombosis. EHPVO was diagnosed on the basis of ultrasonographic evidence of a recanalized or blocked portal vein replaced by a portal vein cavernoma and normal liver function tests. Non-cirrhotic portal fibrosis (NCPF) was diagnosed in children with portal hypertension who had patent spleno-portal axis and normal liver function tests and whose liver histology showed no evidence of cirrhosis or parenchymal injury [21]. Other clinical features like size of spleen on clinical examination, endoscopic documentation of esophageal, gastric varices and follow-up data were recorded.

Grading of gastric varices

Gastric varices (GV) were classified as described by Sarin et al. [11] into gastro-esophageal varices (GOV) and isolated gastric varices (IGV). GOV were sub-classified into GOV1, where the GV were continuous with the esophageal varices (EV) and extended along the lesser curve of the stomach, and GOV2, where the GV extended from the EV toward the gastric fundus. IGV were subclassified as IGV1, which were isolated GV occurring at the fundus, and IGV2, which were ectopic varices located in the antrum, corpus, and around the pylorus. Gastric varices were also graded according to size as F1 (tortuous), F2 (nodular or grapes like) and F3 (tumorous) [22]. Gastric varices were labeled as primary when present at the time of initial endoscopic examination and secondary if they developed after endoscopic eradication of esophageal varices [11]. EV were graded I to IV as per classification by Conn et al [23]. Bleeding from GV was considered if anyone of the following criteria was present**:** (1) active bleeding from GV was seen; (2) a clot or ulcer was seen over the GV; or (3) bleeding occurred in the context of distinct large GV in the absence of esophageal varices or another source of upper gastrointestinal bleeding [24].

Endoscopy

All patients who presented with acute upper gastrointestinal bleeding received resuscitative measures and pharmacologic treatment with bolus intravenous (IV) injection of 1 microgram/kg of octreotide followed by infusion at a rate of 1 microgram/kg/hour for 3 to 5 days. Hemoglobin was maintained around 8 g/dL. Endoscopy was carried out after hemodynamic stabilization under IV sedation using IV midazolam and fentanyl with continuous pulse oximetry monitoring after receiving informed consent from a parent. Endoscopic injection therapy was done with a forward-viewing videoendoscope (Olympus Optical Corporation, Tokyo, Japan) with 22-gauge needle. For initial glue injections, N-butyl, 2-cyanoacrylate (Nectacryl; Dr. Reddy's Laboratories Ltd. Hyderabad, India/ Histoacryl; B.Braun Melsungen AG, Germany) was diluted with lipiodol (1 : 1) before injecting to prevent early polymerization and to allow radiologic monitoring (**Fig. 1**). However, for the last 4 years, because of the risk of embolism, we have stopped using lipiodol. Variceal puncture was confirmed with withdrawal of blood into the injector. The volume of glue injection was restricted to 1 mL/injection to minimize the risk of embolization. The needle was flushed with distilled water after each injection. Successful GV obliteration was determined endoscopically by probing with the tip of an injection catheter. The varices were classified as obliterated if they were felt to be hard on blunt probing

Clinical features		N (%)
Etiology	EHPVO	25 (89 %)
	Isolated splenic vein thrombosis	2 (7 %)
	Non-cirrhotic portal fibrosis (NCPF)	1 (3.5 %)
Bleeding history	Active bleeding	10 (36 %)
	Recent bleeding	18 (64 %)
Presentation of gastric varices	Primary gastric variceal bleeding	11 (39 %)
	Secondary gastric variceal bleeding	17 (61 %)
Grading of esophageal varices (at the time of gastric variceal bleeding)	No esophageal varices/eradicated	14 (50 %)
	Grade I	4 (14 %)
	Grade II	7 (25 %)
	Grade III	2 (7 %)
	Grade IV	1 (3.5 %)
Gastric variceal classification	GOV1	1 (3.5 %) (F3)
	GOV2	2 (7 %) [F2 & F3: 1 each]
	IGV1	25 (89 %) [F3 = 17, F2 = 8]

Table 1 Clinical characteristics of patients (n = 28) with gastric varices.

