SPLENECTOMY AND GASTRIC VEIN LIGATURE IN HEPATOSPLENIC SCHISTOSOMIASIS: EFFECTS UPON ESOPHAGEAL VARICEAL PRESSURE AND ENDOSCOPIC RISK FACTORS OF ESOPHAGEAL VARICEAL BLEEDING

Esplenectomia e ligadura da veia gástrica esquerda na esquistossomose mansônica: efeitos sobre pressão das varizes do esôfago e indicadores endoscópicos de risco de sangramento por varizes esofagogástricas

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ABSTRACT – Background - A significant number of patients with schistosomiasis develop the hepatosplenic form, with portal hypertension, in which bleeding caused by rupture of esophagogastric varices emerged as the leading cause of morbidity and mortality. Aim - To investigate the effects of splenectomy and ligature of the left gastric vein on risk factors for bleeding from esophagogastric varices in patients with schistosomiasis mansoni, hepatosplenic form, with a history of upper gastrointestinal bleeding. Methods - The main risk factors of bleeding from esophagogastric varices were studied in 34 patients. The following parameters were investigated: 1) esophageal variceal pressure, measured by the endoscopic pneumatic balloon technique; 2) size, fundamental color, extension and red signs of esophageal varices, gastric varices and gastropathy of portal hypertension. The evaluations were performed in the preoperative period, immediate postoperative period (between the sixth and eighth postoperative days) and the sixth month of follow-up. Results - The variceal pressure has fallen from 22.3 +/- 2.6 mmHg before surgery to 16.0 +/- 3.0 mmHg in the immediate postoperative period (p<0.001), reaching 13.3 +/- 2.6 mmHg in the sixth month of follow-up. A significant reduction of the frequency of the parameters associated with a greater risk of hemorrhage was observed between the preoperative period and six-month follow-up, when the proportion of large esophageal varices (p<0.05), varices extending to the upper esophagus (p<0.05), bluish varices (p<0.01), varices with red signs (p<0.01) and gastropathy (p<0.05) decreased. Conclusion - In patients with hepatosplenic schistosomiasis with a previous history of variceal hemorrhage, splenectomy and gastric vein ligation was effective in reducing the main hemorrhagic risk factors until the sixth month of follow-up, indicating a good way to control the bleeding episodes.

RESUMO – Racional – Expressivo contingente de pacientes esquistossomáticos com a forma hepatoesplênica e hipertensão portal apresentam hemorragia causada pela ruptura de varizes esofagogástricas, principal causa de alta morbidade e mortalidade da doença. Objetivo - Investigar os efeitos da esplenectomia e ligadura da veia gástrica esquerda sobre fatores de risco de sangramento por varizes esofagogástricas em portadores de esquistossomose mansônica, forma hepatoesplênica, com antecedente de hemorragia digestiva alta. Método - Estudaram-se, de forma prospectiva, 34 pacientes, com idade entre 1 e 74 anos (média 44,14), sendo 18 (53%) mulheres. Analisaram-se: 1) pressão das varizes do esôfago, aferida pela técnica endoscópica do balão pneumático; 2) tamanho, local, cor e sinais de cor vermelha nas varizes do esôfago; 3) varizes gástricas e gastropatia da hipertensão portal. Realizaram-se avaliações no pré-operatório, no pós-operatório imediato e no sexto mês após a ligadura da veia gástrica esquerda. Resultados - A pressão das varizes do esôfago diminuiu de 22.3 +/- 2.6 mmHg, antes da operação, para 16.0 +/- 3.0 mmHg no pós-operatório imediato (p<0.001), caindo para 13.3 +/- 2.6 mmHg no pós-operatório do sexto mês (p<0.001). A proporção de varizes de grosso calibre, varizes no esôfago superior, varizes de cor azul, varizes com sinais de cor vermelho e de gastropatia da hipertensão portal decresceu de forma significante apenas no sexto mês de pós-operatório. Conclusão - A ligadura da veia gástrica esquerda, em esquistossomáticos hepatoesplênicos, com antecedente de hemorragia digestiva alta, revelou-se eficaz em diminuir alguns dos principais fatores de risco de hemorragia por varizes esofagogástricas, indicando boa perspectiva no controle definitivo do sangramento.
INTRODUCTION

The schistosomiasis mansoni affects 200 million of individuals worldwide, occurring on endemic form in 52 countries and territories, distributed through South America, Caribbean, Africa and East Mediterranean, involving 600 million risk people to be contaminated. On Brazil, affects eight million, representing serious problem in public health.

