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High dose, short course prednisolone for acute idiopathic thrombocytopenic purpura (ITP) in children

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ABSTRACT

Background: Immune thrombocytopenia (ITP) is a relatively benign and self-limiting condition. Though its dramatic presentation with skin or mucosal bleeds could be worrisome, the incidence of serious bleeding like intracranial hemorrhage (ICH) is relatively low (<1%) occurs at a very low count of <20,000 /mm³. The aim of the study was to compare a high dose, short course prednisolone with conventional Prednisolone therapy in the treatment of acute ITP of childhood.

Methods: 20 cases and 18 retrospective controls with acute ITP were enrolled. The study group received 5mg/kg/day of oral prednisolone for four days. All the controls had received 2mg/kg/day of oral prednisolone for 14 days, tapered and stopped over the third week.

Results: The study group was found to have significant decrease in clinical bleeding, (p=0.02), and significant increase in platelet count by day 3 of treatment (p=0.03) but no significant difference in platelet counts on day 7 of treatment (p=0.07) when compared with the control group.

Conclusions: We conclude that the high dose short course oral prednisolone is significantly better than the conventional regimen in reducing clinically significant bleeding and raising the platelet count to safe levels within first 72 hours of therapy.

Keywords: Acute, Adverse effects, High dose prednisolone, ITP

INTRODUCTION

Immune thrombocytopenia (ITP) is a relatively benign and self-limiting condition. Though its dramatic presentation with skin or mucosal bleeds could be worrisome, the incidence of serious bleeding like intracranial hemorrhage (ICH) is relatively low (<1%) occurs at a very low count of <20,000/mm³.

Management is individualized based on the clinical profile and severity of bleeding.² Most of the cases of

ICH in ITP occur within the first seven days of illness. Therefore, any rational therapy should aim at elevating the platelet count to a safe level of $>20,000~/\mathrm{mm}^3$ during this period.²

The standard prednisolone regimen for ITP (2 mg/kg/day for 14 days tapered and stopped by day 21) takes at least one week or more to achieve a safe level of platelet count.³ High dose prednisolone therapy (4 mg/kg/day or more) in some studies had been reported to raise the platelet count to a safe level within 72 hours of therapy.^{4,5}

This study compares the high dose short course with the conventional regimen of oral prednisolone in ITP in achieving a safe level of platelet count during the first week of illness.

METHODS

Children with ITP aged 1-15 years attending JIPMER hospital over a period of two years were enrolled prospectively as study group and received prednisolone 5mg/kg/day for 4 days. The age and sex matched controls with similar platelet count who received oral prednisolone (2 mg/kg/day for 14 days tapered and stopped by day 21) were selected from medical records. Since the number of cases were insufficient to design a randomized controlled study, retrospective controls were included.

Diagnosis of ITP was made with the typical history, blood counts, peripheral smear and a bone marrow study. Children with platelet counts in the range of 5,000-50,000/mm³ per cmm were included in the study. This range was chosen because clinically significant bleeding in ITP does not occur beyond a platelet count of 50,000/cmm and life-threatening bleeding could occur below a count of 5,000/cmm requiring platelet transfusions. 1,2 Children with severe bleeding or intracranial bleed, those requiring platelet transfusions, severe anemia, those treated with Anti D immunoglobulin or IVIG outside were excluded from the study.

A platelet count was done after 48 hours, 72 hours and 7 days of therapy. In those with an initial platelet count of <10,000/cmm, count was repeated after 24 hours of therapy to ensure a rise of >10,000/cmm. Follow-up platelet counts were done after 2, 4, 8 and 12 weeks after starting steroids. Recurrences of ITP within six months were treated with the same regimen of steroids and included as cases in the study group. Chronic ITP was defined as thrombocytopenia (<100,000/mm³) persisting for more than 6 months.

During therapy, the patients were monitored for side effects of steroid therapy. Blood pressure and urine test for glycosuria were checked daily. Behavioral changes, if any, were noted. The clinical response time for cessation of any active bleeding and absence of fresh bleeding and the rapidity of rise in platelet count after 3 days and 7 days were considered as primary outcome. The statistical tests used were: unpaired t-test, chi-square test, fisher's exact test.

RESULTS

Thirty-eight cases of ITP (Cases=20, control=18) were studied. The mean age of children in the study group was 7.9 years (2-12 years), in the control group, 7.6 years (2-15 years) (p=0.81) (Table 1). Both the groups were also comparable in terms of sex distribution, severity of bleeds and the initial platelet count.

