

ROLE OF STAGE ENDOSCOPIC VARICEAL BAND LIGATION IN TREATMENT OF CHILDREN WITH PORTAL HYPERTENSION

10.36740/WLek202010105

Dariia I. Voroniak^{1,2}, Oleg S. Godik¹, Larysa Ya. Fedoniuk³, Olena M. Shapoval⁴, Viktoriia V. Piliponova⁴¹BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE²NATIONAL SPECIALIZED CHILDREN HOSPITAL OHMATDYT, KYIV, UKRAINE³I. HORBACHEVSKY TERNOPIL NATIONAL MEDICAL UNIVERSITY, TERNOPIL, UKRAINE⁴NATIONAL PIROGOV MEMORIAL MEDICAL UNIVERSITY, VINNYTSIA, UKRAINE

ABSTRACT

The aim: To evaluate the efficacy of endoscopic variceal band ligation (EVL) after the first esophageal EVL session in children with PH according to endoscopic data.**Materials and methods:** EVL was performed to 39 patients with PH for the purpose of variceal bleeding primary and secondary prophylaxis.**Results:** Esophageal varices grade decrease was observed in 22 (56.41%) children. Cases of early rebleeding (within 14 days after EVL) were not registered. Eradication of varices was successful in 11 (28.2%) of patients. In 1 (2.56%) case the complication (bleeding) occurred while banding procedure. 1 (2.56%) patients had bleeding from gastric varices prior to a control endoscopy. Portal gastropathy grade changes were observed in 17 (43.59%) patients.**Conclusions:** EVL is a safe and effective method of esophageal varices bleeding prophylaxis. This method allows control the esophageal varices grade at different phases of PH treatment in children. Even one EVL session can decrease the grade of esophageal varices ($p < 0.001$). The EVL effect on the severity of portal gastropathy ($p = 0.02$) and on the red marks presence ($p = 0.005$) was also determined. EVL reduced the risk of variceal rebleeding ($p = 0.05$, $RR = 0.05$ (95%CI 0.01-0.32)).**KEY WORDS:** endoscopic variceal band ligation in children; portal hypertension; variceal bleeding

Wiad Lek. 2020;73(10):2133-2137

INTRODUCTION

Acute variceal bleeding is a severe complication of portal hypertension (PH) with high morbidity and mortality rates. 30-60 % of patients with intrahepatic PH and 90-95% of patients with prehepatic PH have esophageal varices (EV) [1, 2, 3] which can be a probable site of bleeding. Gastric varices (GV) are combined with EV in 35% – 40% of patients with prehepatic PH. Despite the therapeutic achievements, mortality rate of acute upper variceal bleeding is 5-19% in children with PH [4].

Esophagogastroduodenoscopy is the obligatory method of diagnostics and treatment for EV and GV in children with PH [5]. At present time the endoscopic variceal band ligation (EVL) is the method of choice in variceal bleeding prophylaxis. It is used as primary (the patient never had variceal bleeding) and secondary (the patient had variceal bleeding) prophylaxis of EV and GV bleeding. Clinical implementation of the EVL in children with PH dictates the need to explore the possibilities and to standardize this method in order to prevent variceal bleeding.

THE AIM

To evaluate the efficacy of EVL after the first esophageal EVL session in children with PH according to endoscopic data.

MATERIALS AND METHODS

39 children with PH who undergone EVL because of EV and GV and high risk of variceal bleeding were included into our retrospective chart review. All procedures were performed between 2017- 2019 in our clinic.

The study has been approved by Bogomolets' National Medical University Ethics committee, the protocol № 127 from 02.12.2019; the chairperson – Yuri Chaikovskiy.

All patients and their parents have given their informed consent for participation in our study.

There were 26 males and 13 females of median age 7 years (1-17 years). In these 39 patients there were 5 with intrahepatic PH ($n = 5$, 12.82%) and 34 with prehepatic PH ($n = 34$, 87.18%) (Tabl. 1).

The causes of intrahepatic PH were liver cirrhosis, as a result of cystic fibrosis ($n=2$, 40%), and congenital liver fibrosis ($n=3$, 60%). The causes of prehepatic PH were portal vein idiopathic cavernous transformation ($n=15$, 44.12%) and portal vein thrombosis ($n=19$, 55.88%). 18 (94.74%) patients with portal vein thrombosis had umbilical vein catheterization performed in the neonatal period and 1 (5.26%) patient had surgical intervention because of hepatoblastoma.

