ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 12, Issue, 07, pp.12643-12646, July, 2020

DOI: https://doi.org/10.24941/ijcr.39154.07.2020

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

POST SPLENECTOMY RESPONSE AND THROMBOTIC EPISODES IN IMMUNE THROMBOCYTOPENIA

Suneeth Kuriakose and Edwin George*

Department of General Medicine, Al Azhar Medical College, Kerala, India,

ARTICLE INFO

Article History:
Received 07th April, 2020
Received in revised form
25th May, 2020
Accepted 27th June, 2020
Published online 30th July, 2020

Key Words:
Immune Thrombocytopenia,
Splenectomy, Thrombosis.

ABSTRACT

Background: In immune thrombocytopenic purpura (ITP) there is premature destruction of platelets in the reticuloendothelial system. Splenectomy is a treatment of choice in chronic ITP refractory to medical management. Objective: The aim of the study is to assess the response to splenectomy, venous thrombotic episodes associated with splenectomy. **Methods:** A retrospective cross sectional study where the data Sentence Reconstruction for ITP in appostrophe Medical college Banglore was analyzed for side effects of treatment presplenectomy; response and thrombotic episodes post splenectomy. **Results:** There was significant improvement in platelet count post splenectomy (p value 0.00). 36.6% patients had complete response and required no treatment after splenectomy; rest of the patient's required medical management to maintain hemostasis. Even though venous thrombosis was high in the laparoscopic and HALS group, it was statistically insignificant (p value 0.08). **Conclusion:** There was significant clinical response to splenectomy in ITP patients either completely or partially. Preoperative vaccinations and proper surgical methods results in lesser infections post procedure, with statistically insignificant thrombotic episodes making splenectomy a safer treatment option.

Citation: ***Suneeth Kuriakose and Edwin George.*** **2020.** "Post splenectomy response and thrombotic episodes in immune thrombocytopenia", *International Journal of Current Research*, 12, (07), 12643-12646.

INTRODUCTION

Immune thrombocytopenic purpura (ITP) also termed as idiopathic thrombocytopenic purpura is an acquired autoimmune haematological disorder (Kronkle, 2018) in which there is immune mediated destruction of platelets. Chronic ITP is defined as persistence of ITP beyond 6 months. In ITP, treatment is tailored according to the clinical scenario and treatment response. Pharmacological therapy gives good response in many patients even though drug related complications may occur. When the disease becomes refractory to drug treatment, splenectomy is a treatment option (George, 1996). It is a surgical procedure which partially or completely removes the spleen and it is done for specific clinical indications rather than specific diagnosis (Taylor, 1985). The aim of treatment is to improve platelet counts, with minimum therapeutic complications and better quality of life. In this study we analyzed 30 chronic ITP patients who underwent splenectomy, the treatment received by them prior to surgery and its related complications. We also analyzed the response to splenectomy and occurrence of thrombotic episodes post splenectomy.

Corresponding author: **Edwin George,**
Department of General Medicine, Al Azhar Medical College, Kerala, India.

MATERIAL AND METHODS

This study was a retrospective cross sectional study done over a period of 2 years from September 2012 to September 2014. Thirty patients who were splenectomised and on follow up in St. Johns medical college hospital for chronic ITP, with willingness to participate in the study were enrolled. Presplenectomy data and post splenectomy data were collected from their medical records. Exclusion criteria included patients with known secondary causes of thrombocytopenia or thrombotic disorder and those who were not willing to participate in the study. The diagnosis of ITP was based on history, physical examination, complete blood count, peripheral smear and bone marrow aspiration.

Diagnostic criteria of ITP (Kuwana, 2006)

- Platelet count lower than 30 x 10^9/L or 50 x 10^9/L with significant mucous membrane bleeding.
- Normal or increased megakaryocytes in the bone marrow aspirate.
- Exclusion of secondary thrombocytopenia.
- The following criteria were used to assess the response to treatment of ITP (Supe, 2009).
- Complete Response (CR) - Platelet count > 100 x 10^9/L while maintained on no therapy.

- Partial Response (PR) - Increase of platelet count between 50-150 x 10^9/L.
- No Response (NR) - Platelet count < 50 x 10^9/L.

Statistical analysis: Statistical analysis was done using spss 16 software. Since the distribution of data was non parametric except age, median was taken and analysis was done by Fischers exact test, Mann Whitney U and Wilcoxons signed ranks test.

RESULTS

Data of 30 splenectomised patients who attended haematology /medicine OPD or admitted in appostrophe Medical college hospital were analysed. Indications splenectomy in the cases were 1.

Failure to respond to medical therapy 2. Frequent relapses with inadequate hemostasis. The study was conducted over a period of two years. At the time of study, post splenectomy interval varied from 6 months to 15 years; with a median of 2 years and interquartile range of 3 years.

