

Study on responses after Splenectomy for Idiopathic Thrombocytopenic Purpura Patients, Kathmandu, Nepal.

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ABSTRACT:

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by accelerated destruction of platelets due to the presence of platelet (Plt) auto antibodies and impaired production of platelets. Splenectomy is still the standard salvage therapy in cases refractory to corticosteroid therapy. Retrospectively we analyzed 34 patients with ITP that underwent splenectomy in the period May 2010 to March 2012 and have been followed for at least 12 months. All patients met the diagnostic criteria for ITP. The median age at diagnosis was 26 years (range: 14-55 years). Overall response rate to splenectomy after 1 year of follow up was 94.1 %, with Complete response in 32 and no response or relapse in 2 (5.8%). Sex didn't influence the outcome after splenectomy in our group of patients. Only preoperative response to steroids (P value = 0.018) and post-operative platelet count (P value = 0.013) were found to be significant statistically. Splenectomy considered as safe and effective treatment for patients with ITP who failed to respond to first-line treatment with corticosteroids. Management of patients who do not respond or relapse after splenectomy represent an important problem for further treatment due to low response rate to other treatment options.

Keywords: Idiopathic thrombocytopenic purpura (ITP), Splenectomy, Patients

INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by accelerated destruction of platelets due to the presence of platelet (Plt) autoantibodies and impaired production of platelets^{1,2}. According to the recent international consensus report³, ITP is characterized by isolated thrombocytopenia, defined as platelet count <100 x 10⁹/L and the absence of any underlying cause for thrombocytopenia. Glucocorticoids and splenectomy have been the primary and most effective treatments of chronic ITP in adults. Glucocorticoids seem to increase the platelet production,⁴ diminish platelet sequestration and destruction of antibody sensitized platelets^{5,6} and this complements the long term immunosuppressive effect of glucocorticoids. Splenectomy is still the standard salvage therapy in cases refractory to corticosteroid therapy. Approximately 60% of the patients will achieve complete remission following splenectomy.⁷

Several large studies with substantial follow-up evaluate the responses of adult patients with chronic ITP to corticosteroid therapy and to splenectomy, alone or in combination. Little information is available on ITP patients undergone to splenectomy in Nepal. The present study describes the short and long-term outcomes of patients with chronic ITP for whom splenectomy done and this study tried to identify and focus on the possible prognostic factors that can predict the response to splenectomy.

MATERIAL AND METHODS

Retrospectively we analyzed 34 patients with ITP that underwent splenectomy in the period May 2010 to March 2012 and have been followed for at least 12 months. All patients met the diagnostic criteria for ITP:

1. Platelet count lower than 30 x 10⁹/L or 50 x 10⁹/L with significant mucous membrane bleeding.
2. Normal or increased megakaryocytes in the bone marrow aspirate.

The medical records of these patients were reviewed for the clinical and laboratory information regarding their diagnosis, initial treatment, and splenectomy and after treatment follow-up. All patients underwent steroid therapy initially (*Prednisolone 1 mg/kg body weight*) and were considered for splenectomy due to failure of steroid therapy to reach or maintain adequate platelet count.

The following criteria were used to assess the response to treatment.

Complete Response (CR) - Platelet count > 150 x 10⁹/L while maintained on no therapy for at least 1 month and continuing for the duration of observation of 12 months.

Partial response (PR)-Increase of platelet count between 50-150 x 10⁹/L

3. No Response (NR) - Platelet count < 50 x 10⁹/L.

The short and long term response to splenectomy at the end

Table-I: Characteristics of Splenectomized ITP patients at Diagnosis.**Age and sex at Diagnosis:**

Age	0-30	31-60	Total (%)	P-value
Sex				P=0.82
Male	4	6	10(29.4)	
Female	6	18	24(70.5)	
Total	10	24	34	

Type of Bleeding at diagnosis:

Type of bleeding	Numbers	%
Asymptomatic	7	20.7
Minor mucosal bleeding	23	67.6
Significant bleeding	4	11.7
Total	34	

Platelet count at presentation:

Platelet Count	Numbers	%
Mild (>50 x 10 ⁹ /L)	Nil	
Moderate (30-50 x 10 ⁹ /L)	7	20.5
Severe (<30 x 10 ⁹ /L)	27	79.4
Total	34	

Initial Steroid response:

	0-30	31-60	Total	P-value
CR				0.018
Male				
Female		2	2	
PR				
Male	1	2	3	
Female	2	4	6	
NR				
Male	3	4	7	
Female	4	12	16	
Total	10	24	34	

Reason for Splenectomy:

Reason	Numbers	%
No response to steroid	24	70.5
Side effects of steroid	5	14.7
Poor compliance	4	11.7
With cholecystectomy	1	2.9
Total	34	

Platelet count at post-operatively:

Platelet Count	Numbers	%
Severe (Plt < 30 x 10 ⁹ /L)	Nil	
Moderate (Plt 30-50 x 10 ⁹ /L)	2	5.8
Mild (Plt > 50 x 10 ⁹ /L)	5	14.7
(>100 x 10 ⁹ /L)	27	79.4

Splenectomy response at end follow up:

	Sex	0-30	31-60	Total (%)	P-value
CR	Male	3	7	10	P=0.032
	Female	7	15	22	
NR	Male			2 (5.8)	
	Female		2	2	

Table-II : Characteristics of patients after Splenectomy, response to splenectomy and additional therapy