EHPVO, extrahepatic portal venous obstruction; GOV1, gastro-esophageal varices type 1; GOV2, gastro-esophageal varices type 2; IGV1, isolated gastric varices type 1.

	Primary gastric variceal bleeding (n = 11)	Secondary gastric variceal bleeding (n = 17)	*P*
Median age (years)	14 (range, 12 – 17)	13 (range, 8 – 18)	0.07
Male	6 (54 %)	13 (76 %)	0.40
Etiology: EHPVO	8 (73 %)	17 (100 %)	0.05
Associated large esophageal varices (grade II/IV)	5 (45.5 %)	5 (29 %)	0.44
Hemostasis achieved	11 (100 %)	17 (100 %)	1.00
Early rebleeding	1 (9 %)	1 (6 %)	1.00
Late rebleeding	0	2 (12 %)	0.50
Ulcer	0	1 (6 %)	1.00
Mortality	1 (9 %)	0	0.39

Table 2 Comparisons between primary gastric variceal bleeding (n = 11) and secondary gastric variceal bleeding (n = 17).

EHPVO, extrahepatic portal vein obstruction.

and as not obliterated if compressible and indentable on pressure. Glue injection was repeated after 3 weeks if the patient had recurrence of bleeding or had unobliterated varices [24]. The criteria for failure of control of acute bleeding episode was used as per Baveno VI consensus [14]. Initial hemostasis was defined by presence of stable vital signs and absence of rebleeding within 48 hours after glue injection [24]. Early rebleeding was defined as occurring within 30 days of initial hemostasis, whereas late rebleeding was defined as occurring after 30 days [24]. The glue injection sessions were carried out until the gastric varices were obliterated. Review endoscopy was done after 3 weeks. The patients were followed-up at 3 months, 6 months and then annually. During follow-up, patients were assessed for feasibility of surgical porto-systemic shunt by Doppler ultrasonography (USG) and computed tomography (CT) venography of portal venous system.

Results

During the study period, 673 cases of variceal bleeding due to non-cirrhotic portal hypertension (EHPVO 640, NCPF: 26, congenital hepatic fibrosis 5, segmental portal hypertension 2) were managed in our center and 28 (4 %) of these patients had bleeding from gastric varices. Clinical characteristics of the patients are summarized in **Table 1**. Their median age at time of bleeding from gastric varices was 13 (range, 8 to 18) years and 19 (68 %) of them were boys. Hematemesis was the mode of presentation in 27 children, while 1 child presented with melena alone. Of the 28 children, 11 (39 %) presented with first-time bleeding from ruptured gastric varices (primary gastric variceal bleeding) while 17 (61 %) children had earlier bleeding episodes from rupture of esophageal varices which were managed with endotherapy and they later presented with bleeding from rupture of gastric varices (secondary gastric variceal bleeding). In 9 of 17 (53 %) children who were on endoscopic follow-up, gastric varices were not present at the time of first bleeding and developed at a median follow-up of 46 months (range, 27 – 93). In the remaining 8 children, gastric varies were present at the first endoscopic session and bled after obliteration of esophageal varices at a median interval of 45 months (range, 2 – 96). None of the patients required balloon tamponade. Of the 28 children, 25 (95 %) had IGV1 (F3 in 17 [**Fig. 1 a**] and F2 in 8) and GOV2 in 2 (F3 1, F2 1) and GOV1 (F3) in 1 child. Ten (36 %) children had active bleeding and 18 (64 %) had bleeding in the recent past. Twenty (71 %) children required a single session of glue injection and 8 (29 %) children required 2 sessions (total 36 sessions of glue injections). Median volume of injected glue in total was 2 (range, 1 to 5) mL. Of the 10 children who had active bleeding from gastric varices, all had immediate hemostasis. None of the 28 children had failure of hemostasis. Obliteration of the gastric varices was achieved in 16 (57 %) children. The comparisons between children who presented with primary gastric variceal bleeding and those with secondary gastric variceal bleeding are given in **Table 2**. There was a tendency of older age in the primary group and EHPVO as the etiology in the secondary group but the differences were not statistically significant due to the small numbers, and other parameters such as gender distribution, rebleeding, and complications did not differ between the groups.