A expressive contingent of patients develops the hepatosplenic form with portal hypertension, in which the bleeding caused by break of esophagogastric varicose veins emerges as the main cause of high morbidity and mortality of the disease. Among the options to control the bleeding, generally is employed the treatment surgery. However, the choice of what type of operation must be used is still controversial.

In portal hypertension the deleterious effects related with the deviation of portal blood from the of liver put the decompression non-selective operations in standing-by, although it is effective on control of hemorrhagic episodes. To same can be said in relationship to the distal splenorenal anastomosis - decompressing only the oesophagogastric territory (local of the bleeding), without divertion of the mesenteric blood on the liver. It proved to be unable to preserve the liver function in schistosomiasis. So, significant encephalopathy cooled off the enthusiasm on selective portal decompression in schistosomiasis.

By other side, the indication of azygo-portal disconnection associated to splenectomy in hepatosplenic schistosomiasis was strengthened after the results of prospective randomized study accomplished by Raia, in São Paulo, Brazil. At end of 85 months it proved to be better due to low mortality, late absence of encephalopathy and hemorrhagic relapse similar to registered with other interventions.

Those results confirmed Kelner ideas - since 50’s in Pernambuco, Brazil -, that the association of splenectomy with the ligation of varicose veins of esophagus in schistosomiasis is interesting. The main physiological bases are the reduction of portal pressure promoted by removal of spleen, and the obliteration of varicose veins in the so called “zone vulnerable” in esophagus. The analysis of 25 years experience with the ligation of varicose veins of esophagus, revealed low mortality, absence of encephalopathy and acceptable hemorrhagic relapse (13.4%). However, the late mortality of 34.1% has no recognized reasons till nowadays.

Driven by the favorable results of the ligation of varicose veins of esophagus, this operation is the most used in Northeast of Brazil on treatment of portal hypertension in schistosomiasis. After angiographic and pressure studies, Lacerda proposed the splenectomy and the ligature of left gastric vein. The ligation of varicose veins of esophagus could be replaced with advantages by endoscopic sclerotherapy, method secure and effective on treatment of varicose veins in schistosomiasis, when associated to surgery.

Advance in portal hypertension studies is the development of parameters with capacity of identify the possibility of occurrence of future bleeding episodes. In that sense stands the endoscopic pressure measurements of varicose veins of esophagus. Indeed, the pressure of varicose veins of esophagus shows good correlation with the portal pressure.

The risk of bleeding also includes the evaluation of endoscopy indicators showing predictive values of hemorrhage as important as criterion to define the indication of what type of operation must be used. Therefore, the present study has the goal to investigate on short and late follow-up on patients with hepatosplenic form of schistosomiasis mansoni with antecedent of bleeding, the effects of ligation of gastric left vein on main factors of bleeding risk of esophagogastric varices.

METHOD

Were studied 34 patients with diagnosis of schistosomiasis mansoni, in form hepatosplenic and with antecedent of varices bleeding, hospitalized for elective surgical treatment.
on Service of General Surgery and Hepatic Transplant of Oswaldo Cruz Hospital, University of Pernambuco, Recife, PE, Brazil. All were treated, before of intervention, with oxamniquine in oral dose of 15 mg/kg.

The protocol was approved by the Ethics Medical Council of the institution. All the participants authorized its inclusion and signed the informed consent term. I was prospective comparing on varices - before and after gastric left vein ligature - , the pressure of esophageal veins; the caliber; the extension; the color; the signs of red color; the varicose on gastric veins and the portal hypertension gastropathy. The assessments were made on pre-operative time in the week preceding the operation (T0); on immediate post-operative period between the sixth and the eighth day after the operation (T1); in six months after the operation (T2).

