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Original Article

Short Term Outcome of High Dose Dexamethasone Versus Prednisone In Children With Acute Immune Thrombocytopenic Purpura: A Single Center Trial

Ahmed Osama Kaddah, Niveen Salama, Doaa Maged Ahmed, Mariam Saad Nassim*
Department of Pediatrics, Faculty of Medicine, Cairo University, Egypt
* Correspondence: nasimmariam@cu.edu.eg
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Abstract:
Background: Corticosteroids are the first line treatment of immune thrombocytopenia (ITP). While high dose dexamethasone (HD-DXM) can be used as a first line therapy in adults, data about its use in children is scarce.
Aim of the work: To compare the efficacy of short-course HD-DXM and standard prednisone (PDN) as a first-line treatment to achieve increase in platelet count among children with previously untreated primary ITP.
Materials and Methods: This prospective randomized controlled open label clinical trial was conducted on 60 children with newly diagnosed ITP randomized to either HD-DXM or PDN (30 patients in each group). HD-DXM was given at a dose of 24mg/m^2/day (maximum dose 40mg/day) for 4 consecutive days and PDN was given at a dose 2mg/kg/day (maximum dose 60mg/day) for 7 consecutive days. Complete blood count was done at days 0,2,4,7,14,30 and 60.
Results: The mean age in HD-DXM and PDN groups were 6 ± 2.9 years and 6 ± 3.5 years respectively (p=0.89). Females and males were 16 (53.3%) and 14 (46.7%) in HD-DXM and 13 (43.3%) and 17 (56.7%) PDN groups (p=0.795). The main symptom was epistaxis in 30(50%) of cases, followed by purpura in 18(30%), gum bleeding in 10(16.6%), and subconjunctival hemorrhage in 2(3.4%). Initial mean platelet count in HD-DXM and PDN was 5.4± 2.9 x 10^3 µl and 5.2 ± 4.2 x10^3 µl (p=0.444). Platelet count was 66.9±42.2 x10^3 µl and 37.3±61.5 x10^3 µl in HD-DXM and PDN groups at day 2 (p=0.002), 176.6±134 x10^3 µl and 108.6±135.8 x10^3 µl at day 4 (p=0.011), 132±134.7 x10^3 µl and 173.8±101.5 x10^3 µl at day 7 (p=0.016). There was no significant difference between the 2 groups in platelet counts at day 14 , 30, 60 (p=0.271), (p=0.982) and (p=0.706) respectively.
Conclusion: HD-DXM achieved an earlier but unsustained rise of platelet count in newly diagnosed ITP than PDN. However, both medicines yielded the same effect during follow up period of two months.

Keywords: immune thrombocytopenia; ITP; pediatrics; high dose dexamethasone; prednisolone; Egyptian; children
Abbreviations: CBC: complete blood count; HD-DXM: high-dose dexamethasone; ITP: immune thrombocytopenic purpura; PDN: prednisone .

Introduction

Immune thrombocytopenic purpura (ITP) is a common autoimmune bleeding disorder characterized by isolated thrombocytopenia less than 100 x 10^9 /L (*1*, *2*). Despite being the most common cause of isolated thrombocytopenia, ITP is a diagnosis of exclusion (*3*). Newly diagnosed ITP is designated to ITP within the first three months of diagnosis (*1*). ITP may be complicated by mucosal bleeding, severe bleeding, intracranial hemorrhage and death (*4*). The main target in the treatment of ITP remains to reduce the incidence and risk of bleeding. Different modalities of treatment of ITP exist. Corticosteroids and intravenous immunoglobulins alone or combined are considered the first line treatment of newly diagnosed ITP (*5*). Regarding corticosteroid therapy in newly diagnosed ITP, many studies compared efficacy of high dose dexamethasone (HD-DXM) and standard prednisone (PDN) in adults (*6*, *7*), however only few studies were performed in pediatric age group. The aim of this study was to compare the efficacy of short-course HD-DXM and PDN as a first-line treatment to achieve increase in platelet count among children with previously untreated primary ITP.