Rebleeding and complications

During median follow-up of 28 months (range, 8 – 102) there was no recurrence of bleeding in 24 (86 %) of the patients. Four children had rebleeding, 2 early and 2 late. One child who had early rebleeding twice (at 3 days and 1 month after glue injection) had a gastric ulcer. The ulcer, which measured 3 cm by 3 cm and was located in the posterior wall of the stomach, was managed conservatively using a proton pump inhibitor. A 13-year-old boy with NCPF had massive rebleeding after 14 days of glue injection and died at home. None of the children in our series had other complications such as distant emboli, pyrexa, bacteremia, or local abscess formation. We did not encounter any procedure-related complications such as detachment of the endoscopic needle in the varices or damage to the endoscope.

Follow-up

All children who presented with bleeding from gastric varices were evaluated for shunt surgery after controlling the index bleed with glue injection as a part of our unit's management policy for non-cirrhotic portal hypertension. Two children who had recurrence of bleeding 1 year and 2 years after glue injection were subjected to repeat glue injection. The first child had rebleeding after shunt surgery due to shunt blockage but there was no recurrence of bleeding for 10 years after the second glue injection. The second child underwent shunt surgery after the second glue injection and remained asymptomatic for 7 years. A total 14 (50 %) children underwent surgery for portal hypertension (shunt surgery in 12 and splenectomy with gastric devascularization in 2 for isolated splenic vein thrombosis (1 with chronic pancreatitis and the other 1 of unknown etiology) after a median gap of 2 months (range, 8 to 27 days) following glue injection. Of the 12 children who underwent shunt surgery, proximal spleno-renal shunt (PSRS) was done in 11 children and interposition mesocaval shunt in 1 patient. Of the remaining 14 patients, 2 had non-shuntable venous anatomy; 2 children were lost to follow up, 9 were awaiting shunt surgery, and 1 died. Eleven children who received glue injection for GV and had not undergone any surgery for portal hypertension had not bled at a median follow-up of 24 months (range, 8 to 98).

Discussion

To the best of our knowledge, this is the largest series in children evaluating the efficacy, safety, and long-term outcome of glue injection therapy in children who had gastric variceal bleeding and the only series so far in NCPH. Previous case series were in 8 infants with gastro-esophageal varices (GOV) [18] and 5 children with GV bleeding [19]. In a recent study, Oh et al. [20] used glue injection in 21 children, 5 of whom had EHPVO, but unlike in the current study, the majority of children (76 %) had GOV1 which was accompanied by large esophageal varices (grade ≥ II in 76 %). Hence, it is difficult to assess whether all these children had bleeding from gastric or esophageal varices because GOV1 varices are, in fact, a continuation of esophageal varices. In 5 cases, Oh et al used glue for esophageal varices as EVL had failed due to the younger age of the patients.

In our study, the majority (89 %) of children had EHPVO and isolated gastric varices (IGV1). Sarin et al. [11] in their seminal paper on gastric varices in 568 portal hypertension patients showed that gastric varices were significantly more common in EHPVO than in cirrhosis (31 % *vs.* 17 %, $P<0.01$). They also showed that bleeding risk was maximal with IGV1 (78 %) than GOV2 (55 %) or GOV1 (12 %). In a study of 274 cases of EHPVO, it was shown that despite having gastric varices in 68 % of cases, none of the patients had primary gastric variceal bleeding. However, after eradication of esophageal varices, the prevalence of high-risk gastric varices (i.e. IGV1) increased significantly (from 1 % to 14 %, $P<0.001$) and 20 % of them had bleeding [9]. This has been substantiated by our previous study in 183 cases of EHPVO [10]. The current study also shows that secondary gastric variceal bleeding is more common than primary bleeding, almost all of which were from IGV1. Nevertheless, 39 % of cases in present series had presented for the first time with gastric variceal bleeding. That was not highlighted in previous pediatric studies [9, 10, 18 – 20]. In a study of 170 adults with gastric variceal bleeding (28 EHPVO), Choudhuri et al [25] showed that only 20 % had primary gastric variceal bleeding, 82 % had F3 and 95 % had fundal varices (IGV1 and GOV2). In another adult study of 29 patients with gastric varices (cirrhosis 13, EHPVO 13 and NCPF 3), 28 % had primary gastric variceal bleeding [26].

