Dicle Tıp Dergisi /
Dicle Medical Journal

2011; 38 (4): 387-391
doi: 10.5798/diclemedj.0921.2011.04.0055

ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Successful endoscopic treatment of bleeding gastric varices with n-butyl-2-cyanoacrylate and lipiodol mixture injection

Kanayan mide varislerinin n-butil-2-siyanoakrilat ve lipiodol karışımı enjeksiyonu ile başarılı endoskopik tedavisi

Yaşar Tuna[1], Adnan Taş[2], Seyfettin Köklü[3]

[1]Department of Gastroenterology, Faculty of Medicine, Akdeniz University, Antalya, Turkey
[2]Department of Gastroenterology, Osmaniye Public Hospital, Osmaniye, Turkey
[3]Department of Gastroenterology, Ankara Education and Research Hospital, Ankara, Turkey

Geliş Tarihi / Received: 17.06.2011, Kabul Tarihi / Accepted: 05.08.2011

ABSTRACT

Objectives: The aim of this study was to determine effect of N-Butyl-2 Cyanoacrylate (CA) and lipiodol mixture injection for hemostasis of bleeding gastric varices or lesions, which had bled from gastric varices.

Materials and methods Fifteen patients with active bleeding or bleeding findings within two weeks who admitted to endoscopic unit of a low volume medical center were evaluated retrospectively between 2003 and 2010. We carried out endoscopic sclerotherapy successfully to gastric varices with combination of N-Butyl-2 Cyanoacrylate and Lipiodol (CALM), with dramatical success over months after sessions of sclerotherapy for each patient.

Results: Sclerotherapy with cyanoacrylate achieved hemostasis in all actively bleeding nine patients initially. Rebleeding occurred in a patient 24 hours later and in another patient two months later (2/15, 13.3%). Eradication of gastric varices was achived in 13 (86.7 %) patients during follow-up. One patient was operated because of rebleeding. One patient died as a result of liver failure. Five-year survival rate of the patients after eradication of gastric varices was 14/15 (93.3%).

Conclution: This study indicated that sclerotherapy with N-Butyl-2 Cyanoacrylate and lipiodol mixture is an effective treatment method for patients with bleeding gastric varices and also for eradication of gastric varices.

Key words: Endoscopic sclerotherapy, cyanoacrylate, Lipiodol, gastric varices

ÖZET

Amaç: Bu çalışmadaki amacımız kanayan veya daha önce kanamış olan gastrik varislerde syanoacrilat ve lipiodol karışımının hemostazdaki etkisini saptamaktır.

Gereç ve yöntem: 2003-2010 tarihleri arasında aktif kanayan veya kanama bulgusu olan ve iki hafta içinde endoskopi ünitesine kabul edilen 15 hasta retrospektif olarak değerlendirildi. Syanoacrilat ve lipiodol karışımını gastrik varisli hastalarda başarılı şekilde uyguladık ve tüm hastalara endoskopik işlem, varisler başarılı şekilde tedavi edilene kadar aylık peryotlarla tekrarlandı.

Bulgular: Syanoacrilatlı skleroterapi ile aktif kanayan 9 hastada başlangıçta hemostaz sağlandı. Tekrar kanama, 1 hastada 24 saat sonra diğer hastada 2 ay sonra görüldü (2/15, %13,3). Takip süresince gastrik varis eradikasyonu 13 hastada (%86,7) başarıldı. Bir hasta tekrar kanamadan opere edildi diğer hasta karaciğer yetmezliğinden öldü. Gastrik varis eradikasyonundan sonra 5 yıllık yaşam 14/15 (%93,3) idi.

Sonuç: Bu çalışmada aktif kanayan ve kanama işareti olan gastrik varisli hastalarda syanoacrilat lipiodol kombinasyonu ile skleroterapinin etkili tedavisi gösterildi.