Subjects and Methods

This prospective randomized controlled open label clinical trial was conducted on 60 children with newly diagnosed ITP at the Children Hospital, Faculty of Medicine, Cairo University Hospitals. The study was approved by the Ethical Committee of the Faculty of Medicine, Cairo University, Egypt (MS-57-2023). All the caregivers willingly consented to the study.

Participants

Sixty newly diagnosed children with ITP who presented to the Cairo University Children's Hospital were included in the study. The children were aged 1- 12 years with platelet count less than 30 x 10^9/ L or platelet count less than 50 ×10^9 /L in presence of bleeding. Patients with other causes of thrombocytopenia, with persistent or chronic ITP, or those with massive bleeding causing hemoglobin drop >2gm/dL or central nervous system bleeding were excluded from the study.

Methods

Patients were randomized to one of two groups (30 patients in each group):

• HD-DXM group: was given orally at a dose of 24mg/m^2/day (maximum 40mg/day) in three divided doses for 4 days (*8*).

• PDN group: was given oral prednisolone at a dose 2mg/kg/day in three divided doses (maximum 60mg/day) for 7 days (*9*).

The patients were randomized according to the day of presentation to our hospital, where patients presenting on Sundays, Tuesdays and Thursdays were randomized to dexamethasone group while patients presenting on Saturdays, Mondays and Wednesdays were randomized to prednisolone group. Ideally, a third control group with no treatment would have been valuable for the results to be valid however it was not possible to deny treatment for patients with newly diagnosed thrombocytopenia.

During the study period all patients fulfilling the inclusion criteria were subjected to detailed history taking, and thorough clinical examination.

Bleeding symptoms were classified into grades 0–5, according to the ITP-specific bleeding scale proposed by Buchanan score (*10*). Grade 0: no new hemorrhage of any kind; grade 1: minor skin bleeding, minor petechiae on palate or buccal mucosa and no active mucosal bleeding; grade 2 includes the possibility of small bruises, buccal hemorrhagic bullae or infiltrates, mild active bleeding; grade 3 involves overt mucosal bleeding (including menorrhagia or gastrointestinal bleeding); grade 4 includes severe mucosal bleeding or internal hemorrhage, requiring intensive care and grade 5: life threatening hemorrhage at any site.

Patients were weighed using a digital scale and surface areas were obtained (*11*).

Laboratory investigations included complete blood count (CBC) was done at Day 0, Day 2, Day 4, Day 7, Day14, Day 30 and Day 60 of treatment

Venous Blood samples (2 mL) were withdrawn from all patients and were collected in sterile tubes, which were used for complete blood count analysis. CBC done automated by Auto Hematology Analyzer machine (Sysmex XN 1000, Sysmex Corporation, Japan) and platelet counts were manually counted as well.

Statistical Analysis

Data was coded and entered using the statistical package SPSS version 21 (Statistical Package for the Social Science; IBM Corp, USA). Data was summarized as number and percent for qualitative variables and as mean, standard deviation, median and range for quantitative variables. Comparisons between groups were done using Chi Square test for qualitative variables, independent sample t test for quantitative normally distributed variables while non-parametrical Mann Whitney test was used for quantitative variables which were not normally distributed. Dependent comparison for quantitative not normally distributed variables were done using Friedman test with multiple comparisons between each two reading using Wilcoxon sign rank test with adjustment. P values less than or equal to 0.05 were considered as a statistically significant.

