pISSN: 2234-8646 eISSN: 2234-8840
http://dx.doi.org/10.5223/pghn.2013.16.4.248
Pediatr Gastroenterol Hepatol Nutr 2013 December 16(4):248-253

Original Article

PGHN

Experiences with Endoscopic Interventions for Variceal Bleeding in Children with Portal Hypertension: A Single Center Study

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Purpose: The aim of this study was to compare the efficacy and safety of band ligation and injection sclerotherapy in the endoscopic treatment of children with variceal bleeding.
Methods: The study population included 55 children, all of whom were treated at the time of endoscopic diagnosis of esophageal varices at Asan Medical Center, Seoul, Korea, between January 1994 and January 2011. The primary outcomes included initial success rates and duration of hemostasis after endoscopic management (band ligation vs. injectionsclerotherapy).
Results: The mean age was 6.7±5.2 years and the mean follow-up time was 5.4±3.7 years. The most common cause of esophageal varices was biliary atresia. Of 55 children with acute variceal bleeding, 39 had band ligation and 16 had injection sclerotherapy. No differences between groups were observed in terms of the size, location, and presence of red color sign. The success rates of band ligation and sclerotherapy in the control of acute bleeding episodes were 89.7% and 87.5%. The mean duration of hemostasis after endoscopic intervention was 13.2±25.1 months. After one year, 19 of 39 patients (48.7%) treated with band ligation and 7 of 16 patients (43.8%) with injection sclerotherapy had experienced rebleeding episodes. Complications after the procedures were observed in 10.3% and 18.8% of children treated with band ligation and injection sclerotherapy.
Conclusion: The results of our current study suggest that band ligation and injection sclerotherapy are equally efficient treatments for the control of acute variceal bleeding and prevention of rebleeding.

Key Words: Esophageal gastric varices, Gastrointestinal endoscopy, Ligation, Sclerotherapy, Hyertension, Portal, Child

INTRODUCTION

Esophageal varices, an important complication of portal hypertension, are a major cause of mortality in both adults and children [1-3]. Whereas the primary etiologies of portal hypertension in children are biliary atresia and extrahepatic portal vein obstruction (EHPVO), the most common etiology in adults is liv-

Received : September 10, 2013, Revised : October 4, 2013, Accepted : October 8, 2013

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er cirrhosis [1-4]. It is conventionally thought that endoscopic intervention, such as band ligation and sclerotherapy, is the best form of treatment for variceal bleeding, until liver transplantation or surgical shunting are unavoidably required as a result of recurrent bleedings [5].

Although evidence-based guidelines for management of portal hypertension in adults were suggested at the Baveno V meeting [6], insufficient pediatric data related to management of variceal bleeding has been accumulated to date [7,8]. Aside from the rarity of esophageal varices in children, band ligation is often not a practical option for small children. These considerations have frustrated efforts to conduct well-controlled studies with members of these specific sectors of the pediatric population. Fortunately, the mortality rate associated with variceal bleeding in infants or small children is less than 10%, which is lower than that of adults reaching up to 30% [2,3,9-11]. Most pediatric studies of variceal bleeding are retrospective and heterogeneous in terms of the population used and the treatment regimens. Few studies have compared the efficacy of band ligation and injection sclerotherapy. To date, pediatric gastroenterologists have attempted to modify a recent Bravo guideline for children [12]. The aim of the present study, which was not a randomized control trial (RCT), was to compare the efficacy and safety of band ligation and injection sclerotherapy in the endoscopic treatment of children with acute variceal bleeding.

MATERIALS AND METHODS

The study population initially included 86 children treated for esophageal varices at Asan Medical Center Children's Hospital, University of Ulsan College of Medicine, Seoul, Korea, between January 1994 and January 2011. Of these, 31 children with gastric varices were excluded. The medical records of the children were reviewed retrospectively. The terminology and selection of variables were based on study guidelines proposed by the Baveno V consensus [6]. The following characteristics were selected: age at the onset of bleeding, sex, underlying etiology, and characteristics of esophageal varices. The characteristics of esophageal varices were classified according to the grading system for esophagogastric varices proposed by the Japan Society for Portal Hypertension [13]. The endoscopic images were reviewed by experienced pediatric gastroenterologists of Asan Medical Center Children's Hospital, and specific etiologies were also reviewed retrospectively. The technical aspects of both band ligation and injection sclerotherapy have been described elsewhere [8]. The primary outcomes included initial success rates and the duration of hemostasis after endoscopic managements (band ligation vs. injection sclerotherapy), which were assessed using medical records. Octreotide was administered at admission and endoscopic evaluation and management performed within 24 hours of admission. All patients received endoscopic treatment as the secondary prophylaxis. Rebleeding was defined as unsuccessful secondary prophylaxis clinically significant rebleeding after 5 days after the initial hemostasis according to the Baveno V criteria [6]. The Fisher's exact test for categorical variables and Kruskal-Wallis test for the continuous variables were used for the statistical analysis, using SPSS ver. 14.0 (SPSS Inc., Chicago, IL, USA). A p-value of less than 0.05 was considered statistically significant.

