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Original Article

OUTCOME OF PARTIAL SPLENECTOMY FOR HYPERSPLENISM IN CHILDREN WITH THALASSEMIA

M RAHMAN[1], SK MONDAL[2], AL KABIR[3], R AMIN[3]

Abstract

Background: Total splenectomy, exposes children to the high risk of overwhelming postsplenectomy infections (OPSI). To avoid these adverse consequences, partial splenectomy has long been practiced for thalasseemia in children. It has been reported that the partial splenectomy keeps the child immunologically competent, hematologically stable with minimum blood transfusion and makes their life more comfortable in comparison to total splenectomy.

Objectives: To compare the results of partial and total splenectomy.

Methodology: This prospective interventional comperative study was done in the department of Pediatric Surgery, BSMMU from 2010 to 2012. Children who underwent partial splenectomy were considered as the case and who underwent total splenectomy as the control. Number of blood (RCC) transfusions (ml/ kg/year), Peripheral blood film (Hb%, WBC count, platelet count, Howell-Jolly body, serum bilirubin), volume of liver (ml), volume of spleen (ml), number of OPSI case, were compared between the case and control groups both pre and postoperatively.

Results: Postsplenectomy blood transfusion requirement is comparatively more decreased in control group than case group. The inter group difference at 6 month is significant (p= 0.004). Peripheral blood pictures are improved in both groups. Post splenectomy hemoglobin level was increased in both groups but it was maintained at a more static fashion in control group than case group (P = 0.114). Howell-jolly body in the partial splenectomy group disappeared almost completely at month 6, while the same inclusion body in the total splenectomy group appeared in all the children (p= 0.001). There was no postsplenectomy infection in case group while two found in control group. After partial splenectomy the residual volume of the spleen was gradually increasing. The increase in volume of the liver was notably greater in the total splenectomy group than that in the partial splenectomy group (p< 0.05).

Conclusion: Partial splenectomy in patients with ²-thalassemia is effective in controlling hemolysis, improving peripheral blood picture while preserving the residual splenic phagocytic and immune function.

1. Dr Mizanur Rahm, Assistant Professor, Dept of Pediatric surgery, Khulna Medical College, Khulna.
2. Dr Susankar Kumar Mondal, Assistant Professor, Dept of Pediatric Surgery, BSMMU, Dhaka
3. Dr Amin Lutful Kabir, Associate Professor, Dept of Hematology, BSMMU, Dhaka
4. Md Ruhul Amin, Professor & Chairman, Dept of Pediatric Surgery, BSMMU, Dhaka
5. Prof. Matiur Rahman, Dept of Pediatric Surgery, BSMMU, Dhaka

Correspondence to : Dr Mizanur Rahm, Assistant Professor, Dept of Pediatric surgery, Khulna Medical College, Khulna, Mobile: 01712260060, Mail: dr.mizanur64@yahoo.com

Introduction

Thalassemias are a diverse group of genetic blood disorders characterized by abnormal production of ± or ² chains of hemoglobin resulting into microcytic hypochromic anemia of varying degree. HbE/²-thalassemia is a variant of thalassemia commonly found in South-East Asian region. [1] Children affected ²-thalassemia show no abnormality at birth but become progressively anemic after six months of age. The features of hypersplenism e.g. anemia, thrombocytopenia, leucopenia and hepatosplenomegaly are also progressively becomes evident [2]. Treatment of thalassemia are mainly symptomatic or palliative e.g. blood transfusion, iron chelation and splenectomy. [3-4] Total splenectomy has long been done to relieve these symptoms. Total splenectomy eliminates the discomforts e.g. dragging abdominal pain, improves the quality of life and peripheral blood picture but the adverse consequences of total splenectomy had since been unwarranted. Total

splenectomy, exposes children to the high risk of overwhelming postsplenectomy infections (OPSI) caused by encapsulated organisms e.g. *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenza* etc. OPSI is a fatal complication of splenectomy and should be treated promptly [5-7] The risk of OPSI is more in children under five years of age. The incidence of OPSI has been estimated to be 4.4% in children and 0.9% in adults. [8] Although, the risk of OPSI may be reduced by routine vaccination and administering prophylactic antibiotics against encapsulated organisms, it still persists due to several causes. [7, 9] Besides OPSI, all the splenectomized patients are liable to many other long term adverse effects. Splenectomy reduces the ability of the reticuloendothelial system to remodel the red blood cells. As a result, reticulocyte count increases in the peripheral blood.

