Original Article

Frequency of Response with Eltrombopag in Patients with Persistent Immune Thrombocytopenia

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ABSTRACT

Objective: Determine the frequency of response with eltrombopag in persistent immune thrombocytopenia.
Design of Study: Descriptive case series study
Place and Duration of Study: This study was conducted at the Department of Hematology, Shaikh Zayed Hospital Lahore from September, 2014 to March, 2015.
Materials and Methods: A total of 40 cases of immune thrombocytopenia were included. Socio-demographic data like name, age and sex was taken. Patients were given eltrombopag (25mg/day) for 3 weeks. Platelet count was noted at day 7, day 14 and day 21 of treatment. These tests were performed on hematology analyzer Sysmex XT1800i. Other variables like partial response and no response were also noted.
Results: Male patients were 23 (57.5%) while female patients were 17 (42.5%) with mean age was 32.97±12.13 years. The mean platelet count was calculated as $109.12 \pm 11.29 \times 10^9$/l. The complete response with eltrombopag in persistent immune thrombocytopenia in 34 (85%) while 6 (15%) had partial response and no cases was recorded with no response.
Conclusion: The frequency of response with eltrombopag in persistent immune thrombocytopenia is goods in our population and in future we can use this drug for the management of immune thrombocytopenia.

Key Words: Frequency, Persistent immune thrombocytopenia, Eltrombopag

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INTRODUCTION

An acquired immune-mediated disorder, Persistent immune thrombocytopenia (ITP), defined as isolated thrombocytopenia (platelet count $<100\times10^9$/L) without any obvious underlying or initiating cause that persists for more than 3 months of duration.[1] The prevalence of ITP in adults ranges from 9.5 to 23.6 cases per 1,000,000 per year.[2]

The mainstay of therapy is glucocoticoids followed by splenectomy. Other options that are available for patients with severe illness, are high dose intravenous immunoglobulin and anti-RhD therapy, but are of temporary benefit only. Rituximab, is the drug that shows more durable responses.

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Other drugs like immunosupressants and cytotoxic agents are less commonly used while danazol may be underutilized.[3] Two novel thombopoiesis-stimulating agents have been developed that have shown their effect to increase platelet count.[4]

Romiplostim, an injectable thrombopoietin (TPO) peptide agonist and eltrombopag, an oral form of non-peptide thrombopoietin receptor agonist, correcting low platelet count in patients with chronic immune thrombocytopenia.[5]

Thrombopoietin, a cytokine produced in the liver, acts on the thrombopoietin receptors (TPO-R) which are present on the megakaryocytes. As a result, the differentiation of the bone marrow precursor cells occur along the megakaryocytic lineage.[6]

Eltrombopag, in association with metal ion (Zn^{2+}) activates the thrombopoietin receptors. Since the interaction between eltrombopag and endogenous thrombopoietin on the the thrombopoietin receptors is non-competitive, their effects are additive.[7] Documented response with eltrombopag in immune thrombocytopenia is 80 to 90%.[8]

Eltrombopag is also being studied in other thrombocytopenic patient populations, including those with hepatitis C, solid tumours, myelodysplastic syndromes, acute myeloid leukaemia and aplastic anaemia.[9]

Eltrombopag is a newly approved drug used in treatment of ITP. It is used when first line therapy fails.

It will provide us with baseline data in our population as well as basis for further research in this regard. No study is available showing its response in Pakistani patients. So we want to see its response in our population.

MATERIALS AND METHODS

This study that is descriptive case series, was conducted at Hematology Department, Shaikh Zayed Hospital Lahore from 2nd September, 2014 to 2nd March, 2015 and comprised 40 cases. Patients age >15years, either gender and diagnosed cases of persistent ITP who have completed more than 1 prior drug therapy for immune thrombocytopenia other than eltrombopag were included. All pregnant women with breast feeding to her child, altered renal function and atrial fibrillation were excluded. Patients were given eltrombopag (25mg/day) for 3 weeks. Platelet count was noted at day 7, day 14 and day 21 of treatment. These tests were performed on hematology analyzer Sysmex XT1800i.Other variables like partial response and no response was also noted. The data was entered and analyzed using SPSS-20.

RESULTS

There were 29 (72.5%) patients between 16-40 years while 11 (27.5%) patients were between 41-60 years with mean age was 32.97±12.13 years. Male patients were 23 (57.5%), while female patients were 17 (42.5%). Thirty four patients (85%) had complete response while 6 patients (15%) had partial response. No case was recorded with absence of response (Table 1).

Mean platelet counts were at day 1 was 29.3± 8.22 $x10^9$/l, day 7 was 41.5± 9.70 $x10^9$/l, day 14 was 77.7±11.68 $x10^9$/l and day 21 was 109.12±11.29 $x10^9$ /l (Table 2).