Table 1: Salient findings in the patients of the two groups.

Parameter	Study group (n=20)	Control group (n=18)	p- value
Mean Age (years)	7.9	7.6	0.81
Mean response time for clinical improvement (days)	2.5 (SD=1.31)	4.0 (SD=1.32)	0.02
Platelet count at presentation			
5000-20,000/cmm	16 (80%)	12 (66%)	0.46
>20,000-50,000/cmm	4 (20%)	6 (33.33%)	
>50,000/cmm	-	-	
Platelet count at 72 hours after treatment			
5000-20,000/cmm	5 (25 %)	6 (46 %)	0.03
>20,000-50,000/cmm	7 (35 %)	7 (54 %)	
>50,000/cmm	8 (40 %)	0	
Platelet count at day 8			
5000-20,000/cmm	1 (7 %)	2 (15 %)	0.07
>20,000-50,000/cmm	5 (36 %)	12 (68 %)	
>50,000/cmm	8 (57 %)	3 (17%)	
Complications during steroid therapy			
Hypertension	0	0	
Glycosuria	1(subsided after 24 hours)	0	
Weight gain	0	7	
Behavioral changes	0	0	
Cataract	0	0	

In the study group, the average time taken to clinical improvement was approximately three days, whereas the

control group children responded with cessation of bleeding after four days of therapy (p=0.02). Eight of the

twenty cases (40%) showed an increase in count to >50,000/cmm at 72 hours of treatment.

In contrast, out of 13 controls who had platelet count measured at 72 hours, none had count above the $50,000/\text{mm}^3$ (p=0.03). Platelet count was available only for 14 cases (out of the 20) and 17 controls (out of 18) on day eight. The remaining did not come for follow up. There was no statistically significant difference in the platelet counts between the two groups on day eight. (p=0.07).

In current study, it was attempted to estimate the sustenance of the response at one month after starting therapy in both the groups but this could not be done satisfactorily as several children were lost to follow up. Only four children in the study group came for follow up at one month. All of them had a platelet count in the normal range (1,50,000-4,50,000/cmm).

Three children in the study group had recurrent episodes in which one child remitted completely at 3 months whereas other two progressed as chronic ITP.

In the control group, out of 10 children who came for follow up at one month, five had a platelet count >50,000/cmm, three had counts from 20,000-50,000/cmm and two children had counts <20,000/cmm. However, all these children achieved a count >50,000/cmm by the second month of follow-up. As the number of children in the two groups was widely disparate (four in the study group and ten in the control), statistical analysis was not attempted.

Hematuria was the presenting feature in one child in the control group but had subsided by day four of therapy. No evidence of intracranial hemorrhage was seen in any of the patients in either group.

There was no death in either group. In the study group, one child had glycosuria on day two of treatment which disappeared by day three and none had other features of steroid excess like hypertension, behavioral abnormalities or weight gain.

In the control group, weight gain was observed in seven of the patients on follow up, however, no hypertension, glycosuria, behavioral abnormalities or cataracts were noticed.

DISCUSSION

The mean age of the children studied in both the groups was 7.5 years, which was slightly higher than the reported peak age of incidence of 5 years.^{1,2} The sex distribution was almost equal in both the groups which is usual in childhood ITP.^{1,2} Most of the cases in both the groups presented with a platelet count of <20,000/cmm (80% and 66.6%). None of them had life threatening hemorrhage in spite of very low platelet counts, which is

typical of childhood ITP.^{1,2} The mean time for clinical improvement was 3 days and 4 days respectively in both the groups. Clinical improvement due to steroid therapy had been observed ahead of rise in platelet count. In terms of clinical improvement, 5 mg/kg/day of prednisolone for 4 days was superior to the conventional regimen of 2 mg/kg /day for 14 days and tapered over a week (p=0.02).

The overall improvement in the platelet count after 72 hours of therapy was significantly better in cases (p=0.03), 40% of cases were found to have a count of >50,000/cmm after 72 hours of therapy. This was significantly faster than the controls, in which none had a count of >50,000/cmm in 72 hours. In a similar study by Carcao et al, 4 mg/kg/day of oral prednisone for four days achieved a platelet count of >20,000/cmm within 7 days in all 22 cases treated for acute ITP.5 Blanchete et al, in another study have demonstrated a rapid rise of platelet count to 50,000/cmm or higher after 72 hours of therapy in cases of acute ITP treated with 4 mg/kg/day of prednisone for 4 days.⁶ Studies in adults with acute ITP, also have demonstrated the benefit of high dose dexamethasone compared with conventional doses as seen in this study.^{7,8} However, the American Society of Hematology (ASH) discourages the use dexamethasone in children due to the high frequency of adverse effects with this drug.9