RESULTS

Of 86 children in our initial cohort with portal hypertension, 55 were noted to undergo endoscopic intervention for esophageal variceal bleedings. The mean age of these 55 children (28 male, 27 female) at the time of the first onset of bleeding was 6.7±5.2 years and the mean follow-up time was 5.4±3.7 years (range, 1.2 to 15.3 years). Table 1 shows the etiologic classification of this population. Of these children, 26 (47.3%) had biliary atresia, 8 (14.5%) had EHPVO, 6 (14.5%) had congenital hepatic fibrosis, and 15 (27.3%) had other various causes. In this cohort also, 39 children had band ligation and 16 had injection sclerotherapy as an intervention. Of the 25 children

with biliary atresia, 12 had band ligation and 13 had injection sclerotherapy. Most children with portal hypertension and congenital hepatic fibrosis underwent band ligations.

Regarding the grade of variceal size, 10 (18.2%), 34 (61.8%), and 11 (20%) children had F1, F2, and F3, respectively. Other characteristics are described in Table 1. The success rates of band ligation and injection sclerotherapy to control acute bleeding episodes were 89.7% and 87.5%, respectively. The mean duration of hemostasis after endoscopic intervention was 13.2±25.1 months (range, 2 months to 10.1 years). During the follow-up period, rebleeding occurred in 65.4% (36/55) patients. Rebleeding was observed in 64.1% (25/39) patients with band ligation and 68.8% (11/16) patients with injection sclerotherapy. Of them, 76.0% (19/25) patients with band ligation and 63.6% (7/11) patients with injection sclerotherapy experienced rebleeding episodes within one year. Complications after the procedures were observed in 10.3% and 18.8% of children with band ligation and injection sclerotherapy, respectively (Table 2).

Statistical analysis indicated no differences between groups in terms of the size, location, color and presence of red color sign. No differences were found between two groups in terms of acute bleeding control, re-bleeding rates, after the treatment and complications, even though the mean age and etiology (biliary atresia) were significantly different between the two groups (Table 3).

Table 1. Characteristics of Study Population and Esophageal Varices (n=55)

Characteristic	Endoscopic intervention	
	Band ligation (n=39)	Sclerotherapy (n=16)
Basic information		
Age (yr), 1st bleeding	8.40	3.57
Sex		
Male	24	4
Female	15	12
Etiology		
Biliary atresia	13	13
Congenital hepatic fibrosis	9	1
Portal vein thrombosis	6	0
Alagille syndrome	2	0
Budd-Chiari syndrome	2	0
Glycogen storage disease type III	2	0
Idiopathic liver cirrhosis	1	2
Others	3	0
Characteristics of esophageal varices		
Location		
Upper	5	1
Middle	11	2
Lower	23	13
Form (size)		
F1	6	4
F2	27	7
F3	6	5
Color		
White/blue	31	16
Red color sign	33	12

DISCUSSION

Many adult RCTs have tried to compare variceal band ligation and injection sclerotherapy to control esophageal variceal bleeding [14,15]. These previous data indicate that band ligation is no less effective than sclerotherapy, while producing fewer occurrences of procedure-related complications such as procedure related perforation, bleeding, ulceration, and stricture formation at the injection site. A detailed review of the complications of endoscopic

Table 2. Results for Patients Who Received Endoscopic Interventions

	Band ligation (n=39)	Sclerotherapy (n=16)
Success, initial hemostasis	35 (89.7)	14 (87.5)
Rebleeding during follow-up period	25 (64.1)	11 (68.8)
Rebleeding within 1 year	19/25 (76.0)	7/11 (63.6)
Complications	4 (10.3)	3 (18.8)

Values are presented as number (%).

