



Immune thrombocytopenia (ITP) with corticosteroids: “Evaluation of Response”

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ABSTRACT

Objective: To evaluate the response of corticosteroids in newly persistent Immune thrombocytopenia (ITP) patients.

Methods: Retrospective Observational from 30th October 2020 to 29th April 2021 at Armed Forces Bone Marrow Transplant Centre Rawalpindi. A total of 74 individuals with ITP who were both males and females of various ages. Prednisolone was administered orally to patients in maximal dose of 1mg/kg. The initial reaction of platelets count was assessed on day 5 and subsequently every two weeks until the full response was attained. An informed consent was obtained.

Results: Age was 32.0 ± 19.1 years on average. There were 1:1.1 patients that were male and female with 48.6% men and 51.4% women. Twenty 27.0% individuals had persistent ITP compared to 54 (73.0%) patients who had just been diagnosed. 45.9% patients had an initial response whereas 43 patients 58.1% showed a full response. The average initial response time was 5.47 ± 2.39 days and 11.79 ± 6.73 days for full response. There was no statistically significant difference in the frequency of initial and complete response and mean time to initial and complete response to various subgroups like age, gender and ITP type.

Conclusion: Regardless of age, gender, or ITP type, steroids were associated with an initial and complete response in a significant majority of patients with immune thrombocytopenia. Keeping in view with their affordability accessibility favors the use of steroids as first line in these patients.

Keywords: Corticosteroids, Complete Response, Initial Response, Immune Thrombocytopenia, Persistent ITP

1. INTRODUCTION

Immune thrombocytopenia is defined as platelet count less than 100×10^9 in the absence of other causes of thrombocytopenia. Immune thrombocytopenia (ITP) is an auto-immune disorder in which there is production of auto antibodies against platelets leading to platelet destruction along with decreased production.¹ ITP may affect patients of any gender, race and age group. Peak incidence is seen in childhood and elderly with an annual incidence of 1.6 cases per 100,000.²

ITP can be divided into primary and secondary disease on etiological basis. Primary ITP is defined when other causes of thrombocytopenia are absent whereas in secondary ITP some identifiable cause of thrombocytopenia is present. Secondary ITP accounts for 20% of the patients.²

Generally treatment is not considered unless platelet count is less than 30×10^9 or there is significant bleeding. New therapeutic options like Rituximab and Thrombopoietin receptor agonists (Eltrombopag) are used in steroid refractory ITP however; corticosteroids still remain the first line treatment agents in patients with newly diagnosed ITP along with IVIG and Anti D.³⁻⁵

Splenectomy or second line therapeutic agents like Rituximab or Thrombopoietin Receptor agonists can be offered to patients who fail to respond to corticosteroids. Response to prednisolone and dexamethasone therapy can be seen within 4-14 days where as for IVIg response is seen within 1 day and for anti-D it is 1-3 days.⁶⁻⁸

International data shows the initial response to prednisolone is 67% and complete response is 26%.⁵ In patients given prednisolone initial response was achieved at 11.4 ± 12.3 days (average \pm standard deviation).⁹ This study is aimed at evaluating the response of steroids as first line treatment

in newly diagnosed cases of ITP. Steroids are the cheapest and most easily available first line treatment option, and no such local study is available to show the response of corticosteroids as first line option in ITP in our population.

2. METHODOLOGY

IT is a retrospective Observational. Study was conducted at armed Forces Bone Marrow Transplant Centre, Rawalpindi From 30th October 2020 to 29th April 2021, a tertiary care setup caring for patients with hematological disorders. All newly diagnosed and persistent ITP (previously untreated or inadequately treated) cases. Patients of all age groups and gender were included. Cases of secondary ITP, Patients with Evan's syndrome, Patients presenting with ITP during pregnancy, previous exposure to second line treatment and Patients with chronic ITP were excluded from the study.

Complete Response: Platelet count more than 100×10^9 and absence of bleeding.

Response: Platelet count doubling from base line and absence of bleeding.

No Response: Platelet count $< 30 \times 10^9$ or less than 2-fold increase of the baseline platelet count or bleeding with maximum dose or steroids up to 4 weeks.

Initial Response: Response seen on day 5.

Time to Response: Time from starting treatment to time to achieve complete response or response.

Inadequate Treatment: Steroids given less than 1 mg/ kg dose, for less than 3 weeks. Disease duration less than 3 month from the time of diagnosis. Disease duration between 3 to 12 months from the time of diagnosis.

Chronic ITP: Disease duration more than 12 months from the time of diagnosis. With the help of World Health Organization sample size calculator, sample size calculated was 74, with: Confidence level = $1 - \alpha = 95\%$. Absolute precision required = $d = 10\%$.

Anticipated population proportion = P = 26.0%⁵.

Formal approval was taken from Hospital Ethical Review Committee. Patients fulfilling the inclusion and exclusion criteria were included in the study. A written consent was taken from each patient. Study variables were age, gender of patient, ITP type (newly/persistent), time to initial and complete response to therapy. A total of 74 patients of newly diagnosed and persistent immune thrombocytopenia from outpatient and inpatient department were included in our study. Patients were started on per oral prednisolone @1mg/kg dose. Further response monitoring was done twice weekly till response was achieved, then weekly until the steroids were tapered off completely and then fortnightly for the next 3 months. Blood glucose monitoring was done weekly till the tapering of steroidtherapy. Data was analyzed by Statistical Package for Social Sciences (SPSS v 25) statistical software. Descriptive Statistics were calculated for qualitative and quantitative variables. Numerical variables; age, number of days to initial and complete response, time to complete response were presented by mean ±SD. Categorical variables; like gender, ITP type, initial response and complete response were analyzed by frequency and percentage. Data was stratified for age, gender and ITP type. Chi-square test was applied for initial and complete response and t-test was applied for time to initial and complete response. p≤0.05 was considered statistically significant.