The inclusion criteria were: age superior to 18 years; prior and recent (five days) history of hematemesis or melena, presumably by break of varicose veins of esophagus; absence of ascites, signs of liver failure and portosystemic encephalopathy; hematocrit above of 22%; endoscopy showing varicose veins of esophagus; abdominal ultrasonography with signs of hepatosplenic schistosomiasis; fibrosis of Symmers in liver histology obtained by biopsy for the operation.

The exclusion criteria were: antecedent of surgical and / or endoscopic treatment of varices; patients in clinical treatment of portal hypertension; chronic alcoholism; thrombosis on portal system detected by Doppler ultrasound and / or by angiography preoperatively; liver cirrhosis or any other disease of the liver.

The age of patients ranged of 19 the 74 years (44.1 +/- 14.4). Were 18 women (53%) and 16 men (47%). All had positive epidemiology to schistosomiasis mansoni. The number of episodes of bleeding ranged from one to ten, with average of 2.9 episodes by patient. Nineteen (55.9%) received blood transfusion, for the hemorrhagic episode. The patients had serological markers to hepatitis B (HBsAg) and hepatitis C (Anti-HCV) negative.

The esofagogastroduodenoscopies were performed by the same examiner on aim of maintain uniform criterion. The endoscopic risk indicators of bleeding were evaluated by Japanese Society to the Research of Portal Hypertension classification. The gastric varicose veins were defined by Sarin and Kumar criteria. The gastropathy of portal hypertension was diagnosed and classified by the criteria established by McCormack et al.

The pressure of varicose veins of esophagus was measured by technique described by Gertsch et al. using Esophageal Varix Manometer unit, pneumatic balloon and polygraph.

After the end of esophagogastroduodenoscopy, were administered intravenously 20 mg of n-butyl scopolamine diluted in 2 ml of distilled water to decrease the peristaltic movements of esophagus. The endoscope and the pneumatic balloon were lubricated with 10% lidocaine gel and introduced on esophagus to arrive in stomach. The balloon was partly inflated and pulled to return to esophagus, 3 cm above the cardia to measure the caliber of varices, fully emptied and soon after, inflated progressively in of 2 ml / sec speed to observe the first collapse of varix wall. In that exact moment the pressure was transmitted to manometer and registered by the polygraph in speed of 5 mm / sec.

The procedure was repeated three times considering the arithmetic average. It was considered the less pressure record to diminish the effect of pressure variations in esophageal lumen caused by its normal movements.

To the statistic analysis was employed the variance with measures repeated to compare the numerical variables obtained on the three periods of evaluation. In binary variables was used the test of Cochran. The tests for multiple comparisons were performed by Tukey or Dunn procedures. Were considered significant p values less the 5 %.

RESULTS

All patients had signs of portal hypertension compatible with hepatosplenic schistosomiasis. The weight of spleen in vitro ranged of 200 g the 1850 g (889 +/- 421). The gastric left vein, reached caliber of 7 +/- 4 mm (3 mm the 17mm).

The average time of operation was 157 minutes (90 the 240 min). The intraoperative more frequent complication was the bleeding by lesion of venous splenic pedicle that occurred in five patients, all controlled without difficulties. Ten cases (29.4%) were submitted to blood transfusion. Half received only concentrated of platelets to correct thrombocytopenia evidenced on pre-operatively.

There was no operative mortality. There were immediate complications in three cases (8.8%) – one paralytic ileum resolved with conservative treatment; one wound bleeding controlled by suture and one left subphrenic collection and respiratory infection treated with antibiotics. The hospital stay was in average 11
In evaluation of sixth month the patients were in good clinician condition. In that time they didn't have ascites, signs of liver failure or episodes of bleeding.

The summary of statistical results of variceal manometry is shown in Table 1.

The analysis of variance found significant difference among the medium of pressure on the three occasions (P <0.001). For the identification of moments that presented differences was used the Tukey multiple test of comparisons (Table 2) giving significant decrease in pressure in the three moments of evaluation (Figure 1).

