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A Preliminary Result of The Frequency of Bacteremia after Endoscopic Injection of Cyanoacrylate for Non Bleeding Gastric Varices

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ABSTRACT

Background: Many studies reported significant transient bacteremia after endoscpic cyanoacrylate injection for active gastric variceal bleeding. The explanation for bacteremia was still unclear, whether it was due to bacterial invasion through ruptured gastric variceal mucosa or introduction of bacteria after cyanoacrylate injection. The aim of our study was to determine the risk of bacteremia in patients with gastric varices who underwent elective cyanoacrylate injection.

Patients and Methods: Cirrhotic patients who underwent elective endoscopic cyanoacrylate injection for gastric variceal obliteration were included as our target group (n = 18), whereas cirrhotic patients who underwent routine endoscopic surveillance were recruited as a control group (n = 17). Blood cultures were taken from all patients at 0 minute (before procedure), 5 minutes and 3 hours after endoscopy. The tip of injected needle was also cultured in the cyanoacrylate group.

Results: No bacteremia was detected from the cyanoacrylate group. In the control group, bacteremia was detected from one patient at 5 minutes. Cultures from the tips of needle were positive in 7 of 18 patients (38.9%). (*Streptococcus viridians*; n = 3, *Staphylococcus coagulase negative*; n = 1, *Streptococcus viridians* and *Streptococcus group D*; n=1, *Streptococcus viridians* and *Streptococcus agalactiae*; n = 1, *Streptococcus viridans* and *Stomatococcus mucilaginosus*; n = 1)

Conclusion: Elective cyanoacrylate injection for non bleeding gastric varices is not associated with bacteremia.

Key words : Bacteremia, Cyanoacrylate, Non bleeding, Gastric varices

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BACKGROUND

Gastric variceal bleeding is a serious complication of liver cirrhosis. Although bleeding from gastric varices is found less often than bleeding from esophageal varices, but the prognosis is poorer.[1-3] Currently, endoscopic injection with N-butyl-2-cyanoacrylate is a standard treatment to obliterate gastric varices[4,5]. The development of transient bacteremia during or after endoscopic procedures is well established[6]. This may be due to endoscopic procedure causing minute trauma to gastrointestinal mucosa. Subsequently this

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may facilitate the entry of host microbial flora into blood stream. Generally, the rate of transient bacteremia after endoscopic variceal sclerotherapy (EVS) was reported to be about 0-53%[7-9]. With the same technique, gastric variceal sclerotherapy with cyanoacrylate may be associated with the same rate of bacteremia. Chen *et al.*, reported that the incidence of transient bacteremia after endoscopic cyanoacrylate injection for bleeding gastric varices was 32%[10]. However, the explanation for bacteremia was still unclear, whether it was due to bacterial invasion through ruptured gastric variceal mucosa or was the result of cyanoacrylate injection itself. Therefore this study was designed to determine the frequency of bacteremia after elective endoscopic cyanoacrylate injection of gastric varices.

PATIENTS AND METHOD

Eighteen cirrhotic patients with previous history of bleeding gastric varices who underwent elective cyanoacrylate injection at King Chulalongkorn Memorial hospital from November 2004 to January 2006 were included as a study group. Other 17 cirrhotic patients who underwent routine endoscopic surveillance were recruited as a control group. Liver cirrhosis was diagnosed by; 1) liver biopsy and/or imaging test such as ultrasonography and/or enhanced computer tomography 2) laboratory data and 3) existent of ascites, hepatic encephalopathy, esophageal varices or other major complication of cirrhosis. Patients were excluded if any of the following were present before endoscopy[10]; body temperature higher than 38.5 ˚C, leukocytosis (white blood cell >10,500/mm^3), antibiotic administration within 72 hours before procedure, active gastrointestinal bleeding and a risk for development of bacterial infective endocarditis.