A randomized controlled trial in adults showed that N-butyl-2-cyanoacrylate injection is superior to sclerotherapy with alcohol [27] and another trial showed its superiority over endoscopic band ligation [28] in gastric variceal bleeding. Acute hemostasis was achieved in more than 90 % of cases with N-butyl-2-cyanoacrylate compared with 62 % with alcohol injection and just 40 % with EVL [27, 28]. In our series, acute hemostasis was achieved in all patients. Cyanoacrylate, in contrast to standard sclerosants, polymerizes immediately and produces vascular obliteration in contact with blood. Mixing cyanoacrylate with lipiodol reduces the rate of solidification of glue and thus facilitates administration of glue without damaging the endoscopes. However, overdilution may predispose to risk of distant embolization [29]. The issue of volume of glue to be injected in children has not been addressed before. Studies in adults showed that the volume depends on the type of gastric varices (less for localized than diffuse [30] and more for IGV than GOV [31]). Oh et al. [20] in their study of 21 children with GOV injected 0.25 mL to 0.5 mL in each aliquot of 1 : 1 mixture of cyanoacrylate and lipoidal. Although they mentioned that a smaller aliquot (0.2 mL) was used for smaller children, they did not report on any age or weight criteria. Whether the volume of glue should be calculated as per the child's age or on the basis of the size of the varices requires further study. Because we had mainly IGV1 and large varices (F2 and F3), we used a 1-mL aliquot and did not encounter any embolization. No cases of embolization were reported by using undiluted glue in a 1-mL aliquot in 170 adult patients by Kumar et al. [32]. Similarly, whether risk of embolization with use of lipoidal depends on the age of the child or severity of portal hypertension requires further study.

In our series, rebleeding was seen in 14 % of children, one of whom had early rebleeding from gastric ulcer at the site of glue injection. Gastric ulcer due to glue injection and rebleeding from it is a known complication reported in 0.1 % to 6.3 % of treated patients [25, 30, 31, 33]. The glue cast causes necrosis and ulceration of the local vessel at the varix, which can lead to fatal hematemesis [34]. Giant gastric ulcers are known to occur if glue injection is done at an extra-variceal location [24, 31]. In some patients, early rebleeding is caused by extrusion of glue cast and reported in 4.4 % of patients in the first 3 months after glue injection [31]. Incomplete obliteration of gastric varies can lead to early rebleeding from the patent vascular channels and was the likely cause of early rebleeding in the one patient in our study who suc-

cumbed to exsanguinous bleeding at home. Rivet et al. [18] documented rebleeding from GV in 38 %, while another study in children [19] did not report rebleeding after glue injection. Late rebleeding was seen in 7 % of children in our study and is reported in 7 % to 28 % of patients after glue injection in adult studies [24, 25, 30, 33, 35].

The retrospective and uncontrolled nature is the major limitation of our study. However, the data collection was from computerized records and endoscopic records, thus limiting recall bias. We did not include a control arm to compare the results of glue injection to any other modality. Because we had a small number of patients, we could not do any subgroup analysis to elucidate factors that predispose to complications.

