

ENDOSCOPIC TREATMENT OF GASTRO DUODENAL VARICES BY CHEMICAL GLUE MIXED WITH GLUCOSE SERUM

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ABSTRACT

Introduction: The incidence of digestive bleedings secondary to the rupture of gastroduodenal varices ranges from 3 to 30%. They represent approximately 10 % of all the high bleedings associated with a portal hypertension. The purpose of this work is to estimate the therapeutic efficiency and the complications of the injection of chemical glue diluted with glucose solution 5% as a technique for endoscopic hemostasis.

Patients and methods: It's a retrospective study concerning 15 patients between 2012 and 2014. All the patients were admitted for upper gastrointestinal bleeding. They all underwent oesogastro- duodenal endoscopy which objectified bleeding caused by rupture of gastroduodenal varices. Patient's consent was mandatory. N-butyl-2-cyanoacrylate was associated with methacryl oxysulfolane (Glubran 2) prepared with glucose serum 5%. The endoscopic treatment was realized under sedation and consisted in the injection of chemical glue intravariceally.

Results: The injection of glue in the gastric varicose veins was realized in 13 patients (86.7%) and in duodenal ectopic varices in two patients (13.3 %). The injection was realized in one or two sites of the ruptured varicose vein. The mean age of the patients was 51 years old [23 - 76]. Female gender was prominent (n= 11; 76 %). The initial hemostasis was obtained in 100 % of cases. We noted a second recurrence in two patients, no immediate or delayed complication were reported.

Conclusion: The hemostatic endoscopic treatment of the upper bleedings, caused by the rupture of gastroduodenal varicose veins, using chemical glue diluted in glucose serum 5% seems effective and less expensive compared to the dilution in Lipiodol. Our results are preliminary and must be confirmed in the future by a more important sample.

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INTRODUCTION

Esogastric varices are present at approximately 50% of the cirrhotic patients. Their presence is correlated to the gravity of the liver disease. Eighty five percent of Child C cirrhotic patients have esogastric varices [1, 2]. The gastric varices are present in approximately 20% of the patients with portal hypertension, remotely or in combination with esophageal varices. The bleeding of varices occurs at an annual rate of 5 % to 15 %, and approximately 20 % of cirrhotic presenting an episode of upper gastrointestinal bleeding die in the 6 weeks following the bleeding [3, 4, 6].

The frequency of the recurrence during the first 06 weeks is between 30 % and 40 % and approximately 40 % of the recurrence occurs in the 5 first days [5, 7]. The gastric varices bleed less

often than the esophageal varicose vein and are the source of bleeding in approximately 10 % to 30 % of patients with portal hypertension. However, the hemorrhage of gastric varicose veins tends to be more severe with a higher mortality [8].

PATIENTS AND METHODS

This is a retrospective study concerning 15 patients collected between 2012 and 2014. All of the included patients were admitted for upper gastrointestinal bleeding, they all underwent an oesogastroduodenal endoscopy which objectified a bleeding caused by the rupture of gastroduodenal varicose veins. Patient's consent was mandatory before the procedure. N-butyl-2-cyanoacrylate associated with Methacryl oxysulfolane (Glubran 2) was prepared with glucose serum 5 %. The

endoscopic treatment, realized under sedation, consisted in the injection of chemical glue mixture in the ruptured varices (1 or 2 sites).

Exclusion criteria:

Were excluded the patients presenting an upper digestive bleeding caused by other etiologies (bleeding of esophageal varicose veins, gastroduodenal ulcers)

Technique of realization:

- The procedure is realized under sedation
- Purge the needle with 1,5ml of glucose serum
- Introduce the needle into the varicose vein,
- Inject 1.5 ml of mixture
- Inject 1.5 ml of glucose serum
- Let the needle at least 20 seconds into the varice and then take it out carefully.
- Repeat the procedure until the varice became hard without exceeding 4 injections.
- Strict surveillance of the hemodynamic parameters.

RESULTS

The mean age of our patients was 51 years old [23-76]. Female gender was prominent (n= 11; 76 %). The average rate of hemoglobin was 6,1g/dl. The injection of glue in the gastric varicose veins was realized in 13 patients (86.7%) and in ectopic duodenal varicose veins in 02 patients (13.3 %). The mixture was injected at one or two sites of the ruptured varicose vein.

Table I: General characteristics of the patients:

	n=15
Gastric varices	13 (86.7%)
Duodenal varices	02 (13.3%)
Average age	51 years old [23-76]
Gender	Female (n=11; 73%) Male (n= 4; 27%)
Average rate of Hemoglobin	6.1 g/dl
Transfused patients	100%
Average number of session	1.1

Table II: results of the glue injection

	%
Rate of initial hemostasis	100%
Recurrence	14% (n= 2)
Immediate or delayed complication	0%

DISCUSSION

The frequency and the severity of the bleedings by rupture of gastric varices depend on their localization [9]. There are four types of gastric varices: gastro-esophageal type I (GOV1) which corresponds to the esophageal varicose veins and which goes on below the oeso-gastric junction,

gastro-esophageal type 2 (GOV2) and the gastric - isolated varicose veins (IGV1) which correspond to fundic - associated varices (GOV2) or (IGV1) with the esophageal varicose veins.