Anahtar kelimeler: Endoskopik skleroterapi, siyanoakrilat, lipiodol, gastrik varis

INTRODUCTION

Gastric varices (GV) are the hemodynamic result in patients with portal hypertension. Approximately 20% of patients with portal hypertension suffer from GV.[1,2] GV associated with esophageal varices named as gastroesophageal varices (GOV) are listed as: type 1 (GOV1), along the lesser curve, or type 2 (GOV2), along the fundus and the ones present in isolated places named as isolated gastric

Yazışma Adresi /Correspondence: Dr. Adnan Taş
Department of Gastroenterology, Osmaniye Public Hospital, Osmaniye, Türkiye Email: dradnantas@gmail.com

varices (IGV), are listed as: in the fundus IGV 1, in the ectopic sites of stomach or in the first part of the duodenum IGV2.[1] GV bleeding is an important lethal complication of cirrhosis, and it's secondary to portal hypertension.[3] Hemorrhage caused by GV is usually severe and hemostatic control is reported to be more difficult, compared with esophageal variceal bleeding. The high early mortality rate of variceal bleeding has been prime motivation for treatment of patients. Incidence rate of bleeding in portal hypertension and cirhosis has been reported as 55 to 78%. Patients who bleed from gastric varices appear to have high mortality.[1]

Several methods have been tried in order to treat GV bleeding with variable success.[4-7] Endoscopic sclerotherapy is an effective theurapeutic modality of fundal varices bleeding. Many sclerosants have been used for variceal sclerotherapy. Intravariceal injection of cyanoacrylate (CA) produced at initial hemostasis has a rate of 87% to 100%. After the initial treatment subsequent sclerotherapy sessions have been required to achieve oblitaration of varices.[8-10] Oblitaration effect of CA is excellent on IGV1. However this effect in patients without active bleeding is controversial.[11] Effective variceal oblitaration is determined, but early rebleeding rate was very high.[12]

The aim of this study was to determine the effect of N-Butyl-2 Cyanoacrylate (Histoacryl, Braun Dexan) and lipiodol mixture (CALM) injection for hemostasis of actively bleeding GV and lesion which had bled from GV.

MATERIALS AND METHODS

The study included 15 patients who were admitted for emergency treatment of gastric fundal variceal bleeding or lesions which had bled from gastric fundal variceal, between 2003 and 2010. The patients were evaluated retrospectively.

Inclusion Criteria

The inclusion criteria were active fundal gastric variceal hemorrhage, a recent history of bleeding attributed to fundal gastric varices. Active bleeding was defined as observed spurting or oozing of blood from a fundal varix or the presence of an overlying clot and absence of any other source of bleeding, such as esophageal varix, portal hypertensive gastropathy, or gastric antral vascular ectasia. Eleven patients presented with acute GV bleeding. Past bleeding: Patients with large GV,with absent esophageal varices, who had bled in the past from GV were included in this category. Four patients presented with past bleeding.

All patients were requested to sign an informed consent before endoscopic procedure.

Exclusion Criteria

Patients who were undergoing endoscopic sclerotherapy or banding for esophageal varices, pregnancy, inability to give informed consent for the procedure, multi-organ failure, patients with hepatorenal syndrome or hepatic encephalopathy and patients not giving informed consent for endoscopic procedures were excluded.

Gastric varices

The gastric varices were classified according to their location using the Sarin classification: Varices in the esophagus and lesser curvature (GOV1); varices in the esophagus and gastric fundus (GOV2); varices in the fundus only (IGV1), or at ectopic sites such as the body, antrum, or duodenum (IGV2). Furthermore, varices were classified based on their size as F1 (mild, linear, tortuous), F2 (moderate, nodular) or F3 (severe, tumorlike). In case of active bleeding, the hemorrhage was described as either oozing or spurting. The presence of a clot or a tear on a varix with blood in the stomach and without any evidence of another bleeding source was also considered a sign of active variceal bleeding.

Endoscopic and medical treatment

In our endoscopy unit, a mixture of N-Butyl-2 Cyanoacrylate (Histoacryl,Braun Dexan) and Lipiodol (CALM) 0,5 mL to 0,5 mL ratio was applied using a front-view type endoscope (Olympus, CV 240, Tokyo, Japan) in the retroflexed position. N-butyl-2 -cyanoacrylate and lipiodol are mixed in equal proportions before use and are injected into the varices using a 23 gauge disposable sclerotherapy needle catheter (Boston Scientific, Tokyo, Japan) that is passed through the biopsy canal. Before administering the mixture, the needles are flushed with just enough isotonic sodium chloride solution for a few drops to appear at the tip. The mixture is then applied in different quantities as needed to achieve he-

mostasis, after which the canal is again flushed with the same amount of sodium chloride solution that was used before. To decrease the risk of a variceal tear the tip of the needle is withdrawn before the glue sets, after which the catheter is held in place for 3–4 s to prevent leakage of the mixture from the varices. CALM was tried to be injected intravaricely without extravasation of solution which may give damage to the endoscopes. 1 mL of CALM was performed for each session of the GV sclerotherapy.