EV grading in this analysis was classified according to Japanese Research Society for Portal Hypertension [6]. GV grading – according to Sarin classification [7].

Table 1. Primary demographic and clinical data of the patients included into study group

Sing	Absolute amount (n)	%
Sex (male/female)	26/13	66.67/33.33
Median age, year (95%CI QI÷QIII)(range)	7 (95% CI 3.87÷9.58) (1-17)	-
Extrahepatic portal hypertension	34	87.18
Intrahepatic portal hypertension	5	12.82
Surgery because of portal hypertension	11	28.2
History of variceal bleeding	22	56.41
Thrombocytopenia (<50,000/L)	4	10.26

EV with high risk of bleeding was defined as an EV grade II with red sings on the mucosal wall (longitudinal red streaks, cherry-red spots, hematocystic spots), EV grade II in a combination with gastric varices along the stomach lesser curvature (GOV1) and/or along the stomach greater curvature, EV grade III [8].

EV eradication was determined as varices reduction up to Grade I, that is extremely thin for suction within ligation procedure, or as absence of visible varices. Rebleeding was determined as an EV, GV or severe portal gastropathy bleeding episode that occurred after the initiation of prophylaxis with need for urgent esophagogastroduodenoscopy and/or blood transfusion [9].

Indications for EVL were: presence of EV with high risk of bleeding (n=39, 100%); presence of EV with high risk of bleeding despite of surgical treatment (n=11, 28.2%), namely Sugiura – Futagawa procedure (n=2, 5.13%), splenorenal shunting (n=4, 10.26%), meso-Rex shunting (n=2, 5.13%), mesocaval shunting (n=1, 2.56%), suturing of esophagogastric junction (n=1, 2.56%). Of those who underwent surgery before EVL 10 patients had fail to achieve EV eradication and rebreeding episodes and 1 patient (90,9%) had recurrence of EV with high risk of bleeding after eradication (9,1%).

Contraindications for EVL were: Grade I of EV; hemorrhagic shock.

Patients underwent general anesthesia with endotracheal intubation and mechanical respiratory assistance during the endoscopic procedure.

Endoscopy was performed using Olympus GIF-H185, GIF-Q150, GIF-XQ260, with an outer diameter of 9.2 mm and working channel diameter of 2.8 mm.

EVL method consisted of two stages. On the first stage diagnostic esophagogastroduodenoscopy was performed to evaluate gastrointestinal mucosa, varicose veins grading and risk of variceal bleeding. On the second stage the EVL was performed using the ligation device. It consisted of transparent distal chamber, single use ligation bands, trigger cord, loading catheter and precision control handle. Transparent distal chamber was put on the distal end of the scope. From 4 to 7 bands were placed outside the chamber. EVL started 2 cm proximal from Z-line.

Selected EV were visualized and aspirated into the banding chamber. Suction was maintained until the screen became red. Then the band was deployed by rotating the handle clockwise until the band release was felt. After the bands were launched onto the selected EV in ascending direction. Varicose vein obliteration was achieved by mechanical strangulation of the varix by band. We imposed from 2 to 10 ligating bands to children of different ages during one EVL session. After the bands fell out, ulcers formed in their location, which was covered by epithelium within 2-3 weeks.

Follow-up. In the postprocedure period we recommended a soft diet, proton pump inhibitors, antacids, hemostatic therapy. After the first EVL procedure esophagogastroduodenoscopy was performed in 12 (95 % CI 9.78÷14.78) weeks.

Statistical analysis. Demographic, clinical and endoscopic data were statistically analyzed. Statistical analysis was performed using BM SPSS Statistics Base v.22. Median value, first and third quartiles values and risk ratio were calculated, and Shapiro Wilk test, Wilcoxon signed-rank test and McNemar's chi-square test were used. The level of significance was adopted a P-values ≤0.05.

For indicators of the EV grade before and after EVL, a difference in the distribution of values from the normal value of $p < 0.001$ was found, and as the samples were related, Wilcoxon signed-rank test was used to compare the averages, $T.V = 253$. A difference in the significance was detected at level $p < 0.001$.

For indicators of the portal gastropathy grade before and after EVL, a difference in the distribution of values from the normal value of $p < 0.001$. was found, and as the samples were related, Wilcoxon signed-rank test was used to compare the averages, $T.V = 121$. A difference in the significance was detected at level $p = 0.02$.