Results

The study population comprised 60 patients of them 27 (45%) were males. Their mean ± standard deviation age was 6±3.5 years. Duration of disease at enrollment ranged between 1-10

days with a mean of 3.9 ±2.5 days. All presented with petechia and ecchymosis of the patients and scored 3 on the Buchanan bleeding scoring system. Half of the patients presented with epistaxis, 18 (30%) presented with wet purpura, 10 (16.6%) presented with gum bleeding and 2 (3.4%) presented with subconjunctival hemorrhage. None of the patients had hepatomegaly or splenomegaly at presentation. Both HD-DXM or PDN groups were age and sex matched (p= 0.89) and (p=0.795) respectively as shown in table 1. There was no significant difference regarding type of bleeding at presentation between both groups (p= 0.88).

There was no significant difference in the hemoglobin and total leucocytic count levels at different days of the trial apart from day 7 in which leucocytic count was significantly higher in the PDN group than the HD-DXM group (p= 0.015). There was no significant difference in the platelets levels at Day 0 (p= 0.444) (Table 1). However, platelet levels were significantly higher among patients in the HD-DXM group than PDN group on days 2 and 4 (p= 0.002) and (p=0.011) respectively.

Table 1. Comparison between patients on high dose dexamethasone and prednisone at enrollment

	High dose dexamethasone (Number=30)		Prednisone (Number=30)		P value
	Mean ± SD		Mean ± SD		
Age (years)	6 ± 2.9		6 ± 3.5		0.89
Disease Duration (days)	3.2 ± 1.9		3.9 ± 2.5		0.37
Baseline platelet count (103/µl)	5.4±2.9		5.2±4.2		0.444
	Number	%	Number	%	
Sex					
Male	14	46.7	13	43.3	0.795
Female	16	53.3	17	56.7	

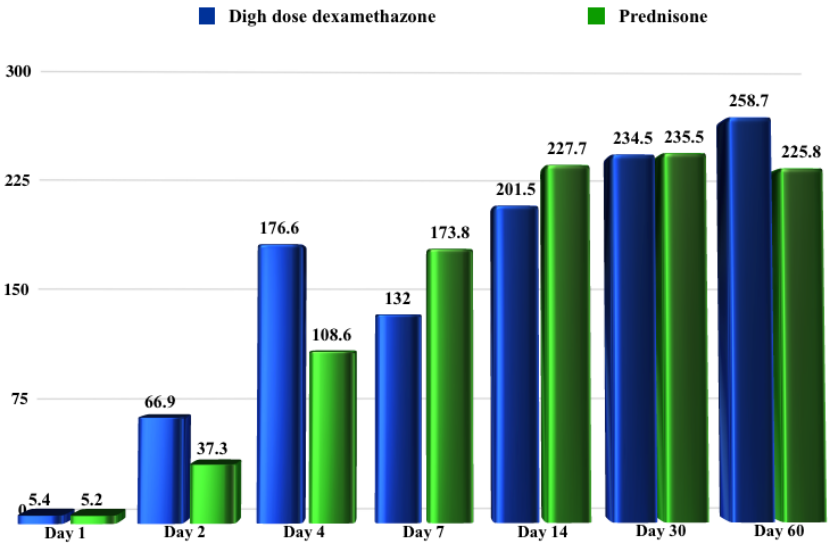

Figure 1. Mean Platelet counts (x10^3/µl) among patients on high dose dexamethasone and prednisone on different days of the study

Table 2. Mean platelet counts among newly diagnosed children with immune thrombocytopenic purpura on high dose dexamethasone and prednisone on different days of the study

	High dose dexamethasone (n=30)	Prednisone (n=30)	P value
Platelet count (10^3/ µl)	Mean ± SD	Mean ± SD	
Day 2	66.9±42.2	37.3±61.5	0.002
Day 4	176.6±134	108.6±135.8	0.011
Day 7	132±134.7	173.8±101.5	0.016
Day 14	201.5±117.5	227.7±108.5	0.271
Day 30	234.5±70.7	235.5±82.7	0.982
Day 60	258.7±55.4	225.9±89.8	0.706

There was a significant decline in platelet counts thereafter in the HD-DXM group so that platelet levels were significantly lower among the HD-DXM group than PDN group in day 7 (p= 0.016). There was no difference in the platelet levels between both groups on days 14, 30 (p= 0.271) and (p=0.982) respectively. Similarly on day 60 there has been a non-significant drop in the platelet count in the PDN group. Despite that, there was no significant difference in the platelet levels between both groups (p= 0.706). (Table 2 and Figure 1). We did not record any side effects in both groups.