We observed and felt when the needle is penetrating the variceal wall. We repeated sclerotherapy with same volume of CALM if the active bleeding was persistant. If GV remained soft and not obliterated enough, sclerotherapy procedure was carried on for eradication of large varices once a week until obtaining the optimum theurapeutic effect according to the endoscopic examination. CALM was tried to be injected intravaricely without extravasation of solution which may give damage to the endoscopes. 1 mL of CALM was performed for each session of the GV sclerotherapy. We observed and felt when the needle is penetrating the variceal wall. We repeated sclerotherapy with same volume of CALM if the active bleeding was persistant. Patients are re-evaluated 4-6 weeks after the index endoscopy, and variceal obliteration is checked by probing with a catheter tip. The glue injection is repeated every 4-6 weeks until obliteration is achieved, after which a follow-up endoscopy is performed at 3-month intervals.

For all patients who presented with gastric bleeding, appropriate fluid resuscitation, prophylactic antibiotics, proton pump inhibitor and somatostatin infusion were initiated before each procedure. All of the acute bleeders received the vasoactive drug somatostatin infusion for 72 hours after admission. We followed up patients for a long time to determine outcome, variables were initial hemostasis rate, early and late rebleeding rate, recurrence rate of GV mortality and sclerotherapy complications.

Statistical analysis

All data were expressed as mean ± SD or percentage. Statistical significance was determined using the chisquare test and significance was taken at $P < 0.05$. The statistical analysis was performed using the SPSS package (version 16.0 J; SPSS Inc., Chicago, Illinois, USA).

RESULTS

A total of fifteen patients (mean age: 51 ± 16.2 years; range 19-75 years; 10 males-5 females) with GV underwent endoscopic sclerotherapy with N-butyl-2-cyanoacrylate (Histoacryl, Braun Dexan) and lipiodol mixture (CALM) injection between 2003 to 2010. The etiology of portal hypertension patients was liver cirhosis (11/15, 73%) and non-cirhotic portal hypertension (NCPH) (4/15, 27%). Cirrhosis was HBV related in five patients, alcohol related in three patients, and with unknown etiology in three patients. NCPH causes of GV included portal vein trombosis (2/4) and splenic vein trombosis (2/4). The number of Child-Pugh A, B, and C cases according to severity of liver disease were 4, 6, and 1, respectively.

All of the patients had gastric varices (10 IGV 1, 4 GOV 1, 1 GOV 2). The majority of GV were IGV 1 (10/15, 66.7 %). The mean number of upper gastrointestinal bleeding was 2.6 ± 2.4 (range 0-10) at the presentation. Nine patients had active GV bleeding during endoscopic examination. Five patients had achieved eradication of esophageal varices before sclerotherapy.

Actively gastric varice bleeding was observed in most of the patients during endoscopic examination (9/15, 60%). CALM injection sclerotherapy achieved hemostasis in all of the actively bleeding patients during initial endoscopic examination (9/9). Only one patient had rebleeding within 24 hours. Eradication of gastric varices was achieved in 13 (86,6%) patients. A mean number of 1.7 ± 1.03 (range, 1-4) sessions was required to eradicate the gastric varices; 9 patients required 1 session; 2 patients required 2 session; three patients required 3 session, 1 patient required four session (range 1-4). The volume of prepared CALM required to control the bleeding gastric varices ranged from 1 to 4 ml with a mean total volume of 1,7 ± 1.03 mL of CA was used. Number os sessions of endoscopic sclerotherapy with CA was 1.7 ± 1.03 (range, 1-4), resulting obliteration of GV in all patients. Only six patients (6/15, 40%) had more than 2 sessions of sclerotherapy.

Recurrence of gastric varices was observed in two patients after 6 months from sclerotherapy (2/15). An early and a late rebleeding was determined in two patients (2/15, 13,3%). Early rebleed-

ing occurred 24 hours artery sclerotherapy. This patient was operated because of uncontrolled rebleeding. One patient died because of liver failure during follow-up (1/15, 6.6%). We observed one damage case of endoscope because of CA leakage. There were no major systemic and local complications such as cerebral stroke, pulmonary embolism, portal vein embolism and splenic infarction. None had remarkable changes in blood tests and vital signs after sclerotherapy.