To determine the effect of EVL on the red marks presence McNemar's chi-square test was used. McNemar's chi-squared=7.69, $df=1$. A difference in the significance was detected at level $p=0.005$.

In our study we observed the decreasing of bleeding episodes occurrence after one EVL session with significance level $p = 0.05$, $RR = 0.05$ (95% CI 0.01-0.32).



Fig. 1. Esophageal varices grade III before EVL.



Fig. 2. The rubber band on the varix.

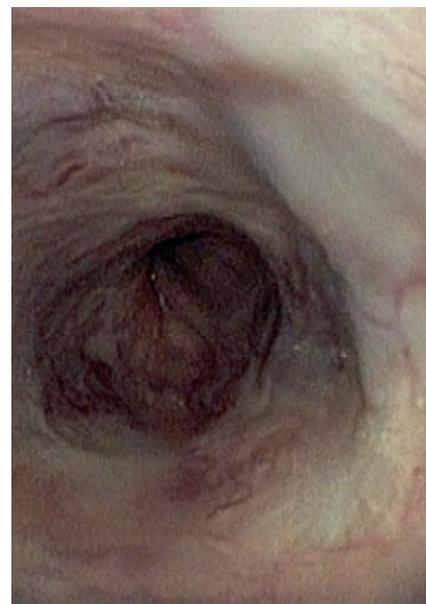


Fig. 3. Esophageal varices eradication after EVL.

RESULTS

56.41% (n = 22) of patients had diagnosed EV grade II and 43.59% (n = 17) had EV grade III (Fig. 1).

GOV1 was found in 51.28% (n = 20) of patients, and GOV2 in 43.59% (n = 17). Red sings (vasa vasorum, red cherry spots, hemocystic spots) as high risk of the variceal bleeding markers were observed in 84.61% (n = 33) of patients with EV. Mild portal gastropathy was observed in 46.15% (n = 18) of patients, and severe – in 28.2% (n = 11) (Tabl. 2).

EVL was performed to all patients (Tabl. 3). The median bands number used by EVL session was 4 (2-10) (Fig. 2). Control esophagogastroduodenoscopy was performed after 12 (95 % CI 9.78÷14.78) weeks (from 2 to 54). The EV grade decreasing after the first EVL session was observed in 22 (56.41%) children.

We achieved EV eradication by single EVL procedure in 11 (28.2%) of them (Fig. 3). The EV grade did not change in 17 (43.59%) children. In 1 (2.56%) case a complication (bleeding) occurred at the moment of band placement, which was taken under control by the Blackmore probe placement and conservative hemostatic therapy.

There were no case of early rebleeding (up to 14 days after EVL). 1 (2.56%) patient had an GV bleeding episode in 6.57 weeks after first EVL procedure. This episode was treated by porto-systemic shunting. GV grade (n = 10, 25.64%) changes were determined clinically after one EVL session in the study group of patients, but the difference was not statistically significant (p > 0.05), which can be explained by small cohort. Portal gastropathy grade changes were observed in 17 (43.59%) patients. Gastropathy severity in-

Table 2. Primary endoscopic data of the patients included into the study group

Sing	Absolute amount (n)	%
Esophageal varices Grade II	22	56.41
Esophageal varices Grade III	17	43.59
Gastroesophageal varices-1	20	51.28
Gastroesophageal varices-2	17	43.59
Red marks	33	84.61
Portal gastropathy (mild)	18	46.15
Portal gastropathy (severe)	11	28.2
Median amount of bands (95%CI QI÷QIII) (range)	4 (95% CI 3÷4) (2-10)	-
Complication during EVL	1	2.56
Median follow-up, weeks (95%CI QI÷QIII) (range)	12 (95 % CI 9.78÷14.78) (2-54)	-

Table 3. The results after the first EVL procedure in the study group

Sing	Before EVL		After the first EVL session		Significance level (p)
	Absolute amount (n)	%	Absolute amount (n)	%	
Esophageal varices Grade I	-	-	11	28.2	p<0,001
Esophageal varices Grade II	22	56.41	25	64.1	p<0,001
Esophageal varices Grade III	17	43.59	3	7.69	p<0,001
Gastroesophageal varices-1	20	51.28	21	53.85	p=0.06
Gastroesophageal varices-2	17	43.59	14	35.9	p=0.06
Absence of gastric varices	1	2.56	4	10.23	p=0.06
Red marks	33	84.61	22	56.41	p=0.005
Portal gastropathy (mild)	18	46.15	15	38.46	p=0.02
Portal gastropathy (severe)	11	28.2	7	17.95	p=0.02
Bleeding	22	56.41	1	2.56	p=0.05

creasing was observed in 4 (10.26%) of them. Gastropathy severity decreasing was observed in 13 (33.33%) of patients. Red marks after the first EVL session were observed in 56.41% (n = 22) of patients.