On day eight, 57 % of the cases had a platelet count of >50,000/cmm as against 18% of children in the control group (three out of seventeen). The overall improvement in platelet counts on day 8 was not statistically significant (p=0.07). Sustenance of the response could not be statistically analyzed as only 4 of the cases came for follow up at one month, while in the control group ten children had come for follow- up. However, all the four children in the study group had normal platelet counts while in the control group only four out of the ten had platelet counts >50,000/cmm. Two children in the control group were found with counts of <20,000/cmm at one month. Till date no study has shown that any treatment in ITP has significantly influenced the long-term outcome of the disease. 1.2

Two out of the seventeen cases (12 %) in the study group had gone on to chronicity. One had complete remission after one year and two months and the other required splenectomy at the end of one-year due to frequent recurrences. Studies report that around 25-30 % of children with ITP experience a chronic course. Seven children in control group had weight gain as a side effect. Side effects observed in cases were transient glycosuria in one, which disappeared on continuation of therapy. None of the cases had weight gain, hypertension or behavioral abnormalities. Though, the data for the control group is insufficient for a statistical analysis, it seems likely that the high dose, short course regimen of oral steroids is associated with fewer side effects than the conventional regimen. Other studies too have shown that

high dose and short course steroids have fewer incidence of adverse effects as against the conventional dose, making it the more compelling therapeutic option.^{5,10,11}

CONCLUSION

Multiple therapeutic options exist for the treatment of childhood acute ITP, including a policy of watchful observation.¹² If a decision to treat the child with steroids is arrived at, high dose short course oral prednisolone is proving to be significantly better than the conventional regimen in raising the platelet count to safe levels during the critical risk period of intracranial hemorrhage- within the first 72 hours of disease onset with fewer adverse effects.

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Institutional Ethics Committee

REFERENCES

- Wilson DB. Acquired platelet disorders. Nathan and Oski-Textbook of hematology of infancy and childhood. 6th ed.1600-10.
- Cines DB, Blanchette VS. Medical progress: Immune Thrombocytopenic Purpura. New Eng J Med. 2002;346:995-1008.
- 3. Buchanan GR, Holtkamp CA. Prednisone therapy for children with newly diagnosed idiopathic thrombocytopenic purpura: a randomized clinical trial. Am J Pediatr Hematol Oncol. 1984;6:355-61.
- 4. Lilleyman JS. Platelet Disorders. Pediatric Hematology. 2nd ed:442-47.
- Carcao MD, Zipursky A, Butchart S, Leaker M, Blanchette VS. Short-course oral prednisone therapy in children presenting with acute immune thrombocytopenic purpura (immune thrombocytopenic purpura). Acta Paediatr Suppl 1998;424:71-4.

- Blanchette V, Adams M, Wang E, McMillan J, Imbach P, Andrew M, et al. Randomised trial of intravenous immunoglobulin G, intravenous anti-D, and oral prednisone in childhood acute immune thrombocytopenic purpura. Lancet. 1994;344(8924):703-7.
- 7. Cheng Y, Wong RS, Soo YO, Chui CH, Lau FY, Chan NP,et al. Initial treatment of immune thrombocytopenic purpura with high-dose dexamethasone. New Eng J Med. 2003;349(9):831-6
- 8. Wei Y, Ji XB, Wang YW, Wang JX, Yang EQ, Wang ZC, et al. High-dose dexamethasone vs prednisone for treatment of adult immune thrombocytopenia: a prospective multicenter randomized trial. Blood. 2016;127(3):296-302.
- 9. Neunert C, Lim W, Crowther M, Cohen A, Solberg L, Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;117:4190-207.
- Ozsoylu S, Sayli TR, Oztürk G. Oral megadose methylprednisolone versus intravenous immunoglobulin for acute childhood idiopathic thrombocytopenic purpura. Pediatr Hematol Oncol. 1993;10(4):317-21.
- 11. Suarez CR, Rademaker D, Hasson A, Mangogna L. High-dose steroids in childhood acute idiopathic thrombocytopenia purpura. Am J Pediatr Hematol Oncol. 1986 Summer;8(2):111-5.
- 12. Provan D, Stasi R, Newland AC, Blanchette VS, Bolton-Maggs P, Bussel JB, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010:115:168-86.

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