Inclusion bodies e.g. Howell-Jolly Bodies, Heinz Bodies and abnormal cells also appear in the peripheral blood. Howell-Jolly Body in the peripheral blood, though not completely sensitive but an important marker to identify the degree of hyposplenism to represent the risk of OPSI. [10]

The adverse effects of total splenectomy, especially the severity of the OPSI has led to the search for alternative surgical techniques that preserve the adequate splenic tissue. Scientists discovered that the presence of splenenculi or autotransplanted splenic tissue has some degree of protective role against OPSI. So, autotransplantation or the preservation of splenenculi after total splenectomy has been practiced to prevent post splenectomy sepsis. [11- 12]

Total splenectomy has been practiced for a long time for palliation for thalassemic children. Conceivably it provides the best opportunity for palliation in thalassemic children by removing a substantial portion of reticuloendothelial system. But it renders children deficient to defensive functions of spleen e.g. risk of infection by encapsulated organisms that may lead to overwhelming post splenectomy infection (OPSI). [13] In order to obviate this problem it has been thought that partial splenectomy may offer a better balance between palliation and retention of some host defense against the aforesaid infection. [12]

It is considered that partial splenectomy is a safe and better alternative to total splenectomy for palliation of thalassemia patients when splenectomy is indicated. Therefore this study has been designed to compare the short term outcomes of partial and total splenectomy in thalassemia patients to testify the above proposition.

Methodology

Study design:

This is a prospective interventional study carried out in the Department of Pediatric Surgery, BSMMU, Dhaka , from July 2010 to June 2012. A total of 30 children from 4 – 13 years of age having thalassemia attending for splenectomy was the study population and was divided into **case** (30 patients undergoing partial splenectomy) and **control** (30 patients undergoing total splenectomy) groups.

Variables of the study:

- Number of blood (RCC) transfusions (ml/ kg/ year).
- Peripheral blood film (Hb%, WBC count, platelet count, Howell-Jolly body, s.bilirubin, reticulocyt count).
- Volume of liver (ml).
- Volume of spleen (ml).
- Number of OPSI case.

The operative procedure adopted for partial splenectomy is summarized as follows:

The segmental blood supply of the spleen is “bisegmental” and in 20% of cases there might be a middle division making the segmental blood supply “trisegmental” [(14-17)] (Morganstern 1979, Decker 1986, Spitz 1995 & Liu 1996). Cut or “splenotomy” was done at the line of demarcation using electrocautery. Bleeding from small arterial branches and venous tributaries were controlled by transfixation ligation using figure of 8 or running suture. When the bleeding was severe, temporary occlusion of the splenic artery with the thumb and forefinger or by drawing a loop around the splenic artery was used till these vessels were occluded. Parenchymatous bleeding, usually from the small sinusoids and this was controlled by electrocautery, horizontal mattress suture from one capsular edge of the cut surface to the other edge.

Patient evaluation and follow-up:

Every patient was evaluated both preoperatively and postoperatively by clinical, hematological, biochemical and ultrasound examination. Clinical evaluation consists of OPSI (fever, cough, tachycardia, tachypnoea, respiratory distress), and hepatosplenomegally etc. Laboratory parameters consist of Hb (gm/dl), platelet count, WBC count, s.bilirubin and reticulocyte count were assessed and compared between groups. Decrease in the amount of blood transfusion (<180ml/

kg/year or <15 ml/kg/month) or increase in interval of blood transfusion, maintenance of Hb % at a static level (8 -10 gm/dl), decrease in s.bilirubin, and reticulocyte count in the postoperative periods were interpreted as effective control of hemolysis after splenectomy.