Conclusion

In conclusion, gastric variceal bleeding, although uncommon, is not rare in children. In almost one-third of cases, patients present with first-time gastric variceal bleeding (primary). Canoacrylate glue injection therapy is effective for secondary prophylaxis of GV with a 100 % success rate for hemostasis in children with non-cirrhotic portal hypertension. Rebleeding was seen in 14 % and injection site ulcer in 3.5 % of children. Long-term follow-up of children who did not undergo shunt surgery showed excellent outcome. However, a large, prospective, controlled clinical trial on the use of cyanoacrylate glue in children is required to confirm our findings.

Competing interests: None

References

1 *Bernard O, Alvarez F, Brunelle F* et al. Portal hypertension in children. Clin Gastroenterol 1985; 14: 33 – 55
2 *Yachha SK, Khanduri A, Sharma BC* et al. Gastrointestinal bleeding in children. J Gastroenterol Hepatol 1996; 11: 903 – 907
3 *Poddar U, Thapa BR, Rao KL* et al. Etiological spectrum of esophageal varices due to portal hypertension in Indian children: is it different from the West? J Gastroenterol Hepatol 2008; 23: 1354 – 1357
4 *Poddar U, Thapa BR, Sing K*. Endoscopic sclerotherapy in children: experience with 257 cases of extrahepatic portal vernous obstruction. Gastrointest Endosc 2003; 57: 683 – 686
5 *Yachha SK, Sharma BC, Kumar M* et al. Endoscopic sclerotherapy for esophageal varices in children with extrahepatic portal vein obstruction; a follow up study. J Pediatr Gastroenterol Nutr 1997; 24: 49 – 52
6 *Zargar SA, Javid G, Khan BA* et al. Endoscopic ligation compared with sclerotherapy for bleeding esophageal varices in children with extrahepatic portal venous obstruction. Hepatology 2002; 36: 666 – 672
7 *Poddar U, Thapa BR, Sing K*. Band ligation plus sclerotherapy versus sclerotherapy alone in children with extrahepatic portal vein obstruction. J Clin Gastroenterol 2005; 39: 626 – 629
8 *Poddar U, Bhatnagar S, Yachha SK*. Endoscopic band ligation followed by sclerotherapy: is it superior to sclerotherapy in children with extrahepatic portal venous obstruction? J Gastroenterol Hepatol 2011; 26: 255 – 259
9 *Poddar U, Thapa BR, Singh K*. Frequency of gastropathy and gastric varices in children with extrahepatic portal venous obstruction treated with sclerotherapy. J Gastroenterol Hepatol 2004; 19: 1253 – 1256
10 *Itha S, Yachha SK*. Endoscopic outcome beyond esophageal variceal eradication in children with extrahepatic portal venous obstruction. J Pediatr Gastroenterol Nutr 2006; 42: 196 – 200
11 *Sarin SK, Lahoti D, Saxena SP* et al. Prevalence, classification and natural history of gastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology 1992; 16: 1343 – 1349
12 *Gonclaves ME, Cardoso SR, Maksoud JG*. Prophylactic sclerotherapy in children with esophageal varices: long-term results of a controlled prospective randomized trial. J Pediatr Surg 2000; 35: 401 – 405
13 *Stringer MD, Howard ER*. Long term outcome after injection sclerotherapy for esophageal varices in children with extrahepatic portal hypertesnion. Gut 1994; 35: 257 – 259
14 *de Franchis R*. Baveno VI faculty. Expanding consensus in portal hypertension: Report of the the Baveno VI consensus workshop: stratifying risk and individualizing care for portal hypertension. J Hepatol 2015; 63: 743 – 752
15 *Soehendra N, Nam VC, Grimm H* et al. Endoscopic obliteration of large esophagogastric varices with bucrylate. Endoscopy 1986; 18: 25 – 26