Other gastric varicose veins localized at the level of the stomach's body, in the cave, in the pylorus or in the initial part of the duodenum, are the isolated gastric varicose veins of type 2 (IGV2) [9, 11]. The GOV2 bleeds more often than the GOV1 (55 vs. 12 %) [9] and their forecast is more difficult in case of secondary GOV2 and IGV2 compared to IGV1, although the hemorrhagic risk is lower 6% [5].

The mortality rates secondary to rupture of gastric varicose veins is 45 to 55 % (9, 12). The presence of gastric varicose veins would increase the global hemorrhagic risk to 2,5 times (69 % vs. 24 %) and would aggravate the forecast of the risk of having a portal hypertension (13).

The efficacy of chemical glue in the treatment of gastric varicose veins is now established. it was described first by Lunderquist and al in 1978 (14). Later in 1986, Soehendra and al [15] reported the first series of endoscopic treatment of gastric varicose veins. Since then, a significant number of series showed a rate of 90 % hemostasis [16, 17]. The techniques of hardening with injection of chemical glue, Histoacryl (n-butyl-2-cyanoacrylate) or Glubran 2 (n-butyl-2-cyanoacrylate associated with Methacryl oxysulfolane) has been developed. These glues solidify immediately in the contact of the blood and allow an immediate closing of varicose veins. Contrary to sclerosing products, the ulcerations with eviction of the mold of glue are late- arising (2 weeks to 3 months after the injection [18], and allow to partially explain the decrease in the risk of premature hemorrhagic secondary offenses.

The histoacryl is usually diluted with Lipiodol which has the additional property to allow the radiological confirmation of the injection and the identification of the embolisation. The glue has a viscosity similar to water, while Lipiodol is very viscous and produces the difficulty in the injection of the mixture [19]. Glubran 2 has a longer duration of polymerization and does not necessarily require a dilution with Lipiodol. [16, 20]. This is interesting, especially as Lipiodol is dear and not always available.

Few studies in the literature were interested in the dilution of chemical glue (Glubran 2) with another product delaying the polymerization other than Lipiodol from where the interest of our study.

An Italian study [21] conducted in 1996 and including 80 patients tried to estimate the role of the injection of undiluted N-Butyl cyanoacrylate in the immediate active hardening of gastroduodenal

varices bleeding and in the eradication of these varicose veins.

The hemostasis was obtained at 89.6 % of the patients. The eradication was obtained at 87.5% of both gastric and duodenal varicose veins. Twelve percent of the patients died during the period of treatment: six patients because of uncontrolled bleedings, two because of the hemorrhagic second offense and two because of hepatic failure.

This study concluded that endoscopic injection of N-butyl-2-cyanoacrylate seems at the same time safe and effective, although the relative value of the injection not diluted glue compared with that diluted must be again estimated.

A Brazilian study [22], led between 2009 and 2010, tried to estimate the importance of dilution of Glubran 2 with some distilled water. Twenty one patients were included in the study and benefited from injection of Glubran 2 mixed with water distilled to calcify the gastric varicose veins. The initial hemostasis was obtained in all the patients and no damages of the endoscope tube or major complication were reported, except epigastric pain in three patients. One patient presented a hemorrhagic secondary offense six months later. This study showed that the injection of Glubran 2 mixed only with distilled water is safe and effective for the hardening of the gastric varicose veins.

An Egyptian study [22] led in April 2015 tried to compare n-butyl-2-cyanoacrylate, iso-amyl-2-cyanoacrylate and a mixture of 72 % of chromate glycerin with hypertonic glucose 25 % in the management of gastric varices. Ninety patients who were presented with gastric varicose veins at the unity of endoscopy at The University Hospital of Ain Shams were included. They were distributed at randomization in three groups; every group included 30 patients handled by sclerosant injections in twice-weekly sessions until complete closing of the gastric varicose veins. Group I, II and III were treated respectively by (n-butyl-2-cyanoacrylate; Histoacryl), (iso-amyl-2-cyanoacrylate; Amcrylate) and a mixture of 72 % of glycerin and chromium Scleremo with glucose serum 25 %]. All the procedures were electively made without active bleeding. The recruited patients were supervised during three months. There was a **secondly** bleeding in 13.3 % of the Histoacryl and Amcrylate group versus 0 % in the group with Scleremo. The mortality rate was 6.6 % in both Histoacryl and Amcrylate groups, while it was 0 % in the Scleremo group. In the first and second sessions, the necessary quantity of Scleremo for closing was sufficiently available, whereas the quantity of Histoacryl was very low. Besides, Scleremo was the least expensive of both treatments. The study concluded that all the

sclerosing substances used showed an efficiency and a success in the management of the gastric varicose veins, but the cost and the global amount of the third group were much lesser compared to the first ones.