Evaluation of splenic function by measuring peripheral blood film:

As splenic function declines, Howell-Jolly body in the blood increase in number and their presence is a strong indicator of risk for bacterial infection (William- 2007) [19]. Decrease or remaining same as preoperative state of Howell-Jolly body, decrease in reticulocyte count in the peripheral blood after partial splenectomy was interpreted as the evidence of retained phagocytic function by the splenic remnant (Corazza 1990 & Brigden 1985) [10, 26].

Ultrasonographic evaluation of liver and spleen:

Ultrasonographic assessment of the liver and spleen performed postoperatively at 7day, 3 month and 6 month period and compared between groups to assess the effect of partial and total splenectomy on them.

Results

Demographic characteristics:

The mean ages of the partial splenectpmy (case) and total splenectomy (control) groups were 6.9 ± 2.0 and 8.1 ± 3.5 years respectively (p = 0.511). The proportion of female patients in the case group was somewhat higher (60%), while males and females were almost equal in the control group.

Table I

Comparison of age and sex between two groups

Age (years)	Group		p-value
	Partial splenectomy (n = 15)	Total splenectomy (n = 15)	
< 5	2(13.3)	4(26.7)	
5 – 10	11(73.3)	7(46.6)	
> 10	2(13.3)	4(26.7)	
Mean ± SD	6.9 ± 2.0	8.1 ± 3.5	0.511
Sex*			
Male	6(40.0)	7(46.7)	
Female	9(60.0)	8(53.3)	

^ Data were analysed using Fisher's Exact Test.

Data were analyzed using the Mann Whitney Test and were presented as mean ± SEM.

Preoperative pictures:

Preoperative hematological pictures of case and control groups are illustrated in table II. All the hematological and other variables (Table II) were fairly comparable between case and control groups (p > 0.05).

Table II

Comparison of preoperative values between groups

Variables	Group		p-value
	Case (n = 15)	Control (n = 15)	
Haemoglobin# (g/dl)	6.5 ± 1.8	6.6 ± 1.2	0.807
Reticulocyte count# (%)	3.4 ± 0.7	2.4 ± 0.3	0.495
Serum billirubin# (mg/dl)	1.9 ± 1.1	2.0 ± 0.6	0.683
Platelet count# (per cu-mm)	92600 ± 16623	83866 ± 12130	0.675
Howell-jolly body* (present)	6(40.0)	8(53.3)	0.358
WBC count# (per cu-mm)	6133 ± 530	7206 ± 555	0.173
Transfusion # (ml/kg/year)	442.7 ± 28.0	451.3 ± 27.3	0.826
Preoperative vol. of spleen# (ml)	1005 ± 363	1060 ± 314	0.581
Preoperative vol. of liver# (ml)	983 ± 1.5	982 ± 2.1	0.636

Data were analyzed using the Mann Whitney Test and were presented as mean ± SEM.

* Fisher's Exact Test was employed to analyze the data

Figures in the parentheses denote corresponding percentage.

Outcomes 7 days postoperatively:

Hematological pictures of case and control groups 7 days postoperatively demonstrate that the level of hemoglobin and percentage of reticulocytes reduced in the case group than those in the control group. The platelet count was considerably higher and total count of WBC was considerably lower in the case group than those in the control group.

Outcome of patients 3 months postoperatively:

Hematological pictures of case and control groups at 3 months postoperatively show that level of hemoglobin was almost equal in both case and control groups ($p = 0.695$). All the cellular counts (reticulocyte <0.001, platelet <0.001 and WBC <0.007) show much wider difference between groups. Howell-jolly body in the case group reduced to 20%, but it increased to 100% in the control group ($p < 0.001$). One patient of control group developed fever while none in the case group (Table IV).

Outcome of patients 6 months postoperatively:

After 6 months of operation the case and control groups were observed to be significantly different with respect to all of the figures of blood picture except serum bilirubin. Considering liver volume, control group experienced more increase than the case group. Regrowth of spleen continued. Another patient developed flue-like symptom and fever (OPSI) in the control group while none in the case group (Table V).