Discussion

This study was conducted to compare the short term efficacy of HD-DXM versus PDN in the treatment of newly diagnosed pediatric patients with ITP. HD-DXM had an earlier but unsustained effect as that platelet counts were significantly higher on days 2 and 4 in the HD-DXM group whereas on day 7 counts were significantly higher in the PND group. There was no significant difference in platelet counts till 2 months follow up.

Many studies compared the efficacy of both drugs in treatment of ITP in adults and preferred HD-DXM over PDN (*6*, *7*, *12*). HD-DXM was reported to be more tolerable than the PDN (*12*, *13*). On the other hand, fewer studies compared both drugs in children and concluded that HD-DXM gave an equal response to PND (*8*, *14*). However, the American Society of Hematology guidelines 2019 recommended PDN at dose 2-4 mg/kg/day maximum 120 mg daily for 5-7 days rather than dexamethasone at a dose of 0.6 mg/kg/day (maximum 40mg) for 4 days (*9*) as the usefulness of HD-DXM was not validated as compared to PDN. Despite that different studies conducted in children used different doses and duration of DXM and PDN respectively other than the ones used in our study, and the conclusion yielded was similar. To exemplify, in a study conducted their study on 211 child, median age less than 3 years used dexamethasone at a dose of 0.6 mg/kg/day for 4 consecutive days, and prednisone at a dose of 2 mg/kg/day for 2 weeks followed by slow tapering over 4-8 weeks in responders (*14*). Others conducted a study on 42 children aged a mean of 8.2 and 8.6 years in the HD-DXM and PDN groups respectively, and used a dexamethasone dose of 40 mg/m^2/day for 4 days for 3 cycles every 28 days and prednisone dose of 2 mg/kg/day for 2 weeks followed by a quick tapering over another 2 weeks (*8).* Both studies concluded that HD-DXM was comparable as PDN as first line of treatment of ITP. Moreover, the former study also deduced that HD-DXM gave less adverse reactions than PDN as the frequency of infections and weight gain was higher among the PDN group (*14*).

Our study shows that HD-DXM is comparable with PDN in terms of raising platelet count. However, HD-DXM gives an earlier and fluctuant onset of action in patients with bleeding symptoms in which a prompt onset of action is desired. The use of HD-DXM gives more prompt increase in platelet count than PDN, while actually both regimens controlled the bleeding irrespective of the platelet count rate of rise. Studies among adults show that the long term effects of HD-DXM last less than the PDN, however studying the long term response to both regimens was beyond the scope of our current study, and remain to be addressed by other future studies (*7*).

The hospital stay and the cost-effectiveness was not assessed in our study. The convenience of both oral treatments render both valid options for management and might actually reduce hospital stay and prompt early discharge. Yet, we are not aware if either regimens reduce need for hospital admission or treatment cost. Our study was a single centered study in which patients were followed up for a relatively short period of time compared to other studies which limit our ability to project on the long term efficacy and side effects of both drugs. A multicenter study with longer follow up period is recommended draw more definite conclusions. As both regimens are effective the choice among both in newly diagnosed ITP might be based on the availability or cost.

Conclusion

High dose dexamethasone had an earlier but unsustained effect than prednisone in newly diagnosed ITP among our studied cohort of children. However, both drugs yielded the same effect during follow up period of two months.

Author Contributions

AOK analyzed the data, provided guidance, reviewed, and approved the final manuscript. DM performed all the data collection needed. NS performed the literature search and collected the data. MSN analyzed the data and drafted the manuscript. All authors approved final draft.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study.

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