Age and Sex distribution: Age of the patients followed a normal distribution curve; and the youngest patient was 22 years old while the oldest was 62 years. Mean age of patients was 38.3 years with a standard deviation of 12.353 years. The male:female distribution was 23.3% and 76.7% respectively.

Type of splenectomy and duration of hospital stay:30 patients who met the inclusion criteria and had undergone splenectomy for chronic refractory ITP were studied. 50% of patients had undergone open splenectomy, while 36.7% had laparoscopic splenectomy and 13.3% had hand assisted laparoscopic splenectomy (HALS). All of the patients tolerated the procedure well and none of the patients had immediate postoperative complications that required prolonged hospital stay. The average hospital stay after splenectomy was 3-5 days for HALS/laparoscopic surgery and 7-10 days in case of open splenectomy.

Presplenectomy treatment: Patients were on medical management according to various treatment protocols. Most of them received steroids with or without other immunosuppressants like danazol, azathioprine, dapsone, cyclophosphamide and vincristine on long term basis. 26.7% received only steroids, 46.7% received steroid with azathioprine, 13.3% received steroid+danazol+azathioprine, 6.7% received steroid+vincristine/cycophosphamide, 3.3% received steroid with danazol, and 3.3% received steroid+ danazol + dapsone. None of the patients received anti D injections, Eltrombopag/romiplostim.7.4% of the patients received rescue treatment in the form of intravenous immunoglobulins or rituximab during crisis (Figure 1)

Side effects related to medical treatment: Various side effects of immunosuppressant therapy, especially to steroids were noted. 30% of patients who were on medical management showed new onset hyperglycemia. Cushingoid features were seen in 26.7%, recurrent lower respiratory infections and acne in 10% each, peripheral neuropathy in 3.3%, cataract in 3.3%. The patients who received azathioprine had no evidence of bone marrow suppression (Figure 2).

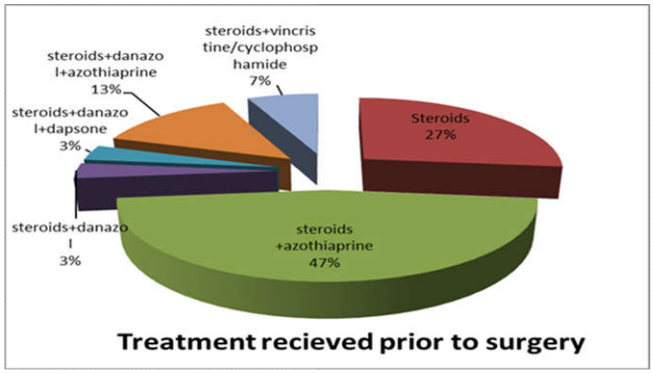

Figure 1: Treatment received prior to surgery

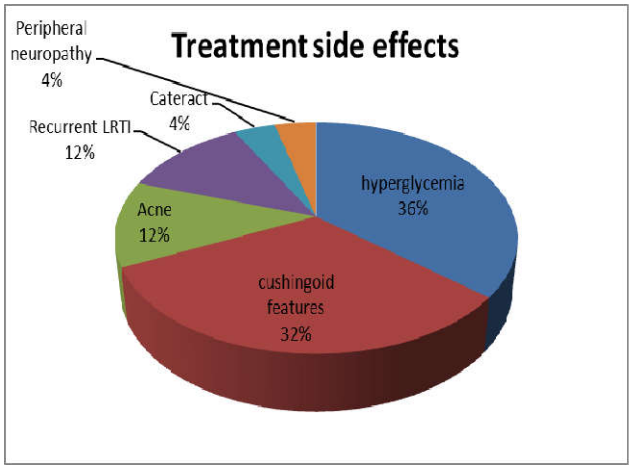

Figure 2 : Side effects of medical treatment

Thrombosis post splenectomy: None of the patients had thrombosis during immediate postoperative period. 13.3% of patients who underwent splenectomy had developed thrombosis later in life when they were ambulant and doing all activities of daily living, of which 50% was deep vein thrombosis of lower limbs, 25% superior mesenteric vein thrombosis and 25% was portal vein thrombosis.