16 *Ramond MJ, Valla D, Mosnier JF* et al. Successful endoscopic obturation of gastric varices with butyl cyanoacrylate. Hepatology 1989; 10: 488 – 493
17 *Oho K, Iwao T, Sumino M* et al. Ethanolamine oleate versus butyl cyanoacrylate for bleeding gastric varices: a nonrandomized study. Endoscopy 1995; 27: 349 – 354
18 *Rivet C, Robles-Medranda C, Dumortier J* et al. Endoscopic treatment of gastroesophageal varices in young infants with cyanoacrylate glue: a pilot study. Gastrointest Endosc 2009; 69: 1034 – 1038
19 *Fuster S, Costaguta A, Tobacco O*. Treatment of bleeding gastric varices with tissue adhesive (Histoacryl) in children. Endoscopy 1998; 30: S39 – S40
20 *Oh SH, Kim SJ, Rhee KW* et al. Endoscopic cyanoacrylate injection for the treatment of gastric varices in children. World J Gastroenterol 2015; 21: 2719 – 2724
21 *Sarin SK, Kumar A, Chawla YK* et al. Non-cirrhotic portal fibrosis/idiopathic portal hypertension: APASL recommendations for diagnosis and treatment. Hepatol Int 2007; 1: 398 – 413
22 *Hashizumi M, Kitano S, Yamaga H* et al. Endoscopic classification of gastric varices. Gastrointest Endosc 1990; 36: 276 – 280
23 *Conn HO*. Ammonia tolerance in the diagnosis of esophageal varices. A comparison of endoscopic, radiologic, and biochemical techniques. J Lab Clin Med 1967; 70: 442 – 451
24 *Seewald S, Ang TL, Imazu H* et al. A standardized injection technique and regimen ensures success and safety of N-butyl-2-cyanoacrylate injection for the treatment of gastric fundal varices (with videos). Gastrointest Endosc 2008; 68: 447 – 454
25 *Choudhuri G, Chetri K, Bhat G* et al. Long-term efficacy and safety of N-butylcyanoacrylate in endoscopic treatment of gastric varices. Trop Gastroenterol 2010; 31: 155 – 164
26 *Dhiman RK, Chawla Y, Taneja S* et al. Endoscopic sclerotherapy for gastric variceal bleeding with N-butyl-2 cyanoacrylate. J Clin Gastroenterol 2002; 35: 222 – 227
27 *Sarin SK, Jain AK, Jain M* et al. A randomized controlled trial of cyanoacrylate versus alcohol injection in patients with isolated fundic varices. Am J Gastroenterol 2002; 97: 1010 – 1015
28 *Lo GH, Lai KH, Cheng JS* et al. A prospective, randomized trial of butyl cyanoacrylate injection versus band ligation in the management of bleeding gastric varices. Hepatology 2001; 33: 1060 – 1064
29 *Bhat YM, Banerjee S, Barth BA* et al. Tissue adhesives: cyanoacrylate glue and fibrin sealant. Gastrointest Endosc 2013; 78: 209 – 215
30 *Iwase H, Maeda O, Shimada M* et al. Endoscopic ablation with cyanoacrylate glue for isolated gastric variceal bleeding. Gastrointest Endosc 2001; 53: 585 – 592
31 *Cheng LF, Wang ZQ, Li CZ* et al. Low incidence of complications from endoscopic gastric variceal obturation with butyl cyanoacrylate. Clin Gastroenterol Hepatol 2010; 8: 760 – 766
32 *Kumar A, Singh S, Madan K* et al. Undiluted N-butyl cyanoacrylate is safe and effective for gastric variceal bleeding. Gastrointest Endosc 2010; 72: 721 – 727
33 *Al-Ali J, Pawlowska M, Coss A* et al. Endoscopic management of gastric variceal bleeding with cyanoacrylate glue injection: safety and efficacy in a Canadian population. Can J Gastroenterol 2010; 24: 593 – 596
34 *Kok K, Bond RP, Duncan IC* et al. Distal embolization and local vessel wall ulceration after gastric variceal obliteration with N-butyl-2-cyanoacrylate: a case report and review of the literature. Endoscopy 2004; 36: 442 – 446
35 *Rajoriya N, Forrest EH, Gray J* et al. Long-term follow-up of endoscopic Histoacryl glue injection for the management of gastric variceal bleeding. Q J Med 2011; 104: 41 – 47