Characteristics	N= 34
Age (years) at splenectomy , median (range)	28
Median follow up from splenectomy in months (range)	12
Median time from diagnosis to splenectomy in months (range)	5
Treatment at last control	
Prednisone	5
No therapy	29
Response to splenectomy	
CR*	32
PR#	None
No response	2

Abbreviations: ITP idiopathic thrombocytopenic purpura;GIT gastrointestinal tract;Plt platelets; IVIG, intravenous immunoglobulin's CR , complete remission PR, partial remission.

of 1 month and 12 months were analyzed. Data collected from medical records were age at diagnosis, gender, symptoms and type of bleeding, platelet count at diagnosis, platelet count after treatment and at the last recorded check up and response to different treatments. The significance of these factors in assessing the response to splenectomy were done by using non-parametric test (Chi-square test) and the level of significance was a P value of < 0.01.

RESULTS

The median age at diagnosis was 26 years (range: 14-55 years). 24 (70.5%) patients were females and 10(29.4%) were males (Table-I.1). Seven (20.5%) were asymptomatic, 23 (67.7%) had minor skin or mucosal bleeding and 4 (11.7%) had significant bleeding from gastrointestinal or genitourinary system (Table-I.2). None of the patients had severe, life threatening bleeding symptoms. The median platelet count at diagnosis was 18 x 10⁹/L (range: 0-91 x 10⁹/L). Number of patients with severe thrombocytopenia at diagnosis was 27(79.4%), with moderate thrombocytopenia was 7 (20.5%). Bone marrow examination was performed in 23 (67.6%) of patients (Table-I.3).

Corticosteroids were initial treatment for all 34 (100%) patients. Among them 12 patients (35.2%) were treated with steroids and intravenous immunoglobulin's (IVIG). Complete response to initial treatment with steroids ± IVIG was achieved in 2 (5.8%), partial response in 9 (26.5%) and no response in 23(67.6%) (Table-I.4).

The median age at the time of splenectomy was 28 years (range 17-58 years). The follow up from splenectomy was 12 months (range 6-12 months). The median duration from diagnosis to splenectomy was 5 months (Table-II). Twenty four (70.5%) patients underwent splenectomy because they didn't respond to corticosteroids or were dependent to steroid therapy, 5 (14.7%) patients had severe side effects from steroid treatment, and 4 (11.7%) patients

had poor compliance and in 1 (2.9%) patient splenectomy was performed during cholecystectomy (Table-I.5). At the first follow up, number of patients with moderate thrombocytopenia was 2 (5.8%), with mild 5 (14.7%), with platelet count $>100 \times 10^9/L$ was 27 (79.4%) and none of them had severe thrombocytopenia. (Table-I.6). At the last control 29 (85.2%) patients were without therapy for ITP and 5 (14.7%) were still receiving prednisone (Table-II).

Overall response rate to splenectomy after 1 year of follow up was 94.1 %, with CR in 32 and no response or relapse in 2 (5.8%). These results indicate that only 29/34 (85.2%) of patients had long-lasting CR without therapy and 5 patients were receiving steroid therapy. (Table-I.7). Two patients with no response cases sent for CT abdomen after operation and found to be presence of small accessory spleen. These patients are under steroid therapy.

We have observed higher response rate in patients above 31 years of age 22/32 (68.7%) than in

Below 30 years 10/32 (31.2%), $p=0.032$. (Table-I.7).

Sex didn't influence the outcome after splenectomy in our group of patients. Complete remission after splenectomy was achieved in 10/32(31.2%) of males comparing to 22/32(68.7%) of females, $p=0.82$. (Table-I.1).

Certain factors like the age at the time of diagnosis, sex, initial platelet count, initial response to steroids, time interval between the diagnosis and splenectomy and the post-operative platelet count at the time of discharge and their association with long term response were studied. The results have been related using a non-parametric test (Chi-square). Of these factors only preoperative response to steroids (P value = 0.018) was found to be significant statistically. Age, sex, initial platelet count and time interval between the diagnosis and splenectomy didn't seem statistically related to splenectomy results.

DISCUSSIONS:

Spleen is the major site of removal of opsonized or damaged platelets that contribute to the thrombocytopenia in patients with ITP. For this reason, splenectomy has been used as therapeutic approach in patients with ITP who were not responsive to corticosteroid treatment.⁸

The initial response rate referred in other studies was 75-85% but it decreased to 50-60% after follow-up longer than one year.⁹ Some studies reported higher long-term response rate of 70-89%, but this can be due to shorter follow-up period, differences in patient characteristics, and higher percentage of patient with severe ITP.¹⁰ Elezovic et al.¹¹ reported that 111/147 (75.5%) splenectomised patients were in remission during follow up of median 62 months. Our results indicate 94.1% long-term response rate in ITP patients and 85.2% of patients were without therapy at the time of last control. In our patients better results after splenectomy were associated with age above 31 years than below 30

years and better response to initial treatment ($p=0.005$), similar to the results in the study of Elezovic et al.¹¹

Splenectomy is relatively safe surgical intervention with postoperative complication rate of 13% in the study by Kojouri et al.¹² and up to 33% in the study of Portielje et al.¹³ We didn't have any severe complication or death due to splenectomy.

CONCLUSION

Splenectomy may be considered as safe and effective treatment for patients with ITP who failed to respond to first-line treatment with corticosteroids. Management of patients who do not respond or relapse after splenectomy represent an important problem for further treatment due to low response rate to other treatment options.

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