DISCUSSION

Spontaneous bleeding from varices is accompanied by life-threatening complications in approximately 20% of cases [8]. Bleeding prophylaxis can significantly improve the quality of life of children with PH regardless of its etiology [9].

Despite the efficacy in obliterating EV, endoscopic methods do not affect the pressure in the portal system, do not restore normal portal blood flow to the liver and therefore do not eliminate the main bleeding cause in patients with PH. EVL has an indirect effect on portal decompression by forming collateral vessels. In most cases, EVL acts as a preparatory stage before surgical treatment. Portosystemic shunts directly reduce pressure in the portal system. It is the single method of the portal system decompression and the restoration of portal blood flow to the liver in patients with prehepatic PH [1]. To our opinion, EVL in children is a method that can be applied when it is impossible to perform portosystemic bypass because of anatomical limitations.

The question of choosing a method for variceal bleeding prevention in children with PH remains debatable. Endoscopic sclerotherapy is an effective treatment for variceal bleeding. However, it is associated with a high risk of complications such as rebleeding (up to 20% of cases), deep esophageal ulcers (up to 14% of cases), esophageal strictures (up to 3% of cases), pneumonia (up to 3% of cases) and pericarditis (up to 3% of cases). For this reason, sclerotherapy is not a method of choice for the variceal bleeding prevention in adults [8]. However, given the anatomical features of the pharynx and esophagus in young

children and the absence of ligating devices for small diameter endoscopes. Therefore, sclerotherapy is used in children to whom EVL is not technically possible [10]. According to our data EVL was successfully performed in patients under 3 years old (n = 5, 12.82%). The smallest patient was 1-year-old and weighed 7800 g.

In comparison to sclerotherapy, the advantages of EVL are the following: mucosal defects are more superficial and, as a consequence, there is a lower risk of bleeding from them; for EV eradication less procedures are needed; lower rate of varices recurrence and rebleeding in the long term follow-up [11, 12, 13, 14, 15].

For the reason of poor evidence to confirm the safety of using beta-blockers in pediatric patients, many studies have advocated EVL as a secondary prophylaxis for all children with a variceal bleeding history, as well as primary prophylaxis for children with EV grade II or III and without a variceal bleeding history [11, 12]. In our practice, we used EVL both as primary and secondary variceal bleeding prophylaxis with efficacy 56.41% in cases of EV grade II or III presence.

Studies have shown that EVL is a safe and effective method, superior to sclerotherapy in terms of eradication, and associated with a lower incidence of rebleeding [2, 6, 11, 13, 14]. Our data showed that after one EVL session the EV grade decreased in 56.41% of studied patients. EV eradication was achieved in 28.2% of them. It was found that EVL reduced the EV bleeding risk (p = 0.05) in the study group of patients. It shows the effectiveness and safety of EVL as a prophylaxis of bleeding from EV in children with PH.

CONCLUSIONS

EVL is a safe and effective method of preventing variceal bleeding in children. This method allows to control the varicose veins grade in different PH treatment phases in children.

The statistical analysis revealed a value decrease ($p < 0.001$ by Wilcoxon signed-rank test) of EV grade in the study group of patients before and after EVL. Therefore, even one EVL procedure is able to reduce the EV grade. The EVL effect on the severity of portal gastropathy ($p = 0.02$ by Wilcoxon signed-rank test) and on the red marks presence ($p = 0.005$ by McNemar's chi-square test) was also determined. Our study showed EVL reduced the risk of bleeding from varicose veins ($p = 0.05$, $RR = 0.05$ (95% CI 0.01-0.32)).