The distribution of local varicose veins is seen in Table 3. The test of marginal homogeneity showed significant difference between distributions of local only between the pre-operative and the late post-operative (p=0.048).

**Fundamental color and signs of red color of varicose veins of esophagus**

The distribution of colors of varicose veins of esophagus is in Table 4. The result of Cochran test showed significant difference between the proportions of varicose veins of blue color and white color on the three occasions of evaluation (p<0.001). The test of McNemar showed varicose veins of blue color in lower quantity on late post-operative (p=0.002) than in the immediate and pre-operative periods (p=0.003).

**TABLE 1 - Pressure of varicose veins of esophagus on pre-operative, immediate post-operative and late post-operative periods**

<table>
<thead>
<tr>
<th>Period</th>
<th>Pressure at the varicose veins of esophagus (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n°</td>
<td>Average</td>
</tr>
<tr>
<td>Pre-operative</td>
<td>30</td>
</tr>
<tr>
<td>Post-operative (immediate)</td>
<td>30</td>
</tr>
<tr>
<td>Post-operative (late)</td>
<td>30</td>
</tr>
</tbody>
</table>

**TABLE 2 - Results of multiple Tukey test to identify the different occasions of varicose veins pressure**

<table>
<thead>
<tr>
<th>Comparisons *</th>
<th>Difference (mean values)</th>
<th>p</th>
<th>95% of confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0 and T1</td>
<td>6.3</td>
<td>&lt; 0.001</td>
<td>4.5 the 8.0</td>
</tr>
<tr>
<td>T1 and T2</td>
<td>2.7</td>
<td>&lt; 0.01</td>
<td>1.0 the 4.4</td>
</tr>
<tr>
<td>T0 and T2</td>
<td>9.0</td>
<td>&lt; 0.001</td>
<td>7.3 the 10.7</td>
</tr>
</tbody>
</table>

* T0 = pre-operative; T1 = post-operative (immediate); T2 = post-operative (late)

**FIGURE 1 – Pressure of esophageal varices in different times**

**TABLE 3 - Distribution of frequencies of caliber and local of varicose veins of esophagus, in relation to the occasions of evaluation**

<table>
<thead>
<tr>
<th>Period</th>
<th>Caliber of varicose veins</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent</td>
<td>Thin</td>
</tr>
<tr>
<td>Pre-operative</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Post-operative (immediate)</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Post-operative (late)</td>
<td>1</td>
<td>8</td>
</tr>
</tbody>
</table>

**TABLE 4 - Colors and signs of red color of varicose veins of esophagus, in relation to the occasions of evaluation**

<table>
<thead>
<tr>
<th>Period</th>
<th>Color of varicose veins</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>White (%)</td>
<td>Blue (%)</td>
</tr>
<tr>
<td>Pre-operative</td>
<td>2 (7.1)</td>
<td>26 (92.9)</td>
</tr>
<tr>
<td>Post-operative (immediate)</td>
<td>3 (10.7)</td>
<td>25 (89.3)</td>
</tr>
<tr>
<td>Post-operative (late)</td>
<td>14 (50.0)</td>
<td>14 (50.0)</td>
</tr>
</tbody>
</table>

**TABLE 3 - Distribution of frequencies of caliber and local of varicose veins of esophagus, in relation to the occasions of evaluation**

<table>
<thead>
<tr>
<th>Period</th>
<th>Signs of red color</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present (%)</td>
<td>Absent (%)</td>
</tr>
<tr>
<td>Pre-operative</td>
<td>22 (78.6)</td>
<td>6 (21.4)</td>
</tr>
<tr>
<td>Post-operative (immediate)</td>
<td>16 (57.1)</td>
<td>12 (42.9)</td>
</tr>
<tr>
<td>Post-operative (late)</td>
<td>8 (28.6)</td>
<td>20 (71.4)</td>
</tr>
</tbody>
</table>
(p<0.001). The test of McNemar showed significant difference only between the pre-operative and the late post-operative times (p<0.05).

**Gastric varicose veins and portal hypertension gastropathy**

The distribution of varicose gastric veins is shown in Table 5. The test of Cochran showed no significant difference among the proportions of gastric varicose veins on the three occasions of evaluation (p=0.495).