Endoscopic and cyanoacrylate injection

After induction of topical pharyngeal anesthesia with 10% lidocaine spray, the disinfected endoscope was introduced into esophagus and stomach. If gastric varices was incompletely obliterated (defined by the varices that was still compressible by tip of biopsy forceps), then a commercial flexible sclerotherapy injectors with 6 mm, 21 gauge needle were inserted through accessory channel. And the gastric varices were injected with a 1.0:1.6 mixture of 0.5 ml. N-butyl-2-cyanoacrylate (Histoacryl blau®, Braun, Melsungen, Germany) and 0.8 ml. Lipiodol (Guerbet Laboratory, Aulnay-Sous-Bris, France). First Lipiodol was drawn into a sterile syringe then subsequently cyanoacrylate was carefully drawn. Another syringe containing sterile Lipiodol was used to flush the needle before and after each session. In this study, no patients required more than 2 injections during each session. The volume of cyanoacrylate in each session was 1.2 ml. The tip of needle was cut and kept in a sterile bottle for culture.

Bacteriology

The forearm skin was prepared with povidone iodine and 70% isopropyl alcohol. A 21-gauge needle with 10 ml. sterile syringe was introduced into the visible vein. Then 10 ml. of venous blood was drawn and inoculated into blood culture bottle (Versa TREK TM REDOX 1TM,TREK diagnostic system, Cleveland, OH). The blood culture bottles were placed in a culture system (Versa TREK and ESPé II system). Blood culture was obtained at 0 minute before endoscopy, 5 minutes and 3 hours after endoscopic procedure in both groups. The tip of needle was also cultured on the blood agar plate.

Statistical Analysis

Results are shown as mean ± SD. Continuous parameters were compared using the Student t test. Non continuous parameters were compared with Chi-square test. Results were considered statistical significant if p value <0.05

RESULTS

There were no significant difference between both groups in baseline characteristics and laboratory data. (Table 1) The most common etiologies of cirrhosis were alcohol and viral hepatitis. All patients had child A and B cirrhosis and no ascites was detected.

There was no bacteremia detected from blood culture before endoscopic procedure in both groups. After endoscopic injection of cyanoacrylate, no bacteremia was detected. But in the control group, positive blood culture was found in one patient (5.8%) at 5 minutes (Table 2). The organism was Streptococcus mitis which is one of the normal flora from the oral cavity. The results of the culture from tips of needle were positive in 7 of 18 patient (38.9%). The organisms detected from culture of the needle tips were nor-

Table 1 Clinical characteristics of patient in both groups

Clinical characteristics	Cyanoacrylate (n = 18)	Control (n = 17)	P value (α = 0.05)
Age (year)	59.2 (13.7)	57.9 (12.1)	NS
Gender (M/F)	13/5	10/7	NS
Etiology of cirrhosis (virus/alcohol/others)	11/7/2	6/9/2	NS
Type of gastric varices (GOV/IGV/absent)	8/10/0	6/7/4*	NS
EV(+/-)	8/10	11/6	NS
PHG(+/-)	9/9	8/9	NS
Child Pugh (A/B/C)	7/9/0	6/6/0	NS
Child Pugh score	6.9 (1.2)	6.8 (1.3)	NS
Hemoglobin (gm/dl)	10.5 (1.8)	11.6 (2.3)	NS
Total Bilirubin (gm/dl)	3.1 (2.5)	2.7 (2.0)	NS
Albumin (gm/dl)	3.0 (0.4)	3.3 (0.7)	NS
INR	1.2 (0.2)	1.2 (0.1)	NS
Volume of cyanoacrylate (ml.)/session	1.2 (0.5)	NA	

** The patients had previous cyanoacrylate injection with completely obliterated gastric varices or had gastric varices without history or sign of recent bleeding.*
NS, not significant; bNA, not available.
GOV, gastroesophageal varices; IGV, isolated gastric varices; EV, esophageal varices; PHG, portal hypertensive gastropathy.