Four patients with NCPH had no signicicant differences in age, sex, number of bleeding episodes, number of sessions required for erredication of gastric varices, complications, and amount of CALM used.

Table 1. Patients demographics and clinical characteristics

Number of patients	15
Male / Female	10 / 5
Mean age	51 ± 16.2 (19-75)
IGV 1	10 / 15 (66.7 %)
GOV 1	4 / 15 (26.7 %)
GOV 2	1 / 15 (6.6 %)
Active bleeding	9 / 15 (60 %)
Recent bleeding	6 / 15 (40%)
Child-Pugh A / B / C	4 / 6 / 1

IGV: isolated gastric varices, GOV: Gastroesophageal varices

Table 2. Etiology of portal hipertension

Cirrhosis	11 / 15 (73%)
HBV	5 / 11
Alcohol	3 / 11
Unknown	3 / 11
NCPH	4 / 15 (27 %)
Portal vein trombosis	2 / 4
Splenic vein trombosis	2 / 4

NCPH: Noncirrhotic Portal Hypertension

HBV: Hepatitis B viruses

Table 3. Hemostasis for gastric varices

Mean volume of CA required	1,7±1.03 mL
Mean sessions of sclerotherapy	1.7
Hemostasis rate for active bleeding of GV	9/9 (100%)
Recurrent bleeding rate	2/15 (13%)
Early rebleeding rate	1/15 (6.6%)
Late rebleeding rate	1/15 (6.6%)
Recurrence of GV	2/15 (13.3%)
Bleeding Mortality	(0/15)

CA: Cyanoacrylate, GV: Gastric varices

DISCUSSION

In the present study, we have documented succesful eradication of either bleeding or non-bleeding gastric varices with CALM. CALM is a cheap and safe method for gastric varice eradication.

The incidence of gastric variceal bleeding is lower than esophageal varices. However, bleeding from GV results in more severe hemorrhage and higher mortality because of large draining veins and abundant blood flow.[1] Efficacy of CA sclerotherapy for emergency and elective IGV 1 bleeding is excellent. Cyanoacrylate sclerotherapy is first line treatment of acute IGV1 bleeding[7] however use of CA in patients without acute bleeding is controversial, because rebleeding rate was relatively high.[11,13] Most rebleeding occurred in first year after CA sclerotherapy during 10 year follow-up.[14]

Cyanoacrylate is a hydrophilic polymer and spontaneously polimerized in water. Because of this property, it has been used to obliterate actively bleeding gastric varices.[12,15,16] We achieved hemostasis in actively bleeding patients during initial endoscopic examination with injection of CALM solution (9/9). This property of CALM was very important for obliteration of gastric varices immediately in emergency conditions. Only one patient had rebleeding within 24 hours (1/15,6.6%) and was operated. One patient with initial hemostasis had recurrent rebleeding after 3 months and died because of liver failure during follow up.

At this study, CALM has no adverse effects on liver function according to Child-Pugh classification. A previous study indicated that N-Butyl-2 Cyanoacrylate injection had little influence on the survival of patient with advanced liver failure.[10,17,18]

One patient died from liver failure during follow up.

At this study most of the patients applied in emergency conditions because of active bleeding. We had demonstrated successful initial hemostasis of active gastric varices bleeding. Early hemostasis rate in actively bleeding patients was 88.8% (8/9) and five-year survival rate of patients with cirhosis was 90.9% (10/11). Rare but serious complications like cerebral stroke, pulmonary embolism, portal vein embolism and splenic infarction[11] of endoscopic sclerotherapy was not observed in our cases and rebleeding rate is lower (2/15, 13.3%) than previous reports (30%).[12,13,19,20] Two patients had recurrent gastric varices and thirteen patients had a clinical course of more than 4 years without any recurrence. Extravasation of solution, which gave damage to the endoscope, was occurred in a case.

There were some limitations to our study. The first is the small number of patients in a retrospective manner. Large number of patients with gastric varices bleeding may be necessary to confirm our results. Second, a control group including a method other than CALM such as band ligation, alcohol injection would further demonstrate the efficacy of CALM.

In conclusion, the optimal treatment of gastric varices remain unclear. Nb2c-lipiodol mixture is a low-cost, effective and easy to use treatment. This study indicated that sclerotherapy with N-Butyl-2 Cyanoacrylate and lipiodol mixture may be an effective treatment method for patients with gastric varice bleeding in emergent and elective conditions. Patients with cirrhosis and NCPH have high eradication rate of gastric varices with -Butyl-2 Cyanoacrylate and lipiodol mixture as a sclerosing agent and relatively low complication rate.