Table III

Outcome of patients 7 days postoperatively between groups

Variables	Group		p-value
	Case (n = 15)	Control (n = 15)	
Hemoglobin# (g/dl)	8.6 ± 0.2	9.8 ± 0.4	0.014
Reticulocyte count# (%)	2.4 ± 0.6	6.9 ± 0.5	< 0.001
Serum billirubin# (mg/dl)	1.6 ± 0.2	1.5 ± 0.1	0.495
Platelet count# (per cu-mm)	398666 ± 40069	336000 ± 29869	0.220
Howell-jolly body* (present)	6(40.0)	8(53.3)	0.358
WBC count# (per cu-mm)	19066 ± 933	22133 ± 2080	0.189
OPSI	None	None	
Transfusion# (ml/kg/year)	Not needed	Not needed	——-
Volume of spleen# (ml)	197.6 ± 12.3	——-	——-
Liver volume# (ml)	983 ± 0.4	982 ± 0.5	0.426

Data were analyzed using the Mann Whitney Test and were presented as mean ± SEM.
* Fisher's Exact Test was employed to analyze the data
Figures in the parentheses denote corresponding percentage.

Table IV

Outcome of patients 3 months after operation between groups

Variables	Group		p-value
	Case (n = 15)	Control (n = 15)	
Haemoglobin# (g/dl)	9.8 ± 0.4	9.8 ± 0.2	0.695
Reticulocyte count# (%)	1.7 ± 0.2	6.1 ± 0.4	<0.001
Serum billirubin# (mg/dl)	1.7 ± 0.1	1.0 ± 0.1	0.726
Platelet count# (per cu-mm)	242866 ± 21833	402333 ± 28371	< 0.001
Howell-jolly body* (present)	3(20.0)	15(100.0)	< 0.001
WBC count# (per cu-mm)	12000 ± 941	17720 ± 1741	0.007
Transfusion# (ml/kg/year)	107.3 ± 3.7	97.7 ± 2.6	0.402
OPSI	None	1(6.7)	0.62
Volume of spleen# (ml)	237.3 ± 42.3	——-	——
Liver volume# (ml)	985 ± 0.4	987 ± 0.4	0.714

Data were analyzed using the Mann Whitney Test and were presented as mean ± SEM. * Fisher's Exact Test was employed to analyze the data
Figures in the parentheses denote corresponding percentage

Table V

Outcome of patients 6 months after operation between groups

Variables	Group		P-value
	Case (n = 15)	Control (n = 15)	
Hemoglobin# (g/dl)	8.4 ± 0.6	9.6 ± 0.4	0.114
Reticulocyte count# (%)	1.7 ± 0.2	5.1 ± 0.6	< 0.001
Serum billirubin# (mg/dl)	1.0 ± 0.1	0.9 ± 0.1	0.726
Platelet count# (per cu-mm)	211333 ± 23500	344666 ± 33578	0.003
Howell-jolly body* (present)	1(6.7)	15(100.0)	< 0.001
WBC count# (per cu-mm)	9193 ± 621	14366 ± 1015	< 0.001
Transfusion# (ml/kg/year)	133.0 ± 7.8	107.0 ± 2.7	0.004
OPSI	None	1(6.7)	0.62
Volume of spleen# (ml)	296.3 ± 63.3	——-	——-
Liver volume# (ml)	988 ± 1.3	991 ± 1.6	0.073

Data were analyzed using the Mann Whitney Test and were presented as mean ± SEM.
* Fisher's Exact Test was employed to analyze the data
Figures in the parentheses denote corresponding percentage.

Postpartialsplenectomy residual splenic enlargement:

Residual splenic size after partialsplenectomy is gradual increase in pattern. The initial size after partial splenectomy was 197 ml. At three month postoperative follow up it was 237 ml and at six month it was 297ml.

