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Splenectomy in Patients with Beta Thalassaemia Major

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Abstract

Objective: To evaluate the effect of splenectomy, in patients with beta thalassaemia major, on blood transfusion rates and blood counts

Methodology: In this prospective descriptive study patients with beta thalassaemia major, who underwent splenectomy were included. The study was conducted at deptof thalassaemia, Pakistan Institute of Medical Sciences, Islamabad from January 2018 to December 2018. Thalasseamics with signs of growth retardation, poor health, leucopenia, thrombocytopenia, increased transfusion demand (more than 250 ml/kg/year or more than four transfusions per month) or respiratory embarrassment (mechanical discomfort) from massive splenomegaly were included. The pre- and post-splenectomy transfusion requirement was calculated by dividing the volume of packed red cells used for transfusion in one year by the patient's weight at mid-year and expressing the result as ml/kg/year.Hypersplenism was established in patients having splenomegaly with accompanying anaemia, leucopenia, thrombocytopenia or any combination of these with hypercellular bone marrow.

Results: The majority were male (60.65%). The average hospital stay was six days. Pre-splenectmy, majority of patients had transfusion requirements of more than 350 ml/kg/l. Blood tranfusion requirements revealed a significant fall (less than 250 ml/kg/l) post splenectomy. One year follow up showed significant fall in transfusion rateand significant increase in haemoglobin. In 23.94% of patients, splenectomy was performed at an age less than ten years old.

Conclusion: Splenectomy has a positive outcome on blood transfusion rates and haemoglobin levels in patients with beta thalassaemia major.

Key Words: Splenectomy, Beta Thalassaemia Major, blood transfusion rate, hypersplenism.

Introduction

Beta Thalassaemia Major remains a significant health problem throughout the world. It represents a heterogeneous group of inherited diseases characterized by the lack of or reduced production of β- chains. The typical patho-physiology leads to increased destruction of red blood cells by reticuloendothelial system, in particular by the spleen, resulting in its enlargement. There is also an extramedullary haemopoiesis. All this leads to increase in size of spleen with peripheral blood cytopenias. Blood transfusion and iron chelation are the main stay of thalassaemia major management. The excessive destruction of red blood cells and extramedullary haemtopoiesis cause splenomegaly which increase the transfusion requirements. Splenectomy is an option to avoid this complication, thus reducing the frequency of blood transfusion.[1-4]Splenectomy is justified in a case where there is massive splenic enlargement, hypersplenism and an increased transfusion requirement.[5-8]

With proper transfusion, supported by judicious iron chelation, patients with thalassaemia are expected to have minimal splenomegaly and marrow expansion complications. However, massive splenemogaly and hypersplenism with increasing transfusion requirements is commonly seen in inadequately managed thalassaemics more commonly splenectomy is contemplated in localities where management is suboptimal .[9-11]

Patients who require more than 200 – 250 mg/kg of red cell concentrates per year to maintain a haemoglobin level of 10 G /dl are supposed to benefit from splenectomy.[12] .If a decision to perform splenectomy is made, then partial , full and laparoscopic splenectomy are the options.[13,14]Partial splenectomy is a complicated surgery utilized to preserve some splenic function. It should be reserved for infants requiring splenectomy. Full splenectomy can usually be performed by laparoscopic technique. However open procedure is preferred in cases of marked splenomegaly.[15]

Authorship Contribution: [1,2]Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work,[1,2,3]drafting the work or revising it critically for important intellectual content· ·[3]Data Analysis, literature review.

Funding Source: none
Conflict of Interest: none
Received: July10, 2021
Accepted: Feb 09, 2022

Splenectomy is known to be associated with short and long term complications such as infective, hypercoagulability and thromboembolism. Recurrence of anaemia may occur due to the presence of splennuculi which may enlarge following splenectomy. Therefore it is required to detect any accessory spleen and remove during surgery.[1]Beforesplenectomy bone marrow examination can be helpful in demonstrating that the marrow is producing sufficient new cells to correct the cytopenias in the absence of spleen. [16]

Splenectomy is associated with overwhelming post splenectomy infections (OPSI). The main incriminated organsims for this complication are encapsulated bacteria, like Strep Pneumococcus, Neisarria Meningititus and Haemophilus Influenzae. It is characterized by evolution in a just few hours in association with hypotension, alteration of consciousness, or shock. It has a mortality rate of 40-50%. Preventive measures, like conjugate vaccines, antibiototic prophylaxis, increased awareness and patients' education, are believed to considerably reduce the risk of OPSI. [4, 17]