Our study, using Glubran 2 mixed with serum glucose 5%, showed its efficiency in the initial hemostasis of bleeding gastroduodenal varicose veins and. there were no initial or delayed complication and the process proved to be much less expensive than the dilution with Lipiodol

CONCLUSION

Chemical glue (Glubran 2) diluted in glucose serum is a less expensive and effective method compared to the dilution in Lipiodol which is expensive and not always available in our context. These results are preliminary and must be confirmed in the future by a more important sample

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REFERENCES

1. Navasa M, Pare´s A, Bruguera M, and al. Portal hypertension in primary biliary cirrhosis. Relationship with histological features. *J Hepatol* 1987; 5: 292–8.
2. Sanyal AJ, Fontana RJ, Di Bisceglie AM, et al. The prevalence and risk factors associated with esophageal varices in subjects with hepatitis C and advanced fibrosis. *Gastrointest Endosc* 2006; 64: 855–64.
3. Carbonell N, Pauwels A, Serfaty L, and al. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. *Hepatology* 2004; 40: 652–9.
4. Shiv K. Sarin, Awinash Kumar. Endoscopic Treatment of Gastric Varices. *Clin Liver Dis.* 18 (2014) 809–827
5. D'Amico G, De Franchis R, Cooperative Study Group. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. *Hepatology* 2003; 38: 599–612.
6. El-Serag HB, Everhart JE. Improved survival after variceal hemorrhage over an 11-year period in the Department of Veterans Affairs. *Am J Gastroenterol* 2000; 95:3566–73.
7. Graham DY, Smith JL. The course of patients after variceal hemorrhage. *Gastroenterology* .1981;80: 800–9.
8. 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;16:1343-9
9. Sarin SK, Lahoti D, Saxena SP, Murthi NS, Makwane UK. Prevalence, classification and natural history of gastric varices: a long term follow-up study in 568 portal hypertension patients. *Hepatology*. 1992; 16: 1324-49.
 10. Sarin SK, Jain AK, Lamba GS, Gupta R, Chowdhary A. Isolated gastric varices : prevalence, clinical relevance and natural history. *Dig Surg* 2003; 20: 42-7.
 11. Lo G-H, Lai K-H, Cheng J-S, Chen M-H, Huang H-C, Hsu P-I, and al. Endoscopic variceal ligation plus nadolol and sucralfate compared with ligation alone for the prevention of varicea rebleeding: a prospective, randomized trial. *Hepatology* 2000; 32: 461-5.
 12. Trudeau W, Prindiville T. Endoscopic injection sclerosis in bleeding gastric varices. *Gastrointest Endosc* 1986; 32: 264-8.
 13. Kleber G, Sauerbruch T, Ansari H, Paumgartner G. Prediction of variceal hemorrhage in cirrhosis: a prospective follow-up study. *Gastroenterology* 1991; 100:1332-7.
 14. Lunderquist A, Borjesson B, Owman T, et al. Isobutyl 2-cyanoacrylate (bucrylate) in obliteration of gastric coronary vein and esophageal varices. *AJR Am J Roentgenol* 1978; 130: 1-6.
 15. Soehendra N, Nam VC, Grimm H, et al. Endoscopic obliteration of large esophagogastric varices with bucrylate. *Endoscopy* 1986; 18:25-6.
 16. Petersen B, Barkun A, Carpenter S, et al. Tissue adhesives and fibrin glues. *Gastrointest Endosc* 2004; 60: 327-33.
 17. Binmoeller KF. Glue for gastric varices: some sticky issues. *Gastrointest Endosc* 2000; 52: 298-301.
 18. Sarin SK, Jain AK, Jain M, Guptar A. Randomized controlled trial of cyanoacrylate vs. alcohol injection in patients with isolated fundal varices. *Am J Gastroenterol* 2002;97:1010-15
 19. Binmoeller KF, Soehendra N. New haemostatic techniques: Histoacryl injection, banding/endoloop ligation and haemoclipping. *Baillieres Best Pract Res Clin Gastroenterol* 1999; 13:85-96
 20. D'Imperio N, Piemontese A, Baroncini D, Billi P, Borioni D, Dal Monte PP, Borrello P. Evaluation of undiluted N-butyl-2-cyanoacrylate in the endoscopic treatment of upper gastrointestinal tract varices. *Endoscopy* [1996, 28(2):239-243]
 21. Gustavo F. Gomes, Lucianna M. Correia, Danielle Bonilha, Luciano Lenz, Frank S. Nakao, Gustavo A. De Paulo, Ermelindo Della Libera. Efficacy and Safety of Endoscopic Treatment With Cyanoacrylate Metacrilosilfolano Without Lipiodol® for Gastric Varices. *Gastrointestinal endoscopy* Volume 73, No. 4 S : 2011
 22. Reda El Wakil and al. N-butyl-2-cyanoacrylate, isoamyl-2-cyanoacrylate and hypertonic glucose with 72% chromated glycerin in gastric varices. *Ain Shams University, Egypt. World J Gastrointest Endosc* 2015 Apr;7(4):411-6