

Post Butyl-cyanoacrylate (Histoacryl) Endoscopic Injection Sclerotherapy Pulmonary Haemodynamic Changes

Nasr H. Khalil¹, Gamal M. Soliman², Mohamed Abd El-Rasheed², Mahmoud Abd El-Rasheed³, Nabil Fathy Esmail Hassan⁴ and Gamal Zakaria Elmorsy Elkhatib⁴

¹Chest Department - Ahmed Maher Teaching Hospital, ²Tropical Medicine Department - Al-Azhar University, ³Internal Medicine Department - Al-Azhar University, ⁴Clinical Pathology Department - Al-Azhar University, Egypt. m-allam74@hotmail.com

Abstract: Background: Endoscopic injection sclerotherapy (EIS) for gastric variceal bleeding using butyl-2-cyanoacrylate (Histoacryl) began to be used in the mid-1980's. As Histoacryl is rapidly polymerized on contact with blood, the use of Histoacryl is the initial treatment of choice for gastric variceal bleeding. Although Histoacryl is considered to be best suited for larger varices due to ease of intravariceal injection, it is more difficult to calculate the exact volume needed for variceal obliteration. The occurrence of systemic embolization with Histoacryl injections has been reported. **Aim:** Post endoscopic intravariceal Histoacryl injection pulmonary vascular complications evaluation. **Patient and Methods:-** Thirty patients with bleeding from gastric varices who were treated with N-butyl-2-cyanoacrylate (Histoacryl) were enrolled in this study from October 2013 to October 2014, 22 patients were emergency cases and 8 patients as a follow up sclerotherapy cases. For all patient, full clinical assessment, routine laboratory tests and D-dimer were done. Pulmonary imaging as x-ray and Helical CT scanning were done. Echocardiography supplemented with Doppler was done before, 10 minutes and 24 hours post procedure. **Result:** Acute variceal bleeding was initially controlled in all patients with Histoacryl injections. But, rebleeding was reported in 5 cases (16.6%). Apart from, 2 patients presented with hypotension and shock, no significant post procedure clinical findings was detected. One patient was admitted to ICU for 72 hours, where he was diagnosed as stable acute pulmonary embolism (3.3%). The diagnosis of pulmonary embolism was based on Helical CT scan. Tracing the mean pressure of pulmonary artery before and after the procedure showed no significant changes. **Conclusion:** However Histoacryl injection for controlling gastric variceal bleeding is considered as an invasive maneuver, the incidence of major complications as pulmonary embolism is low. Further study with more number of patients is recommended for evaluating the risk factor for post histoacryl pulmonary embolism.

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1. Introduction

In patients with portal hypertension, acute gastroesophageal variceal bleeding is one of the main causes of death. Therefore, the treatment and prevention of variceal bleeding are important for successful patient management (*Marco et al., 2004*).

For this reason, the demand for palliative treatment of acute gastroesophageal variceal bleeding continually increases. Various treatment modalities, such as pharmacological therapy, balloon tamponade, endoscopic injection sclerotherapy and endoscopic variceal ligation have all been used for this purpose (*Yoshida et al., 2006*).

Endoscopic injection of Histoacryl has been recommended for gastric variceal bleeding. This long-chain Cyanoacrylate glue polymerises and solidifies within seconds following contact with aqueous media such as blood within a varix. This leads to obliteration

of the varix from which the cast extrudes after 2–4 weeks. Mixing the Histoacryl with the oily agent Lipiodol delays polymerization. Histoacryl injection has reported immediate haemostasis (*Stavros et al., 2015*).

Endoscopic injection of N-butyl-2-cyanoacrylate (Histoacryl) is widely used for the control of gastric variceal bleeding with initial hemostasis rates of 87-100% (*Huang et al., 2000*).

However, Histoacryl injection has been associated with major complications, including embolism, sepsis, fistula and adherence of the needle within the varix (*Seewald et al., 2008*).

The first-line treatment for gastric variceal bleeding is endoscopic obliteration with Histoacryl® (N-butyl-2-cyanoacrylate). However, it has been used worldwide for the treatment for gastric varices, data regarding the long-term efficacy and safety of this

procedure are still lacking. Indeed, although rare, fatal complications do occur (*Eun et al., 2011*).