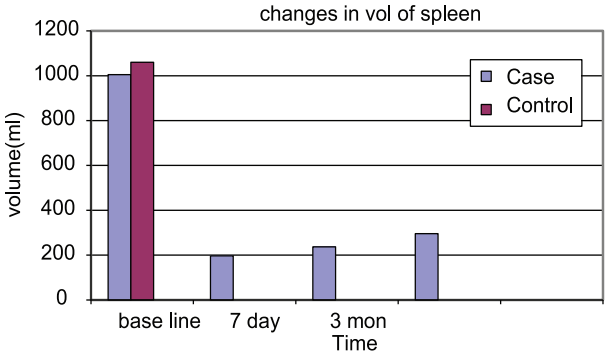

Fig. 1: *Changes in volume of spleen from baseline to endpoint*

Discussion

Total splenectomy has long been the procedure of choice for patients with thalassemia since mid 19th century. It has been a logical treatment modality for palliation in children with thalassemia patients. The spleen has several immunological functions to perform. It may phagocytose blood-borne antigens in the presence of low concentrations of antibodies, participate in opsonisation, generate specific antibodies and maintains the integrity of the complement pathway and has an 'immune memory'. As the spleen plays unique role in the clearance of particulate antigens including pathogenic bacteria from the peripheral blood and is also a key lymphoid organ in early childhood. Therefore the decision to perform total splenectomy before the age of 5 years is not a wise one .[19-20] To preserve these functions, partial splenectomy, as an alternative to total splenectomy has been proposed in thalassemia patients.

In the present study, the age and sex (Table-I) distribution between partial and total splenectomy groups were fairly comparable at the baseline. All the hematological variables (hemoglobin levels, reticolocyte count WBC

count, platelate count, Howell-Jolly body), frequency of blood transfusion, volume of the spleen and liver were fairly comparable between partial and total splenectomy groups before surgical intervention.

Preoperative blood transfusion requirement (Table-II) was almost equal in both groups. In the postoperative periods (7 days, 3 months and 6

months) the blood transfusion requirement has decreased in both groups but the rate of reduction is more pronounced in the control group. In the case group it had reduced from 442.7 ml/kg/year (36.9ml/kg/month) to 107ml/kg/year (8.9ml/kg/month) at three months (Table VI). At six month it had increased to133.0 ml/kg/year (11.08 ml/kg/month) for the same group. On the other hand in the control group, blood transfusion requirement had reduced from 451.3 ml/kg/year (37.6ml/kg/month) to 97 ml/kg/year (7.3ml/kg/moth) at three months and to 107 ml/kg/ year (8.91 ml/kg/month) at six months. Bahador and his associates [21] showed in a comparative study between partial and total had reduced threefold from 10 to 25ml/ kg/month every 1 to 2 weeks to every 4 to 6 weeks which is consistent with our study.

At the same time the Hb level had increased at least about 2 gm/dl from its preoperative value at three months (Table IV) and remained static up to 6months (Table V) postoperatively. At three months postoperatively the amount of Hb had increased in both groups and became equal (9.8 gm/dl) (p = 0.695). It remained stable at this level (9.8 gm/dl) at six months postoperatively in the control group while it had reduced to some extent (8.4 gm/dl) in the case group but the difference is not significant (p= 0.114). de Buys and his associates [22] in a study of partial splenectomy on 5 children demonstrated that the level of hemoglobin had increased from 4.7 g/dl before surgery to 8.7 g/dl after surgery which is consistent with the findings of the present study. However, Rice and his colleagues [23] demonstrated in a series of follow up of 25 children from one month to 4 years with symptomatic hemolytic anemia showed that though hemoglobin level increases rapidly in first month following partial splenectomy, it is no longer kept at this level in long-term follow up. As our follow up period was only 6 months, we are not in a position to comment on the change in hemoglobin level in the long run.

The cellular counts e.g. platelet and WBC showed (Table III) a sudden rise in both groups but in case of platelet count it was considerably higher in the partial splenctomy group than that in the total splenectomy group. The abrupt rise in WBC count was significantly more in the total splenectomy group than that in the partial splenectomy group. The WBC count in the former group was reduced to a normal range on the 3rd month while the same variable in the latter group also reduced but still maintained at a much higher level than the upper limit of normal range.

