Rate and Associated Risk Factors of Rebleeding after Endoscopic Variceal Band Ligation

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Abstract

Bleeding esophageal varices is associated with a high mortality rate. Despite advances in management, the mortality rate remains at 30-80 per cent. Endoscopic variceal band ligation (EVL) is a new technique designed to manage esophageal varices with the aim of reducing the complication rate.

Variceal rebleeding which occurs in 6-36 per cent of patients is common during the treatment period before variceal obliteration is achieved but related factors remain unknown. Thirty-one patients with a history of esophageal variceal bleeding and endoscopically confirmed between February 1999 and February 2001 received regular EVL until variceal disappearance and were reviewed retrospectively. There was no major complication. Rebleeding was documented in 8 patients (25.8%). Portal hypertension-related conditions, such as gastric varices and portal hypertensive gastropathy, were the most common sources of rebleeding. Platelet count and prothrombin time were not found to be closely related to rebleeding (p-value=0.79, 0.08) but Child-Pugh's C patients had a significantly higher rebleeding rate compared with Child-Pugh's B and A respectively (p-value=0.047). Mortality was high in the rebleeding group significantly (p-value=0.006) and exsanguinations were the major cause of death. In conclusion, the authors suggest that long-term follow-up is required.

Key word : Cirrhosis, Portal Hypertension, Esophageal Varices, Child-Pugh's Classification, Endoscopic Variceal Band Ligation

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Cirrhosis is the end result of a variety of mechanisms causing hepatocellular injuries. Alcoholic cirrhosis and viral hepatitis B and C are the two most common causes in Thailand. The pathologic response is hepatocellular necrosis followed by fibrosis and nodular regeneration. The distorted hepatic architecture and perisinusoidal fibrosis cause increased hepatic vascular resistance, resulting in portal hypertension and portosystemic collateralization and associated complications of variceal hemorrhage, hypersplenism, ascites and encephalopathy.

Varices in the distal esophagus may rupture depending on the magnitude of portal pressure, variceal size and variceal wall thickness. Bleeding from esophageal varices is the single most life-threatening complication of portal hypertension, responsible for about one third of all deaths in patients with cirrhosis. Mortality of an episode of variceal hemorrhage ranges between 25 per cent and 30 per cent[1] and occurs mostly in patients with severe liver disease and in those with early rebleeding. Balloon tamponade and pharmacotherapy are associated with a significant incidence of rebleeding. Endoscopic injection sclerotherapy (EIS) has gained wide popularity for both control of acute bleeding episode and prevention of early rebleeding and has become the gold standard in the management of acute variceal hemorrhage. This technique controlled hemorrhage in more than 85 per cent of patients[1] but recurrent bleeding still occurred in about half of the patients and there were more serious complications such as esophageal perforation, worsening of variceal hemorrhage, and aspiration pneumonitis.

Investigations have suggested that rubber band ligation of varices may be more effective and associated with fewer complications and mortality rates than sclerotherapy[2-5]. The rebleeding rate appears to be between 6 per cent and 36 per cent[6]. Possible predictive factors for rebleeding have not been established but may be associated with residual small varices that cannot be ligated, recurrent varices and Child-Pugh classification[7].

In Sawanpracharak Hospital, the exact rebleeding rate is still unknown. Two assumed risk factors for rebleeding are thrombocytopenia and prolonged prothrombin time, both of which are well-known complications of advanced stage liver disease. The present study was undertaken in order to identify the rebleeding rate and associated risk factors in patients with bleeding esophageal varices after variceal band ligation.

MATERIAL AND METHOD

Between February 1999 and February 2001, patients with bleeding esophageal varices admitted to Sawanpracharak Hospital were enrolled in the study. All patients underwent upper gastrointestinal endoscopy and diagnosis of bleeding varices was confirmed when spurting or oozing was seen from a varix, or variceal size was larger than one-third of esophageal lumen, or when patients presented with red color signs on their esophageal varices with no other potential site of bleeding identified. Patients with a history of injection sclerotherapy were excluded. Thirty-one patients were included in this study. Variceal ligation was performed with the multi-band ligator until the bleeding ceased. Further sessions of ligation were performed to reduce the rate of subsequent hemorrhage at an interval of 2 weeks until all varices were eradicated and then underwent follow-up endoscopic examination at 6-month intervals. Patients who had severe portal hypertensive gastropathy were on beta-blocker to prevent recurrent bleeding. Most of them received diuretics and/or lactulose.