Response to eltrombopag was also analyzed among two genders. In Male patients, mean platelet count at Day 1 was 27.04±7.88 $x10^9$/l, at Day 7 mean platelet count was 39.73 ±8.74 $x10^9$/l, at Day 14 mean platelet count was 78.73 ±11.67 $x10^9$/l and at Day 21 mean platelet count was 110.65 ±8.58 $x10^9$/l.

In Female patients, mean platelet count at Day 1 was 32.35±7.88 $x10^9$/l, at Day 7 mean platelet count was 43.88±10.68 $x10^9$/l, at Day 14 mean platelet count was 76.35 ±11.91 $x10^9$/l and at Day 21 mean platelet count was 107.05 ±14.18 $x10^9$/l.

The mean platelet counts at day 1, showed statistically significant (P<0.05) difference between response of male and female patients while no significant (P>0.05) difference was seen between response of male and female patients at days 7, 14 and 21 (Table 3).

Table No.1: Demographic status of the patients

Parameter	No.	%
Age (years)		
16-40	29	72.5
41-60	11	27.5
Gender		
Male	23	57.5
Female	17	42.5
Type of response		
Complete Response	34	85.0
Partial Response	6	15.0
No Response	-	-

Table No.2: Mean platelet count of persistent immune thrombocytopenia taking eltrombopag before and during therapy (n=40)

Treatment (day)	Platelet count ($x10^9$/l)
1	29.3±8.22
7	41.5±9.70
14	77.7±11.68
21	109.12±11.29

Table No.3: Stratification of mean platelet count of gender according to treatment

Treatment (day)	Platelet count ($x10^9$/l)		P value
	Male	Female	
1	27.04±7.88	32.35±7.88	0.04
7	39.73±8.74	43.88±10.68	0.18
14	78.73±11.67	76.35±11.91	0.53
21	110.65±8.58	107.05±14.18	0.32

DISCUSSION

An acquired immune-mediated disorder, Persistent immune thrombocytopenia (ITP) defined as having isolated thrombocytopenia (platelet count <100 × 10^9/L) without any obvious underlying and/or initiating cause that persists for more than 3 months of duration.[1] Bussel et al[8] who revealed that response to eltrombopag in immune thrombocytopenia was 80-90% while in the present study it is 85% agreement with the international study. The rise in platelet count ≥50$x10^9$/l or ≥2 time baseline value is considered response to eltrombopag.

Kim and co-workers[10] in a recent trial analyzed in Korean ITP patients, the dose of eltrombopag that is needed to get and maintain safe platelet counts. They recorded that patients who achieved platelet counts >100 x 10^9/l (complete response) were 66.7%, who achieved platelet counts between 50 x 10^9/l and 100 x 10^9/l (partial response) were 5.6%, and 27.8% were unable to achieve the target platelet count i.e. > 50 x 10^9/l (no response). The present study showed that complete response was seen in 85% and partial response in 15% while absence of response is not seen. In patients who achieved the target platelet count, the median duration of ITP was significantly shorter and concluded that in refractory adult ITP patients, eltrombopag showed excellent treatment outcomes and was well tolerated. The target platelet count was maintained effectively with low-dose eltrombopag.

However, in some patients, especially in longer cases of ITP or who are heavily pre-treated, longer or higher-dose of treatment is required to maintain the target count of platelets.

Saleh et al[11] reported that 79% were white, 15% Asian and 6% belong to other ethnic groups. Reduction in symptoms like bleeding and sustained elevation of platelet counts along with use of ITP medications were observed for prolonged periods of time (months) in many patients, that confirmed the extension of eltrombopag response in the pivotal 6-week and 6-month trials. Overall response is seen in 80–88 % of cases with well tolerated treatment with eltrombopag. This figure closely resembles our study response in 85% of cases.

Cheng et al[12] also reported that 75% were white, 16% were Asian and 10% belonged to other ethnic groups. This study in patients with chronic immune thrombocytopenia during a 6-month periods, compared the once daily eltrombopag response versus placebo. Patients in the eltrombopag group, who showed response to treatment at least once during the study was 79%, in comparison with patients in the placebo group who were 28%. The odds of response to treatment throughout the 6 months period were more in the eltrombopag group patients in comparison with the patients in the placebo group. The results are close to response rate 85% in our study. The findings of our study provide us with baseline data in our population as well as basis for further research in this regard while no local study was available showing its response in Pakistan. We found higher efficacy in our population.

CONCLUSION

The frequency of response to eltrombopag in persistent immune thrombocytopenia is good in our population and in future we can use this drug for the management of ITP.

Author's Contribution:

Concept & Design of Study:	Amna Arooj
Drafting:	Madiha Islam
Data Analysis:	Mona Aziz, Sadia Taj
Revisiting Critically:	Amna Arooj, Madiha Islam
Final Approval of version:	Amna Arooj

Conflict of Interest: The study has no conflict of interest to declare by any author.

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