3. RESULTS

Range of age was from 2 years to 87 years with a mean age of 32.0±19.1 years. Majority (n=50, 67.6%) of the patients were less than 40 years of age followed by 24 (32.4%) patients with age 40 years and above. There were 36 (48.6%) male and 38 (51.4%) female patients with a male to

female ratio of 1:1.1 as shown below in figure no 01. Fifty four (73.0%) patients had newly diagnosed while 20 (27.0%) patients had persistent ITP.

Initial response was observed in 34 (45.9%) patients while 40 (54.1%) had no response. Complete response was observed in 45 (60.8%) and 29 (39.2%) patients had no response. Mean time to initial response was 5.47±2.39 days while mean time to complete response was 11.79±6.73 days. There was no statistically significant difference in the frequency of initial and complete response and mean time to initial and complete response to various subgroups like age, gender and ITP type as shown below in Tables 1,2,3 and 4 respectively.

Table-1:

Frequency of Initial Response across Various Subgroups

Characteristics	n	Initial Response n (%)	P-value
Age (years)			
<40 years	50	24 (48.0%)	0.609
≥40 years	24	10 (41.7%)	
Gender			
Male	36	20 (55.6%)	0.106
Female	38	14 (36.8%)	
ITP Type			
Newly Diagnosed	54	26 (48.1%)	0.532
Persistent	20	8 (40.0%)	

Table-2:

Frequency of Complete Response across Various Subgroups

Characteristics	n	Complete Response n (%)	P-value
Age (years)			
<40 years	50	31 (62.0%)	0.327
≥40 years	24	12 (50.0%)	
Gender			
Male	36	25 (69.4%)	0.054
Female	38	18 (47.4%)	
ITP Type			
Newly Diagnosed	54	32 (59.3%)	0.742
Persistent	20	11 (55.0%)	

Table:3

Comparison of Mean Time to Initial Response across Various Subgroups

Characteristics	n	Time to Initial Response (mean±sd)	P-value
Age (years)			
<40 years	24	5.29±2.22	0.507
≥40 years	10	5.90±2.85	
Gender			
Male	20	5.25±2.40	0.528
Female	14	5.79±2.42	
ITP Type			
Newly Diagnosed	26	5.31±2.11	0.482

Persistent	8	6.00±3.25	
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Table-4: Comparison of Mean Time to Complete Response across Various Subgroups

Characteristics	n	Time to Complete Response (mean±sd)	P-value
Age (years)			
<40 years	31	11.61±5.73	0.784
≥40 years	12	12.25±9.11	
Gender			
Male	25	10.64±7.35	0.190
Female	18	13.39±5.55	
ITP Type			
Newly Diagnosed	32	12.00±7.32	0.732
Persistent	11	11.18±4.85	

4. DICSCUSSION

ITP is an auto-immune disorder in which there is production of auto antibodies against platelets leading to platelet destruction along with decreased production leading to decreased platelet count ($\leq 100 \times 10^9$).¹ Corticosteroids still remain the first line option of treatment in patients with newly diagnosed ITP.

In our study, the mean age of the patients was 32.0±19.1 years. A similar results was reported by Naz et al in 2016 (mean age 32.1±13.5 years) in patients

presenting with ITP.¹⁰ Dutta et al. (2017) reported similar mean age of 32.1 ± 11.4 years from India, while Dash et al. (2014) reported it to be 36.3 ± 18.34 years in UK.^{11,12} We reported thirty six (48.6%) male and thirty eight (51.4%) female patients with a male to female ratio of 1:1.1. A similar result of female predominance with male to female ratio 1:1.1 has been reported by Alhammadi et al. (2016) in Qatar.¹³ while Sultan et al. also observed similar female predominance with male to female ratio of 1:1.5.¹⁴ Humayun et al. in 2017 at Sheikh Zayed Postgraduate Medical Institute, Lahore and Sheema et al. (2017) from Karachi reported similar female predominance with male to female ratio of 1:1.9 and 1:1.7 respectively.^{15,16} Dayama et al. in 2017 reported male to female ratio of 1:1.5 in Indian patients.¹⁷

In our study, 54 (73.0%) patients had newly diagnosed while 20 (27.0%) patients had persistent ITP. A similar distribution of newly diagnosed (73.5%) and persistent (26.5%) ITP was reported by Dayama et al. from India. In our study, complete response was observed in 43 (58.1%) patients. A similar frequency of complete response with steroids has been observed by Hollander et al. who reported similar frequency of 54.0% for complete response after steroid therapy in American children.¹⁸ Wei et al. and Cheng et al. reported similar frequency of 50.5% and 42.4% respectively for complete response in Chinese patients with ITP with steroid therapy.^{19,20}

In the present study, the mean time to complete response was 11.79 ± 6.73 days. Our results were similar to study reported by Spahr et al. In his study mean time to complete response of 11.4 ± 12.3 days with steroid therapy in patients with ITP.⁵

Our study from our local population and has shown that steroid therapy was associated with initial and complete response in a substantial proportion of patients with

immune thrombocytopenia regardless of patient's age, gender and ITP type which along with low cost and easy availability favor the use of steroids in such patients in future practice.

Limited follow-up of 3 months is single most important limitation in our study. There is need for long term follow-up to see persistence of response and any need for additional medication or procedure like splenectomy. Such a study would definitely help in the management planning of such patients and is highly recommended in future research.

5. CONCLUSION

Steroid therapy was associated with initial and complete response in a substantial proportion of patients with immune thrombocytopenia regardless of patient's age, gender and ITP type which along with low cost and easy availability favor the use of steroids in such patients in future practice.

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