Type of surgery and thrombosis: Thrombosis was seen in 6.6% (1/15)of open splenectomy cases, in 9% (1/11)of laparoscopic splenectomy cases and in 50% (2/4) of hand assisted laparoscopic surgery (Figure 3)

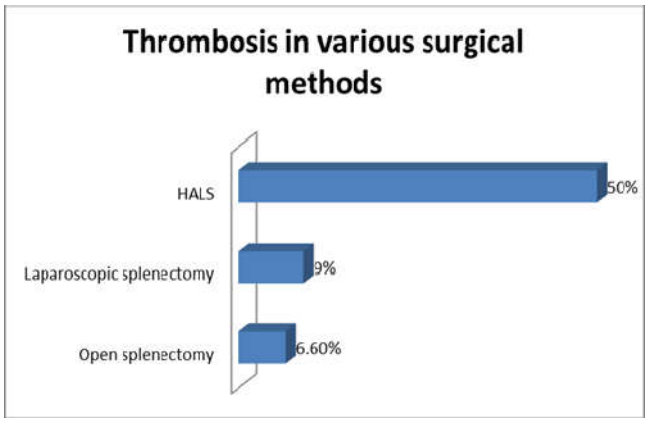

Figure 3: Thrombosis in various surgical methods

Platelet count pre and post splenectomy: Median platelet count pre splenectomy was 9000/mm^3 and median platelet count post splenectomy was 2.1

Lakh, which is statistically significant (Wilcoxons signed rank test showed p value of 0.00)

Treatment response tosplenectomy: Patients who maintained >1 lakh/mm^3 platelet count without further treatment were considered as complete responders. 36.6% individuals were complete responders, 30% were partial responders who required pharmacological treatment and 33.3% were non responders. Among nonresponders 20% required serial blood transfusions to maintain adequate haemostasis (Figure 4).

DISCUSSION

Chronic idiopathic thrombocytopenia is caused by production of antibodies against circulating platelets and destruction of antibody coated platelets in the reticuloendothelial system especially spleen. Hence the treatment is based on decreasing the antibody production and preventing the removal of platelets by spleen. Splenectomy was done for the first time as a definitive therapy for ITP in 1916 (Kaznelson, 1916). The discovery of steroids and its use in the treatment of ITP, followed in 1950. Since then, steroids are the primary modality of therapy in adults with chronic idiopathic thrombocytopenic purpura. The decision to do a splenectomy is taken usually when the patient is refractory to medical management or relapsing frequently with inadequate hemostasis. It is also done when the side effects of medical treatment is impairing the patient's quality of life. In our study, majority of patients were on steroids or combination like steroid with other immunosuppressants like azathioprine, danazol and dapsone. In severe cases cyclophosphamide and vincristine were tried (6.7%). Rescue treatment was given to 7.4% of patients with Rituximab or Intravenous immunoglobulins (Akwari, 1987). None of our patients received anti D injections/eltrombopag/romiplostim.

The common side effects of medical therapy included steroid induced side effects like hyperglycemia, cushingoid features, cataract and acne. None of the patients who received azathioprine had pancytopenia caused by azathioprine. 3.3% of patients who received vincristine had peripheral neuropathy Recurrent infections was present in all treatment groups in the form of recurrent respiratory tract infections, urinary infections and skin infections (10%). Spleen can be removed by open splenectomy, laparoscopic surgery or by hand assisted laparoscopic surgery(HALS). It can be made dysfunctional by splenic artery embolization also. Laparoscopic splenectomy/HALS is now the procedure of choice, and it can be performed even in thrombocytopenic patients. Two late complications of splenectomy are overwhelming septicemia and atherosclerotic heart disease (Robinette, 1939). In our study 50% of patients underwent open splenectomy while 50% had undergone laparoscopic splenectomy/ HALS (Delaitre, 2002). None of the patients had acute infective/thrombotic complications/ OPSI following the surgery. All the patients were given pneumococcal and influenza vaccinations prior to surgery (George, 1996). 13.3% of patients developed venous thrombosis in the form of femoral vein thrombosis, superior mesenteric vein thrombosis, and portal vein thrombosis (Taher, 2006; Stewart, 1996) after returning to normal activities of daily living. But the association was found to be statistically insignificant (P value 0.08). 80% of patients who developed venous thrombosis later in life had undergone laparoscopic splenectomy or HALS. This finding was comparable with many international and national studies (Stamou, 2006; Skarsgard, 1993). The incidence of thrombosis involving the portal venous system after splenectomy ranges from 5-37% as per various studies. A higher incidence of this complication appears with laparoscopic than open splenectomy and it may be due to the result of increased surgical site manipulations during the procedure. In our study HALS carried maximum incidence of thrombosis, which may be attributed to the increased splenic size which might have resulted in a difficult procedure.

Response after splenectomy varied from patient to patient. All patients who had undergone splenectomy had an increase in platelet count. Splenectomy removes the primary site of platelet clearance and autoantibody production that offers the highest rate of durable response compared with other medical therapy. The post splenectomy platelet count showed a rise which was statistically significant (p value 0.00). Even though there is an increase in the median number of platelets, 33.3% were non responders while 36.6% were complete responders as per the criteria. 20% of patients required platelet transfusions for clinically significant bleeding.36.6 % were off treatment after splenectomy but the rest required medical therapy to maintain the partial response (Srinivasan, 2003).