Pulmonary embolism may escape prompt diagnosis since the clinical signs and symptoms are non-specific. In most patients, PE is suspected on the basis of dyspnoea, chest pain, pre-syncope or syncope and/or haemoptysis. Arterial hypotension and shock are rare but important clinical presentations, since they indicate central PE and/or a severely reduced haemodynamic reserve. Finally, PE may be completely asymptomatic and be discovered incidentally during diagnostic work-up for another disease or at autopsy (*Stavros et al., 2015*).

Echocardiography supplemented with pulsed and continuous wave Doppler facilities is a potent diagnostic tool in many cardiovascular disorders. Its potential role in the management of patients with suspected pulmonary embolism, though less extensively studied (*Stavros et al., 2015*).

Admittedly, in the majority of cases echocardiography provides only indirect signs of PE, predominantly consisting of signs of RV pressure overload. Such signs have been reported to be reasonably specific for PE in patients without prior cardio-respiratory diseases (*McConnell et al., 1996*).

D-dimer levels are elevated in plasma in the presence of acute thrombosis, because of simultaneous activation of coagulation and fibrinolysis, the negative predictive value of D-dimer testing is high and a normal D-dimer level renders acute PE unlikely (*Stavros et al., 2015*).

Helical CT scanning has become the method of choice for imaging the pulmonary vasculature in patients with suspected PE. It allows adequate visualization of the pulmonary arteries down to at least the segmental level (*Patel et al., 2003*).

2. Patient and Methods:-

Thirty patients with bleeding from gastric varices were enrolled in this study. Complete blood count (CBC) using Swelab Alfa basic "Boule Medical AB, Stockholm, Sweden", Routine laboratory tests using Humalyzer 3000 "Human, Gesellschaft for Biochemical and Diagnostics, Wiebaden, Germany" and D-dimer using human D-Dimer ELISA Kit Supplied by RayBiotech, Inc. "3607 Parkway Lane suite 100 Norcross, GA 30092" were done . Pulmonary imaging as x-ray and Helical CT scanning were done. Echocardiography supplemented with Doppler was done before, 10 minutes and 24 hours post procedure.

3. Results:

Acute variceal bleeding was controlled in all patients with Histoacryl injections, but rebleeding was reported in 5 cases (16.6%), so second session was

done. The average volume of pure Histoacryl injected was 1.7 ml/patient

After endoscopic therapy, three patients (9.9%) complained of abdominal pain, shortness of breath and chest pain with Hypotension and shock were detected in 2 (6.6%) of them with only one (3.3%) was shifted to ICU.

Abdominal pain and chest discomfort were noticed by 7 (23.3%) patients for a short time. seventeen patients (65.6%) complained from abdominal distension only.

Diagnosis of abnormal X-ray finding was based on *David et al., (1974)* criteria as, Westermark's sign (oligemia in area of involvement), increased size of a hilum (caused by thrombus impaction), atelectasis with elevation of hemidiaphragm and linear or disk shaped densities, pleural effusion, consolidation and Hampton's hump (rounded opacity). In the case of pulmonary infarctions, the main radiographic feature is multifocal consolidation at the pleural base in the lower lungs.

Table 1 : Patient characteristics

Age (Mean±SD)	(51.0 ± 11.9)
Male : Female	23:7
Aetiology (n) (%)	
Hepatitis C	19 (63.3%)
Hepatitis B	3 (10%)
Mixed HCV and HBV	7 (23.3%)
Cryptogenic cirrhosis	1 (3.3%)
Childs grade (n) (%)	
A	4 (13.3%)
B	16 (53.3%)
C	10 (33.3%)

Table 2: endoscopic findings:-

GOV-1	GOV-2	IGV-1	IGV-2
9 (30%)	19 (63.3%)	2 (6.6%)	-

Table 3: Post endoscopic pulmonary changes

- D-dimer (abnormal high levels).	9 (30%)
- Chest x-ray abnormalities	3 (3.3%)
- Helical CT scanning abnormalities	1 (3.3%)
Echocardiography	
- Positive McConnell sign	2 (6.6%)
Doppler:- Mean Pulmonary artery pressure (X±SD) and range/mm.Hg	
• Before	15±4.4 (7-23)*
• After 10 minutes	17±4.1 (3-27)*
• After 24 hours	14±3.4 (5-27)*

*Non-significant

Helical C.T. scan chest was performed from aortic arch to lung bases with intravenous contrast medium. Images were acquired in mediastinal and lung windows. Image interpretation was performed on the console and hard copies for main branch and segmental thrombus.