Methodology

In this prospective descriptive study patients with beta thalassaemia major, who underwent splenectomy were included. Inclusion criteria was thalasseamics with signs of growth retardation, poor health, leucopenia, thrombocytopenia, increased transfusion demand (more than 250 ml/kg/year or more than four transfusions per month) or respiratory embarrassment (mechanical discomfort) from massive splenomegaly even with lesser transfusion requirements were included. All the patients were from Thalassaemia Centre Pakistan Institute of Medical Sciences, Islamabad from January 2018 to December 2018.

The transfusion requirement, pre- and post-splenectomy, was expressed as the volume of packed red cells used for transfusion in one year divided by the weight of the patient in mid-year and expressed as ml/kg/year. Volume of each unit of packed red cells was taken as 245 ml. Mean pre-transfusion haemoglobin levels were calculated from values obtained prior to each transfusion during the year of study.[18,19]Hypersplenism was established in patients having splenomegaly with accompanying anaemia, leucopenia, thrombocytopenia or any combination of these with hypercellular bone marrow.

Preoperative vaccination against Streptococcus pneumoniae, Haemophilus influenzae type B and Neisarria meningitidus was administered to all patients 2-4 weeks before surgery. Injection Penta (against Haemophilus influenzae, Diphtheria, Pertusis, Tetnus and Hepatitis B), injection Menactra A(against Neisseria meningitidus) and injection Sanflorix (against Strep pneumoniae) was the administered regimen. Preoperatvie haemoglobin was maintained between 8-10 gm/dl. Splenectomy was performed through left transverse incision in the left hypochondrium.

Statistical analysis were carried out using statistical package for social sciences.Data are expressed as mean $\pm$ SD for continuous variables and percentages for categorical variables. An independent sample t-test was used to assess the significance of differences between preoperative and postoperative measurements for different parameters. The p-value was considered statistically significant when less than 0.05

Results

Majority were male (60.65%).Average hospital stay was six days. Two patients died due to spesis and two died because of thromboembolic episodes. All this fatal events took place three to four years post splenectomy. (Table I)

In 23.94% patient's splenectomy was performed at an age less then years. (Table II)One year follow up showed significant fall in transfusion rate and significant increase in haemoglobin. (Table III) Haemoglobin, white blood cells count and platelets count showed significant increase post-spelnectomy. (Table IV) Majority of patients had transfusion requirements more than 350 ml/kg/year, before splenectomy. (Table V) Blood transfusion requirements revealed a significant fall, less than 250 ml/kg/l) post splenectomy. (Table VI)

Table I : Patients' profile

Parameter	No(%)
Male	43(60.65)
Female	28(39.36)
Age Range (years)	6.0 – 25
Mean Age (years)	10.2 $\pm$ 2.9
Hospital stay (Days)	5 – 16
Average hospital stay (Days)	6 (79.2%)
Morbidity	02 (2.8%)
Mortality	04(5.6%)

Table II: Age range

Age (Years)	No (%)
>20	13(18)
>15 – 20	22(30.98)
>10-15	19(26.76)
<10	17(23.94)

Table III: Response to splenctomy after one year

	Before Splenectomy (Mean ± SD)	After Splenectomy (Mean± SD)	p-value
Haemoglobin (g/dl)	5.02± 1.06	7.80±0.83	<0.000
Transfusion (ml/kg/year)	352.15± 168.2	56.54± 2.97	<0.000
Ferritin (ng/ml)	7791.8± 1134.6	6327.73±119.03	0.449

Table IV: Blood counts pre- and post-splenectomy.

Parameter	Pre-Splenectomy Mean (Range)	Post-Splenectomy Mean(Range)
Haemoglobin (g/dl)	6.6(4.8-10.1)	9.2 (7.3-11.0)
WBC (X10 ^{9}/l)	5.6 (1.2-7.8)	12.8(11.2-75.2)
Platelet count (X10 ^{9}/l)	60 (40.2-67.0)	620.2(245-972)

Table V: Transfusion requirements-Presplenectomy

ml/kg/year	No(%)
>250- 350	20(28.1)
>350-450	10(14.08)
>450-550	23(32.39)
>550-650	14(19.71)
>650	4(5.63)