REFERENCES

1. Sarin SK, Lahoti D, Saxena SP, Murthy NS, Makwana UK. Prevalence, classification and natural history ofgastric varices: a long-term follow-up study in 568 portal hypertension patients. Hepatology 1992; 16(6): 1343-9.
2. Thakeb F, Salem SA, Abdullah M, el Batanouny M. Endoscopic diagnosis of gastric varices. Endoscopy 1994;26(3):287–9.
3. Graham DY, Smith JL. The course of patients after variceal hemorrhage. Gastroenterology 1981;80(4):800–9.
4. Ramond MJ, Valla D, Mosnier JF, et al. Successful endoscopic obliteration of gastric varices with butyl cyanoacrylate. Hepatology 1989;10(4):488–93.
5. Gimson AE, Westaby D, Williams R. Endoscopic sclerotherapy in the management of gastric variceal hemorrhage. J Hepatol 1991;13(3):274–8.
6. Soehendra N, Nam VC, Grimm H, Kempeneers I. Endoscopic obliteration of large esophagogastric varices with bucrylate. Endoscopy 1986;18(1):25–6.
7. Yoshida T, Hayashi N, Suzumi N, et al. Endoscopic ligation of gastric varices using a detachable snare. Endoscopy 1994;26(5): 502–5.
8. Huang YH, Yeh HZ, Chen GH, et al. Endoscopic treatment for bleeding gastric varices by N-butyl-2-cyanoacrylate (Histoacryl) injection: longterm efficacy and safety. Gastrointest Endosc 2000;52(2):160-7.
9. Iwase H, Maeda O, Shimada M, et al. Endoscopic ablation with cyanoacrylate glue for isolated gastric variceal bleeding. Gastrointest Endosc 2001;53(6):585-92.
10. Lo GH, Lai KH, Cheng JS, Chen MH, Chiang HT. A prospective, randomized trial of butyl cyanoacrylate injection versus band ligation in the management of bleeding gastric varices. Hepatology 2001;33(5):1060-4.
11. Binmoeller KF. Glue for gastric varices: some sticky issues. Gastrointest Endosc 2000;52(2):298-301.
12. Akahoshi T, Hashizume M, Shimabukuro R, et al. Long-term results of endoscopic Histoacryl injection sclerotherapy for gastric variceal bleeding: a 10-year experience. Surgery 2002;131(1):176-81.
13. Sarin SK, Jain AK, Jain M, Gupta R. A randomized controlled trial of cyanoacrylate versus alcohol injection in patients with isolated fundic varices. Am J Gastroenterol 2002; 97(4):1010–1015
14. Soehendra N, Grimm H, Nam VC, Berger B. N-butyl-2-cyanoacrylate: a supplement to endoscopic sclerotherapy. Endoscopy 1987;19(6):221–4.
15. Cheng PN, Sheu BS, Chen CY, Chang TT, Lin XZ. Splenic infarction after Histoacryl injection for bleeding gastric varices. Gastrointest Endosc 1998;48(4):426–7.
16. Jutabha R, Jensen DM, Egan J, Machicado GA, Hirabayashi K. Randomized, prospective study of cyanoacrylate injection, sclerotherapy, or rubber band ligation for endoscopic hemostasis of bleeding canine gastric varices. Gastrointest Endosc 1995;41(3): 201–5.
17. Ng WD, Chan YT, Ho KK, Kong CK. Injection sclerotherapy for bleeding esophageal varices in cirrhotic patients with hepatocellular carcinoma. Gastrointest Endosc 1989;35(1):69–70.
18. Sung JJ, Yeo W, Suen R, et al. Injection sclerotherapy for variceal bleeding in patients with hepatocellular carcinoma: cyanoacrylate versus sodium tetradecyl sulphate. Gastrointest Endosc 1998;47(3):235–9.
19. Greenwald BD, Caldwell SH, Hespenheide EE, et al. N-2-butyl-cyanoacrylate for bleeding gastric varices: a United States pilot study and cost analysis. Am J Gastroenterol 2003;98(9):1982–1988
20. Oho K, Iwao T, Sumino M, Toyonaga A, Tanikawa K. Ethanolamine oleate versus butyl cyanoacrylate for bleeding gastric varices: a nonrandomized study. Endoscopy 1995; 27(5):349–54.