Table 2 Results of blood culture and tip culture in both group

Group	Blood culture results						Tip culture results	
	Before procedure		5 minutes		3 hours			
	Pos.	Neg.	Pos. (%)	Neg.	Pos.	Neg.	Pos. (%)	Neg.
Cyanoacrylate (n = 18)	0	0	0	0	0	0	7 (38.9%)	11
Control (n = 17)	0	0	1 (5.8 %)	0	0	0	-	-

Pos.: positive; Neg.: negative.

mal flora of gastrointestinal tract. (Table 3)

No clinical evidence of systemic embolism occurred in cyanoacrylate injection group. Half of the patients in this group complained of having mild retrosternal pain after the procedures but the symptom disappeared within 24 hours. No recurrent bleeding was observed in any patients. No patient developed any serious complication that require further treatment.

Table 3 Organisms from tips culture in cyanoacrylate group

Organism from tip culture	No
Streptococcus viridans	3
Staphylococcus coagulase negative	1
Streptococcus viridans and *Streptococcus group D*	1
Streptococcus viridans and *Streptococcus agalactiae*	1
Streptococcus viridans and *Stomatococcus mucilaginosus*	1

DISCUSSION

Cirrhotic patients are prone to bacteremia because of multifactorial impairments of the immune system[11]. Kao, *et al*. reported the incidence of bacteremia was 8.8% during a 5-year period in a study of 197 cirrhotic patients with 228 episode of bacteremia, and the incidence was higher in child C cirrhosis (17.1%)[12]. Yoneyama *et al*. confirmed that the important risk factors of bacteremia were advanced cirrhosis, presence of ascites, low serum albumin and high serum total bilirubin[13]. Most of the cirrhotic patients undergone many endoscopic procedures such as EVS which were reported to be associated with a high incidence of bacteremia. Many studies reported that the incidence of bacteremia after EVS was 0-53%[7-9]. In the present

study, we hypothesized that endoscopic cyanoacrylate injection was done by the same technique as EVS, therefore it should also produce the same risk for bacteremia. However, the results from our study did not support this hypothesis. The results maybe explained by the difference in antimicrobial effect between sclerosants used in EVS and cyanoacrylate. Cyanoacrylate is a class of synthetic glues that rapidly form polymers when contact with blood thus rendering hematogenous spread less likely[14]. In addition, some investigators claim that cyanoacrylate has in vitro antibacterial property[15,16]. Therefore, cyanoacrylate injection might limit bacterial invasion and reduce the frequency of bacteremia. Furthermore, several injections into varices are required in each session of EVS. But in our study we performed just 1-2 injections in each session. Multiple injected-varices may prone to bacterial invasion into the circulation. In addition, the stomach may contains fewer resident organisms than the esophagus because of the lethal action of gastric hydrochloric acid and peptic enzyme on bacteria. Therefore, injection into the varices in the area that has higher bacterial flora may enhance the risk of bacteremia. Unfortunately, there was no data to support this hypothesis[17].

Chen, *et al*. reported that the risk of bacteremia after endoscopic cyanoacrylate injection for bleeding gastric varices was 32 %[10]. However, the severity of cirrhosis was different between their study and our study. Half of the patients in their study were cirrhosis Child C with ascites. But in our study, all patients had cirrhosis child A and B and no ascites. As mentioned above, advanced cirrhosis is associated with a high frequency of bacteremia. In addition, the previous study required 1-6 injections in each session to control bleeding gastric varices but in our study we completely obliterated varices with only 1-2 injections. Moreover, majority of their patients had bleeding gastric varices therefore the cause of bacteremia in their study maybe due to bacterial invasion through ruptured gastric variceal mucosa.

The limitation of our study was only a small number of patients were recruited and we did not include bleeding gastric varices as another control group. Future study should compare the frequency of bacteremia from cyanoacrylate injection between bleeding and non bleeding gastric varices.

In conclusion, elective cyanoacrylate injection for non bleeding gastric varices is not associated with bacteremia. Therefore, prophylactic antibiotic may not necessary for cirrhotic patient who undergone elective cyanoacrylate injection to obliterate gastric varices.

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