This inadequate response/relapse may be due to the following reasons 1) the presence of accessory spleen 2) the spillage of splenic tissue at the time of surgery 3) hypertrophy of remaining of splenic tissue 4) liver acting as a site for platelet sequestration after splenectomy. In our study also laparoscopic splenectomy was changed to hand assisted laparoscopic procedure in view of increased spleen which might have resulted in spillage of splenic tissue. Preoperative abdominal imaging with USG/CT sometimes fails to find accessory spleen. Although 99mTc nanocolloid scintigraphy is the investigation of choice for finding accessory spleen, it is not done routinely (Leo, 2015). An intraoperative search for accessory spleens is mandatory and remains the most successful method for its detection.

Conclusion

In this study we noted significant improvement in platelet count post splenectomy (p value 0.00). 36.6% patients had complete response and required no treatment after splenectomy; rest of the patient's required medical management to maintain hemostasis even though all of them had improvement in platelet count post procedure. Occurrence of venous thrombosis was less in open splenectomy in comparison to laparoscopic procedures. Even though venous thrombosis was high in the laparoscopic and HALS group, it was statistically insignificant (p value 0.08). None of the patients had acute infective/ thrombotic complications/ OPSI in the immediate post-operative period hence splenectomy is a relatively safe procedure with minimal complications offering substantial response in ITP patients. A perioperative advanced Imaging to rule out accessory spleen and intra operative search for the same is advised to decrease relapse and increase the response rate.

REFERNCES

Akwari OE, Itani KM, Coleman RE, Rosse WF. 1987. Splenectomy for primary and recurrent ITP. Current criteria for patient selection and results. *Annals of Surgery.,* 206:529

Delaitre B, Blezel E, Samama G, *et al*., 2002. Laparoscopic splenectomy for idiopathic thrombocytopenic purpura. Surgical Laparoscopic Endoscopic Percutaneous Techniques. 12:412.

George JN, Woolf SH, Raskob GE, *et al*., 1996. Idiopathic thrombocytopenic purpura: A practice guideline developed by explicit methods for the American Society of Haematology. Blood 88:3-40

Kaznelson P. 1916. Verschwinden der haemorrhagischen diathese bienenfalle von "essentieller thrombopenie nach Milzexstirpationsplenogene thrombolytische purpura. Wein Klin Wochenschr; 29:1451-4

Kronkle BA. Disorders of platelets and vessel wall. In Jameson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Loscalzo J. 2018. editors. Harrison's principles of internal medicine. 20th ed. New York: McGraw-Hill, 825

Kuwana M, Kurata Y, Fujimura K, *et al*., 2006. Preliminary Laboratory based diagnostic criteria for immune thrombocytopenic purpura: evaluation by multi-center prospective study. *Journal of Thrombosis and Haemostasis.* 4:1936-43

Leo CA, Pravisani R, Bidinost S, *et al*., 2015. Post splenectomy recurrence of idiopathic thrombocytopenic purpura: role of laparoscopic splenectomy in the treatment of accessory spleen. *Giornale di Chirurgia*. 36:153-7.

Robinette CD. 1939. Fraumeni JF Jr. Splenectomy and subsequent mortality in veterans of The 1939-45 war. Lancet. 1977; 2:127-9.

Skarsgard E, J Doski, T Jaksic, *et al*., 1993. Thrombosis of the portal venous system after splenectomy for pediatric hematologic disease. *Journal of Paediatric Surgery*. 28: p. 1109-12.

Srinivasan S, Sabapathy K, Bharadwaj TPR, Sethuraman S. 2003. Role of splenectomy in chronic idiopathic thrombocytopenic purpura. Journal of Association of Physicians India. 51:159-62.

Stamou KM, Toutouzas KG, Kekis PB, *et al*. 2006. Prospective study of the incidence and risk factors of postsplenectomy thrombosis of the portal, mesenteric and splenic veins. *Archives of Surgery*. 141: 663-9.

Stewart GW, Amess JA, Eber SW, *et al*., 1996. Thrombo-embolic disease after splenectomy for hereditary stomatocytosis. *British Journal of Haematology*. 93:303-10.

Supe A, Parikh M, Prabhu R. *et al*., 2009. Post splenectomy response in adult patients with immune thrombocytopenic purpura. *Asian Journal of Transfusion Science*. 3: 6-9

Taher A, Ismaeel H, Mehio G. *et al*. 2006. Prevalence of thromboembolic events among 8860 patients with thalassemia major and intermedia in Mediterranean area and Iran. *Journal of Thrombosis and Haemostasis*. 96:488-91.

Taylor MA, Kaplan HS, Nelson TS. 1985. Staging laparotomy with splenectomy for Hodgkin's disease: The Stanford experience. *World journal of surgery.,* 9:449.

****