Table 3. Comparison of Characteristics between Band Ligation and Sclerotherapy

Variable	Characteristic	Univariate analysis
		p-value
Age, 1st bleeding	Continuous	0.001
Etiology	BA vs. others	0.008
Location	Upper vs. inferior	NS
Form (size)	F3 vs. F1	NS
Color	Present vs. absent	NS
RCS	Present vs. absent	NS
Success, initia l hemostasis	Continuous	NS
Rebleeding within 1 year	Continuous	NS
Complications	Continuous	NS

BA: biliary atresia, NS: not significant, RCS: red color sign.

management is described elsewhere [16]. For children, those findings are inconclusive owing to the lack of appropriate RCTs and the inadequacy of the sample sizes for robust statistical analysis [7]. Notwithstanding the limitations of these studies to guide the treatment of pediatric patients, it is generally accepted that octreotide effectively controls variceal bleeding in a significant number of patients and that endoscopic therapy with band ligation or injection sclerotherapy is suitable for children with variceal bleeding [17,18].

In our present study, we performed band ligation in 39 children and injection sclerotherapy in 16 children as an initial form of therapy. We observed that both esophageal band ligation and injection sclerotherapy were equally effective in controlling active variceal bleeding and preventing rebleeding during the first year after treatment (Table 2), although this observation incorporates a selection bias because of two main limitations. First, band ligation was preferred over injection sclerotherapy as an initial form of treatment for variceal bleeding. This preference is based on a pediatric RCT study on secondary prophylaxis, in which band ligation was found to be more efficient than injection sclerotherapy [7,17,18]. In addition to its superior effectiveness, band ligation also showed fewer complications than injection sclerotherapy [18,19]. Second, for small children (whose etiology is mainly biliary atresia), it is difficult to insert the device-attached endoscopic probe into their small esophageal lumen in an attempt to control variceal bleeding by band ligation, whereas injection sclerotherapy is feasible even for small infants. Therefore, although band ligation is the best treatment methods for children with liver cirrhosis, injection sclerotherapy is recommended if band ligation is not feasible [8,12]. In our present study, the significantly lower mean age of patients that underwent injection sclerotherapy compared with those that underwent band ligation was attributed to the small esophageal lumen of younger children who were unable to accept band ligation probes. Notwithstanding these two limitations, both band ligation and injection sclerotherapy were shown to be highly successful in controlling variceal bleedings. There was no difference in complications between the band ligation and injection sclerotherapy groups. The most commonly encountered complications were short-term fever and abdominal pain. One of our patients who underwent band ligation developed subcutaneous emphysema caused by a tearing of the mucosa. Hazardous complications, such as esopageal stricture and perforation and bacteremia did not occur in our injection sclerotherapy group even in infants.

To date, our center has not investigated either primary or secondary prophylaxis extensively, owing to our belief that endoscopic intervention cannot change the long-term outcome of children with portal hypertension. Two important facts support this belief. First, a recent study in the United States of the long term outcome of biliary atresia showed that only one-third of children who underwent endoscopic intervention were able to preserve their naive liver function until the age of 20 [20]. Despite measures that included the Kasai operation and endoscopic interventions, many of these children died or underwent liver transplantation. Liver transplantation is the best treatment for children with end-stage liver disease [21], with surgical intervention, such as the Rex shunt, a further possibility for children with EHPVO [5]. Second, there is no evidence that endo-

scopic intervention can prevent hepatopulmonary syndrome or portopulmonary hypertension [22]. Hepatopulmonary syndrome and portopulmonary hypertension are more critical complications that even make the attempt of liver transplantation unfeasible [23]. In addition, given that these complications are found at late stages, clinicians usually make their diagnosis at a clinically advanced stage, when the issue can be detected using contrast echocardiography. In such instances, repeated endoscopic interventions might be unwise for children with irreversible hepatopulmonary syndrome or portopulmonary hypertension.

In conclusion, band ligation and injection sclerotherapy are both efficient and safe for the control of acute variceal bleeding and the prevention of rebleeding in children. Although endoscopic intervention is not accepted as the preferred modality for the treatment of variceal bleeding, the high success rates shown in the present study suggest that esophageal varices in children with portal hypertension can initially be managed by endoscopic approaches.

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