At month 3 (Table IV), the platelet count greatly reduced in the partial splenectomy group from its 7th postoperative value, while the same parameter in the total splenectomy group had a further rise showing a wider difference between the groups. At 6 months, platelet count of both groups was reduced and was maintained within the normal range (Table V). de Montalembert and associates [12] in a similar study reported that 9 out of 24 patients had thrombocytopenia before surgery with the mean platelet count being 20600/Cu-mm of blood. In the third week after surgery all of them changed to thrombocytosis with a mean platelet count of 831000/Cu-mm of blood. But one year after surgery the mean platelet count had fallen to 411000/Cu-mm of blood which is quite consistent with the findings of the present study. Consistent with the present study, Nouri et al [24] in an another study demonstrated that the platelet count after partial splenectomy increased from 134000/Cu-mm of blood before surgery to 540000/Cu-mm of blood immediately after surgery.

Howell-Jolly Body (HJB) in the partial splenectomy group started decreasing while it is increasing in total group in the postoperative periods. Preoperatively, six (40%) patients of partial group and 8 (53.3%) patients of total group showed HJB in their peripheral blood (Table II). At 7 day postoperatively the picture was same (Table III). At 3month and 6 month postoperatively HJB was found only in 3(20%) and 1(6.7%) patients of partial group respectively, while the same inclusion body was found in all the patients (100%) of total group (p< 0,001) (Table IV & V). Rice et al [23] and Vasilescu et al [25] reported clearance of the Howell - Jolly body after partial splenectomy but they did not mention how it was possible. In the present study, clearance of Howell-jolly body in five patients after partial splenectomy in contrary to total splenectomy indicates preservation of splenic phagocytic function.

The rate of postsplenectomy infection (OPSI) was only 13. 3% in total group while 0% in partial group. One patient of control group near three months postoperative period reported fever and another one at six months complained flue-like symptom and fever (table-IV & V), while none in the case group reported

any symptoms of OPSI. These two patients were given admitted in the hospital and were evaluated clinically, hematological, blood culture and sensitivity test. Finally they were recognized as mild OPSI. Intravenous fluid, injection penicillin, paracetamol suppository and other supportive therapy were administered to treat (OPSI). de Montalembert (1990)[12] found no infection after partial splenectony in six children which is consistent with our study. The less incidence of postsplenectomy infection in the partial group in our study indicates that the immune and the phagocytic function of the spleen were preserved.

Regrowth of the residual spleen was observed in our study after partial splenectomy (Fig- I). The preoperative mean splenic volumes were 1005 ml and 1060 ml in the case and control groups respectively. In the immediate (7^{th}) postoperative period, the mean residual splenic volume was 197.6 ml (19.6% of preoperative value). After three months the volume increased to 237.3 ml (23.6%) and after six months to 296.4 ml (29.4%). The mean size of the splenic remnant remained between 19.6% and 29.4% of the baseline volume through the study period. Rice and his colleagues [23] in a study throughout two years showed that splenic regrowth was between 15% and 30%. As our study period was only 6 months, it is obvious that the rate of regrowth is more pronounced in our study. Although the objective of our study was to retain 5% to 10% of its preoperative value we could not do that for several causes.

In our study postsplenectomy liver volume is increasing in both groups but the increase is greater in the total splenectomy group (from 982ml to 991ml) than that in the partial splenectomy group (from 983 ml to 988 ml) suggesting that difference is not significant ($P < 0.05$) (TableIII & Table V).

From the above discussion it is evident that partial splenectomy in patients with thalassemia major is effective in controlling hemolysis, preserving the hematological variables, splenic functions and precluding postsplenectomy hepatomegaly. But splenic regrowth is a drawback which may convert it into secondary total splenectomy in the future.

Regarding small sample size and short follow up period, it is recommended further randomized controlled with prolonged follow up study to be done in such type of study.

Conclusion

From the findings of the present study it can be concluded that partial splenectomy in patients with ²-thalassemia is effective in decreasing transfusion requirement and haemolysis, improving peripheral blood pictures and preserving splenic phagocytic and immune functions. Although the reduction in haemolytic rate is not as much as that observed in total splenectomy, it is of sufficient magnitude to provide clinical benefit. Partial splenectomy also reduces the extramedullary hemopoitic activity

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