The distribution of gastropathy is in Table 5. The test of Cochran revealed significant differences among the proportions of gastropathy on the three occasions of evaluation (p=0.006). The paired comparison based on McNemar, showed significant difference only between the pre-operative and the late post-operative periods (p<0.05).

<table>
<thead>
<tr>
<th>Period</th>
<th>Gastric varicose veins</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present (%)</td>
<td>Absent (%)</td>
</tr>
<tr>
<td>Pre-operative</td>
<td>16 (53,3)</td>
<td>14 (46,7)</td>
</tr>
<tr>
<td>Post-operative (immediate)</td>
<td>15 (50,0)</td>
<td>15 (50,0)</td>
</tr>
<tr>
<td>Post-operative (late)</td>
<td>12 (40,0)</td>
<td>18 (60,0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Period</th>
<th>Gastropathy</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present (%)</td>
<td>Absent (%)</td>
</tr>
<tr>
<td>Pre-operative</td>
<td>22 (73,3)</td>
<td>8 (26,7)</td>
</tr>
<tr>
<td>Post-operative (immediate)</td>
<td>20 (66,7)</td>
<td>10 (33,3)</td>
</tr>
<tr>
<td>Post-operative (late)</td>
<td>13 (43,3)</td>
<td>17 (56,7)</td>
</tr>
</tbody>
</table>

**TABLE 5 - Gastric vein varicose and gastropathy, in relation to the occasions of evaluation**

**DISCUSSION**

On the last two decades the endoscopic measure of pressure of varicose veins of esophagus proved to be efficient in the identification of patients with elevated risk of bleeding allowing definition of more accurate criteria to the prevention of primary high digestive bleeding, especially in cirrhosis. Also proved to be effective evaluation of several modalities of treatment. In that connection, was used the manometry of varicose veins of esophagus, to investigate the effects of ligation of gastric left vein.

In present paper, the evaluation pre-operative period revealed pressure of 22,3 + / -2,59 mmHg. These results indicate the existence of a high regime pressure at the varicose veins of patients with hepatosplenic schistosomiasis and prior bleeding, reinforcing the need of surgical treatment order to control the bleeding.

Contrary to cirrhosis, the pressure of varicose veins of esophagus in schistosomiasis has been object of few papers. The results obtained at the investigations are next to the observed on present study, assuring manometry of varicose veins of esophagus by the method of balloon a good position on research.

In bleeding, is not recognized yet a varicose value of pressure of veins of esophagus with capacity to discriminate the more risky population. Therefore, it is used balloon Freire technique to compare the pressure of varicose veins, considering value equal or superior to 20 mmHg as more risky. So far, 85% of patients of this study had pressure level above it.

The confrontation of hemodynamic state of varicose veins with other parameters to predictive the bleeding - as their endoscopic aspects - has shown correlation between them. The present study confirms the importance of varicose veins size as criterion more associated with the risk of hemorrhage. The decrease of pressure of varicose veins of esophagus, after the ligation of gastric left vein is based in hemodynamic concepts well known. Invoking the law of Ohm, that establishes the pressure as product of flow by resistance, the fall of pressure is consequent to reduction of blood flow on territory of varicose veins, after the operation. Therefore, the ligation of gastric left vein interrupts the main blood pathways to the region of varicose veins, and the splenectomy, to the decrease the portal pressure.

The pressure levels at the varicose veins remained below of 20 mmHg in all the cases revealing a good response to operation by absence of hemorrhagic elapse. The endoscopic characterization of varicose veins assumes particular importance. However, by the fact of containing element of subjectivity, the criteria have been modified. In that connection stands the classification proposal by Japanese Society that standardized four aspects of varicose veins of esophagus (size, fundamental color, extension and signs of red color) and the presence of erosive esophagitis. Such aspects proved to be useful in evaluation of risk of bleeding.

The size of varicose veins of esophagus is considered the endoscopic indicator that maintains more close relationship with the risk of bleeding. This paper confirmed such evidence. The endoscopic control of varicose veins of esophagus, after the surgical treatment, in portal hypertension has been utilized to assess the effectiveness of the operation. The disappearance or the decrease of size of varicose veins are accepted as criteria of successfully therapy.