Table VI: Transfusion requirements-Postsplenectomy

ml/kg/l	No(%)
<250-150	15(21.12)
<150-50	35(49.29)
<50	21929.57)

Discussion

Although a surgical cure is not a goal in thalassaemia, overall these patients experience better quality of life after splenectomy.[11,20,21] Different procedures are adopted for splenectomy in thalassaemics. Total splenectomy, partial splenctomy and laparoscopic splenectomy are perfromed in patients with beta thalassaemia major.[1,5,22-25] From a technical point of view , the spleen in thalassaemics is easier to handle .Due to haemosidrosis the splenic tissue us not friable and allows for easier manipulation .[10,26]

After splenectomy an increase in haemoglobin level is observed. Most of the patients have a decrease in blood transfusion requirements , from four to five a month to a single transfusion.[2,20,24,25,27,28] Studies demonstrated fall in transfusion requirements to <150 ml/kg/ year after splenectomy, thus reducing hospital visits and improving quality of life. [1,3,21,29]

For thalassaemics, on standard treatment, the chance to be splenectomized is low during childhood. According to Piga et al (2011) the probability of undergoing splenectomy within the first 10 years of life is 57,22,16 and 07% for patients with thalassaemia born in the 1960s,1970s,1980s, and1990srespectively.[5] But in our set up, as is evident from present study ,a high proportion still undergoes splenectomy in early childhood.

Patients with thalassaemia major are predisposed to infection by altered complement activation, decreased immunoglobulin levels and increased iron. Splenectomy further increases the risk of infection. In the context of splenectomy, term Overwhelming Post Splenectomy Infection(OPSI) defines sepsis, meningitis or pneumonia, mainly caused by encapsulated bacteria .The time interval between splenectomy and OPSI could vary from days to years and overall mortality could reach 50%.[9,20] In present series it was registered in two patients. Presplenectomy vaccinations are believed to considerably reduce the risk of OPSI. Post splenectomy repeat vaccinations are advised against Strep pneumoniae (repeat five yearly) and Neissaria meningitidus (repeat five yearly). No booster vaccination is suggested against Haemophilus influenzae. Influenza virus vaccination is advised yearly.[4,9,17] Antibiotic prophylaxis is required after splenectomy. Recent guidelines recommend that patients at high risk of infections, including less than 16 or more than fifty years of age, those with inadequate response to pneumococcal vaccination or a previous episode of invasive pneumococcal disease should receive lifelong prophylaxis.[21] Broad spectrum antibiotic cover is given pre-splenectomy and continued post operatively.

Penicillin is the first option. Alternative antibiotics for patients unable to take penicillin include amoxicillin, erythromycin and trimethoprim – sulfamethoxazole. In children, for at least five years, and for adults, at least for twoyears, post-operatively antibiotic prophylaxis is usually recommended. [30,31]

Splenectomy leads to immediate reactive thrombocytosis and increase in circulating microparticles, with an increased risk of subsequent venous thromembolism, particularly within the spleno-portal system, which ranges from 0.7 – 8.0% in different studies. Patients usually present with fever and abdominal pain.[4,17,32-34] Patients who develop thromboembolism post splenectomy are treated with intravenous heparin followed by oral anticoagulants for a variable period ranging from 3 to 6 months .[35,36]

Zahra F et al (2005) reported frequency of per-operative complications 3%, early post-operative complications 10% and late complications 1.6%.[6] But now better prophylaxis with better operative procedures these complications are reduced . In present study two patients had fatal thromboemoblic episodes, at least three years after splenectomy. Splenectomy results in a hypercoagulable state, by preventing circulation of greater number of red cells altered membranes and an increase in the number of platelets. Thalassaemic red cells facilitate thrombin formation as a consequence of altered asymmetry of the membrane phospholipids with enhanced exposure of phosphotidylserine.[1,16,37-40]

Conclusions

1. Splenectomy has a positive outcome on blood transfusion rates and haemoglobin levels in patients with beta thalassaemia major
2. Immunization, proper antibiotic cover and anti-thrombotics can be considered as few of paramount measures to decrease post splenectomy infection up to a minimum level
3. Unfortunately in our set up still thalasseamics underwent splenectomy at an early age. Better the child is managed , less likely the child will develop problems which contemplate to go for splenectomy
4. Splenectomy in thalassaemics, where indicated, is a safe procedure and along with other positive outcomes leads to a better quality of life.

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