The charts and endoscopic reports of the patients were reviewed. Three clinical data such as the patients' demographic, biochemical tests and endoscopic data were recorded for statistical purposes: age, gender, etiology of liver cirrhosis, ascites, encephalopathy, serum albumin, prothrombin activity, and serum bilirubin. Pugh's modification of Child's grading[7] was calculated for assessment of liver function by giving a value of 1, 2, or 3 for increasing abnormality and the values were summed up over the five variables (ascites, encephalopathy, bilirubin, albumin, prothrombin time). All analyses were conducted with SPSS 9.0 statistical software. Descriptive analyses and Chi-square test were used in this study. P-value$\leq$0.05 was considered significant.

RESULTS

The present study covered the period from February 1999 to February 2001, there were 31 patients with variceal hemorrhage under band ligation. Fourteen patients who had prior sclerotherapy

were excluded from the study. There were 25 males (80.6%) and 6 females (19.4%) with ages ranging from 31 to 80 years (mean age 49 years 10 months ± 11 years 5 months). The mean length of follow-up for all patients was 7 months 22 days ± 5 months 19 days (range 12 days-1 year 8 months). The patients were alcoholic in 74.2 per cent. Chronic hepatitis B and C in 19.4 per cent and 12.9 per cent respectively. Concomitant hepatoma was present in 3.2 per cent. Thrombocytopenia (platelet count<$150x10^3$) was found in 75 per cent, and prothrombin time prolonged (>15 sec) in 100 per cent. Severity of liver disease was classified into three grades according to the modified Child classification: 7.7 per cent of the patients were labelled as Child-Pugh's grade A, 61.5 per cent Child-Pugh's grade B, and 30.8 per cent Child-Pugh's grade C. Variceal bleeding was controlled in 96.8 per cent, the remaining 3.2 per cent died because of massive hemorrhage. Esophageal varices were completely eradicated in 29 per cent. An operation was performed in 6.45 per cent for large gastric varices and severe portal hypertensive gastropathy. New varices had developed in 6.5 per cent. There was no major complication. Rebleeding rates were 25.8 per cent, which was from gastric varices 12.5 per cent, from portal hypertensive gastropathy 37.5 per cent and the remaining 50 per cent did not undergo endoscopic examination. During the study ten patients (32.3%) died. Deaths caused by rebleeding accounted for 60 per cent of cases, whereas 10 per cent were from hepatoma, 10 per cent from heart failure and 10 per cent from renal failure respectively. No significant difference was seen between the patients with rebleeding and without rebleeding with regard to factors of platelet count and prothrombin time (p-value=0.79 and 0.08 respectively). Those patients in Child- Pugh's grade C had a higher rebleeding rate than patients in Child-Pugh's grade B and A. (p-value=0.047). Statistical differences were noted as a factor of death rate between the patients with and without rebleeding (p-value=0.006).

DISCUSSION

Gastroesophageal varices are the most important porto systemic collaterals because of their propensity to rupture, constituting the most lethal complication of cirrhosis. Associated mortality after variceal bleeding is high, and recurrent bleeding after the first episode accounts for additional deaths. Variceal wall tension, which is related to vessel diameter, as well as the intravariceal pressure, is believed to be critical in the pathogenesis of bleeding esophageal varices.

Endoscopic variceal band ligation (EVL) is a non-portal pressure-reducing method to treat varices with the objective of interrupting blood flow and subsequently developing necrosis of mucosa and submucosa and replacement of varices by scar tissue. Even though EVL can achieve variceal obliteration, rebleeding will eventually recur. Variceal eradication is achieved in only 25 per cent compared to others which are usually successful in about two thirds of patients[1]. The rebleeding rate after band ligation in this study was 25.8 per cent, which is consistent with a previous report[6]. There are several factors that influence rebleeding. The first is the extent of eradication of the varices, either residual or completely obliterated. The second is the newly developed, small-size, dilated varices in the lower esophagus. Although these potential sources of bleeding are controlled, rebleeding remains in patients with portal hypertension. The presence of portal hypertensive gastropathy, gastric varices and the worsening of the Child-Pugh score after band ligation may predict an increase of the risk of rebleeding.

In the present study, thrombocytopenia and prothrombin time failed to demonstrate any significant effect on the occurrence of rebleeding rate. The authors have shown that the Child-Pugh C is a significant prognostic predictor of rebleeding ($p \leq 0.05$), yet it does not significantly influence the survival. Only the increase in Child-Pugh score appeared to be a significant predictor of rebleeding. Mortality was significantly high in the rebleeding group (p-value=0.006). It is clear that their quality of life was improved by band ligation and a life-threatening situation was removed. Because only liver transplantation can save these patients from the natural outcome of this clinical state, band ligation helps patients survive bleeding episodes until a liver can be transplanted.