On post-operative six months follow-up
was found significant reduction in proportion of varicose veins of thick caliber (from 63.3% on pre to 30% on post). Also increased significantly the percentage of varicose veins of thin caliber (6.7% to 26.7%) and of average caliber (30% to 40%). However, considering the evolutionary aspect of size of varicose veins, was observed disappearance in a case (3.3%) and reduction in 14 (46.7%), that makes 50% of series.

In this paper, the ligature of gastric left vein proved to be effective in reducing the number of varicose veins with more risk of bleeding. However, in terms of reduction of size, there is reason of concern, because only half of patients had disappearance or decrease of size. However, the considerable fall of pressure of varicose veins of esophagus observed in that time, could neutralize the effects of size of varicose veins and, thus, decrease the impact on the tension (considered the main responsible for the bleeding).

The risk of bleeding remain low after the ligature of gastric left vein. Such aspect highlights the importance of measure of pressure of varicose veins and at the same time raises questions to effectiveness of control based only in dimension of varicose veins. Although recognized important up to 40 years, the signs of red color became more valuable in the last two decades considering the size of varicose veins as indicator more correlated to risk of bleeding. The signs of red color represent anatomical distortion of vascular plot on territory of varicose veins. The evolution of signs of red color at the varicose veins, after the ligature of gastric left vein, is identical to size of varices. On post-operative immediate period decreased the proportion of patients with signs of red color (from 78.6% to 57.1% difference not significant). Six months after the operation only eight cases (28.6%) exhibited signs of red color at the varicose sites, with significant reduction in relationship to pre-operative (p<0.001).

On regards to location the varicose veins, they superiorly reached the upper parts. It possible that such phenomenon occurs by a mechanism of accommodation to more blood flow resulting in formation of cords of more extension. In present paper, was observed varicose veins up to superior esophagus (50%). After the ligature of left gastric vein the proportion of varicose veins located to the superior third of esophagus fell to 39.3% on immediate reaching 28.6% on late follow-up of six months. Therefore, the operation showed efficiency in decrease the varicose veins of more extension.

The fundamental color of varicose veins, defined as white or blue translates the degree of vascular congestion. Varicose veins of blue color are recognized as independent factor of risk of bleeding. In this paper, there was high prevalence of varicose veins of blue color (92.3%) before operation - evidencing good correlation between that indicator and the occurrence of bleeding. The proportion of varicose veins of blue color decreased significantly after the operation (89.3% on immediate and 50% in late evaluation). In compensation, was observed increase on percentage of varicose veins of white color (10.7% and 50%).

The classification of JSRPH adopted in this paper also included the evaluation of erosive esophagitis, not found in any case. This reinforce the varicose break as the result of portal hypertension.

On present study were identified varicose gastric veins in 53.3% of cases on pre-operatively phase. All had continuity with varicose veins of the esophagus and were classified as esophagogastric varicose veins type 1. In contrast with the effects on the varicose veins of esophagus, the ligature of gastric left vein determined only tenuous repercussion on the varicose veins of the stomach. These varicose veins decreased from 53.3% on pre-operative to 50% on immediate post-operative period coming to 40% on six months.

The hypertension portal gastropathy has been associated to more risk of bleeding both in cirrhotic as in schistosomiasis. In present series, gastropathy was found in 73.3% of cases, 53.3% in light form and 20% in intense, close to observed in other studies. The frequency of gastropathy decreased gradually after the ligature of gastric left vein. The intensity of gastropathy also decreased on late post-operative time reflecting the decrease of venous congestion on splanchnic territory due of the reduction of portal pressure by splenectomy. Additionally, the ligature interrupts part of blood contribution to the proximal stomach, decompressing the regional vascular territory.

CONCLUSION

In patients with hepatosplenic schistosomiasis with a previous history of variceal hemorrhage, splenectomy and gastric vein ligation was effective in reducing the main hemorrhagic risk factors until the sixth month of follow-up, indicating a good way to control the bleeding episodes.
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