REFERENCES

1. Giouleme O., Theocharidou E. Management of Portal Hypertension in Children with Portal Vein Thrombosis. *J Pediatric Gastroenterology Nutr* 2013; 57:419-425.
2. Thomson M., Tringali A., Dumonceau J.M. et al. Paediatric Gastrointestinal Endoscopy: European Society for Paediatric Gastroenterology Hepatology and Nutrition and European Society of Gastrointestinal Endoscopy Guidelines. *Pediatr Gastroenterol Hepatol Nutr* 2017; 64:133-53.
3. D'Amico G., Luca A. Natural history Clinical-haemodynamic correlations Prediction of the risk of bleeding. *Baillieres Clin Gastroenterol*. 1997; 11:243-256.
4. Dos Santos J.M., Ferreira A.R., Fagundes E.D. et al. Endoscopic and pharmacological secondary prophylaxis in children and adolescents with esophageal varices. *J Pediatr Gastroenterol Nutr*. 2013; 56(1):93-8.
5. Cardey J., Le Gall C., Michaud L. et al. Screening of esophageal varices in children using esophageal capsule endoscopy: a multicenter prospective study. *Endoscopy* 2019; 51(01):10-17.
6. Shneider B.L., Bosch J., de Franchis R. et al. Expert Panel of the Children's Hospital of Pittsburgh of UPMC. Portal hypertension in children: expert pediatric opinion on the report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. *Pediatr Transplant* 2012; 16:426-437.
7. Sarin S.K., Kumar A. Gastric varices: profile, classification, and management. *Am J Gastroenterol* 1989; 84: 1244-1249.
8. Duche M., Ducot B., Ackermann O. et al. Portal hypertension in children: High-risk varices, primary prophylaxis and consequences of bleeding. *J of Hepatol*, 2017; 66:320-327.
9. Zargar S.A., Javid G., Khan B.A., et al. Endoscopic ligation versus sclerotherapy in adults with extrahepatic portal venous obstruction: a prospective randomized study. *Gastrointest Endosc* 2005; 61:58-66.
10. Kang K.S., Yang H.R., Ko J.S. et al. Long-term Outcomes of Endoscopic Variceal Ligation to Prevent Rebleeding in Children with Esophageal Varices. *J Korean Med Sci* 2013; 28:1657-1660.
11. Mahmud S., Ahmed S.S., Gulshan J. et al. Outcome of Band Ligation in Esophageal Varices of Bangladeshi Children: A Tertiary Centre Experience. *Bangladesh J Child Health*, 2017; 41(1):28-33.
12. McKiernan P., Abdel-Hady M. Advances in the management of childhood portal hypertension. *Expert Rev Gastroenterol Hepatol* 2015; 9:575-83.
13. Shneider B.L., Abel B., Haber B. et al. Portal hypertension in children and young adults with biliary atresia. *J Pediatr Gastroenterol Nutr* 2012; 55:567-73.
14. Kim S.J., Kim K.M. Recent Trends in the Endoscopic Management of Variceal Bleeding in Children. *Pediatr Gastroenterol Hepatol Nutr* 2013; 16:1-9.
15. Pimenta J.R., Ferreiro A.R., Tavares Fagundes E.D. et al. Evaluation of endoscopic secondary prophylaxis in children and adolescents with esophageal varices. *Arq Gastroenterol*, 2017; 54(1):21-26.

The work is carried out within the framework of the initiative research work of the Bogomolets National Medical University "Development and implementation of modern approach to diagnostic and treatment methods for children with congenital malformations and abdominal cavity diseases" (state registration No. 0118U100562)

Acknowledgement

The Authors express their sincere gratitude and deep appreciation to Dr. Daria Diehtiarova for the valuable advice and comments on the article, for the text edition and translation into English.

ORCID and contributioship:

*Dariia I. Voroniak: 0000-0003-3201-6632^{A, B, E}
Oleg S. Godik: 0000-0002-1084-9484^{A, C, D, E}
Larysa Ya. Fedoniuk: 0000-0003-4910-6888^{B, E, F}
Olena M. Shapoval: 0000-0002-1868-7811^{C, F}
Viktoriia V. Piliponova: 0000-0002-5465-5809^{E, F}*

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Dariia I. Voroniak

Diagnostic Department,
National Children Specialized Hospital «Ohmatdit»
28\1 Chornovola, 01175, Kyiv, Ukraine
tel: +380934974913
e-mail: dania19@icloud.com

Received: 21.05.2020

Accepted: 28.08.2020

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article