In conclusion, the present data showed the rebleeding rate of 25.8 per cent after band ligation in patients with variceal hemorrhage. Child-Pugh's C patients had significantly higher rebleeding rates compared with Child-Pugh's B and A respectively (p-value=0.047). Mortality was significantly high in the rebleeding group (*p*-value=0.006) and exsanguination was the major cause of death.

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อัตราเลือดออกซ้ำและปัจจัยที่เกี่ยวข้องภายหลังการรัดหลอดเลือดดำโป่งพองในหลอดอาหารด้วยยาง

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เลือดออกจากหลอดเลือดดำโป่งพองในหลอดอาหาร เป็นภาวะแทรกซ้อนที่รุนแรงในผู้ป่วยโรคตับแข็ง มีอัตราตายมากร้อยละ 30 ถึง 50 ปัจจุบันนิยมให้การรักษาโดยใช้ยางรัด(Endoscopic variceal band ligation) ซึ่งมีประสิทธิภาพเทียบเท่าการฉีด sclerosing agent (Endoscopic injection sclerotherapy) มีภาวะแทรกซ้อนน้อยกว่า แต่ยังประสบปัญหาเลือดออกซ้ำ ร้อยละ 6 ถึง 36 ผู้ป่วยเลือดออกจากหลอดเลือดดำโป่งพองในหลอดอาหารที่มารับการรักษาด้วยการใช้ยางรัดในโรงพยาบาลสวรรค์ประชารักษ์ ตั้งแต่วันที่ 25 กุมภาพันธ์ 2542 ถึงวันที่ 25 กุมภาพันธ์ 2544 จำนวน 31 ราย ผู้ป่วยทุกรายได้รับการส่องกล้องเพื่อยืนยันการวินิจฉัยว่ามีเลือดออกจากหลอดเลือดดำโป่งพองในหลอดอาหารจริงและได้รัดยางตามระยะเวลาที่กำหนดจนกว่าจะกำจัดหลอดเลือดที่โป่งพองหมด (Eradication) ทำการวิเคราะห์ข้อมูลด้วยโปรแกรม SPSS for Windows และวิเคราะห์หาค่าความสัมพันธ์ทางสถิติด้วยวิธี Chi-square test กำหนดค่าความเชื่อมั่นไม่น้อยกว่าร้อยละ 95 ผลการศึกษาพบว่า อัตราเลือดออกซ้ำร้อยละ 25.8 โดยอย่างน้อยร้อยละ 50 มีสาเหตุของเลือดออกซ้ำจาก portal hypertensive-related bleeding จากการวิเคราะห์ปัจจัยที่เกี่ยวข้องกับภาวะเลือดออกซ้ำพบว่าค่า platelet count และ pro-thrombin timeไม่พบความแตกต่างกันทางสถิติ (p-value=0.79, p-value=0.08) แต่ Child-Pugh classification มีความเกี่ยวข้องกับภาวะเลือดออกซ้ำอย่างมีนัยสำคัญ (p-value=0.047) โดยผู้ป่วยกลุ่ม Child-Pugh's C มีอัตราเลือดออกซ้ำร้อยละ 60 Child-Pugh's B ร้อยละ 20 และ Child-Pugh's A ร้อยละ 20 อัตราการเสียชีวิตทั้งหมดร้อยละ 32.3 ในกลุ่มที่มีเลือดออกซ้ำมีอัตราการเสียชีวิตมากกว่ากลุ่มที่ไม่มีเลือดออกซ้ำอย่างมีนัยสำคัญ (p-value=0.006) โดยจำแนกเป็นกลุ่มที่มีเลือดออกซ้ำมีอัตราการเสียชีวิตร้อยละ 75 และกลุ่มที่ไม่มีเลือดออกซ้ำมีอัตราการเสียชีวิตร้อยละ 17.4

คำสำคัญ : โรคตับแข็ง, ความดันหลอดเลือดดำในระบบ portal สูง, หลอดเลือดดำโป่งพองในหลอดอาหาร, ระดับความรุนแรงของสภาพการทำงานของตับ (Child-Pugh's classification), การรัดหลอดเลือดดำโป่งพองด้วยยาง

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