Diagnosis of Echo findings was based on "McConnell sign" which was defined by *McConnell et al., (1996)* as right ventricular (RV) free wall hypokinesia in the presence of normal RV apical contractility. McConnell sign has been suggested as a useful criteria for the diagnosis of acute PE mostly because it was observed in the setting of acute but not chronic pulmonary hypertension (*McConnell et al., 1996*).

Mean pressure of pulmonary artery before and after the procedure showed no significant changes.

4. Discussion

Gastric varices and their association with portal hypertension were first described in 1931 (*Soehendra et al., 1987*). The overall incidence of gastric varices in patients with portal hypertension is 18%-70% (*Ryan et al., 2004*).

The incidence of bleeding from gastric varices is relatively lower, ranging from 10%-36%, compared with bleeding from esophageal varices. Mortality associated with a first variceal bleed appears to have improved in recent years but remains as high as 20% within 6 weeks (*Eun et al., 2011*).

A recent study compared Histoacryl to propranolol for prevention of gastric variceal rebleeding. The authors reported significantly reduced rebleeding and mortality with Histoacryl (*Mishra et al., 2010*).

Few randomized studies have compared Histoacryl injection with other endoscopic modalities. Histoacryl had faster rates of variceal obliteration, improved control of acute bleeding and reduced need for rescue surgery compared with ethanol injection for fundal varices (*Sarin et al., 2012*).

Sarin et al. (2002) reported a 72% variceal obliteration rate in gastric variceal bleeds treated with ethanolamine sclerotherapy, significant complications and rebleeding rates of 50-90% have been reported using this technique.

Endoscopic injection of Histoacryl® is the currently recommended in recent consensus and guidelines as the initial treatment for acute gastric variceal bleeding (*Eun et al., 2011*).

Endoscopic injection of tissue glue for gastric variceal bleeding was first reported in 1986 by *Soehendra et al., (1987)*.

However, the rebleeding rate remains high, at 22%-34% and episodic complications such as systemic embolism have been the main issues.

Cerebral stroke, portal vein embolization, splenic infarction, coronary embolism and nonfatal pulmonary emboli in 4.6% of cases were reported as complications of tissue adhesive use (*Eun et al., 2011*).

In the present study, acute variceal bleeding was initially controlled in all patients with Histoacryl injections.

This finding come in agreement with that of *Huang et al., (2000)* who stated that, Endoscopic injection of N-butyl-2-cyanoacrylate (Histoacryl) is widely used for the control of gastric variceal bleeding with initial hemostasis rates of 87-100%.

Usman et al., (2003) have shown that contrast enhanced helical CT has sensitivities and specificities of approximately 90% in the diagnosis of PE involving segmental or larger vessels.

In our study, diagnosis of pulmonary embolism was based on Helical CT scan. Pulmonary embolism was diagnosed in one patient (3.3%).

We are in a tight match with *Hwang et al., (2001)* who reported, radiographically evident PE in 4.3% of patients after endoscopic injection sclerotherapy for gastric variceal bleeding.

We found that, only 2 (6.6%) patients presented with post procedure hypotension and shock, and no significant post procedure clinical findings was detected.

This findings found to be in agreement with *Eun et al., (2011)* who reported that, complication rate of Histoacryl® injection therapy was relatively low and most of the complications were not severe. The common adverse effects include fever and abdominal discomfort.

In the largest study published so far *Nazeyrollas et al., (1996)* used the parasternal M-mode echo. They reported a sensitivity of 93% with a specificity of 81% in 137 patients free from known cardio-respiratory disease. Unfortunately, in real life we often deal with patients known or suspected of having previous cardio-respiratory problems.

Hwang et al., (2001) reported that, affected patients were either mildly symptomatic or asymptomatic and there were no direct fatalities of this complication.

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