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Comparison of Single Course High-Dose Dexamethasone and Prednisone for Initial Treatment of Primary Immune Thrombocytopenia in Children: A Prospective Randomized Trial

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Abstract :
Introduction: *Prednisone (PDN) is the most commonly used first-line treatment for primary immune thrombocytopenia (ITP) in children. Recently, a short-course high-dose dexamethasone (HD-DXM) therapy has been reported to be efficacious in childhood primary ITP. However, the choice of best corticosteroid as an initial therapy in primary ITP in children is still a matter of debate.*
Methods: *This single-blind prospective randomized clinical trial was conducted at Pediatrics Department, NRS Medical College and Hospital, Kolkata, a tertiary care teaching institute in the state of West Bengal from the month of July 2014 to June 2017 to compare the efficacy and safety of HD-DXM and conventional PDN as first-line strategies for newly diagnosed primary ITP in children. Patients enrolled were randomized to receive DXM 20 mg/m^2/day for 4 days (n=49) or PDN 2.0 mg/kg/day for 10 day and then tapered over 2-3 weeks (n=47).*
Results: *Single courses of HD-DXM resulted in a higher incidence of overall initial response (95.92% vs 82.98%, P = 0.049) and complete response (69.39% vs 34.04%, P = 0.001) compared with prednisone. Median time to response was shorter in the HD-DXM group [4 days (1-6) vs 6 days (2-9), P = < 0.0001). Bleeding was more effectively controlled on day 3 (P = 0.009) in children who had received HD-DXM compared with prednisone. Sustained response was achieved in 71.43% of patients in the HD-DXM arm and 42.55% in the PDN arm (P = 0.007). Initial complete response was associated with a decreased likelihood of loss of response. Both the corticosteroids were tolerated better with no statistically significant difference regarding treatment related overall toxicities (P = 0.0604).*
Conclusion: *We concluded that HD-DXM could be a preferred corticosteroid strategy for first-line management of primary ITP in children.*
Keywords : *Randomized clinical trial; Newly diagnosed primary immune thrombocytopenia; Children; High-dose dexamethasone; Prednisone.*

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I. Introduction

Immune thrombocytopenia (ITP) is an acquired autoimmune disease where the platelet count is < 100×10^9/L. The abbreviation ITP stood for idiopathic thrombocytopenic purpura until recently, but current awareness relating to the immune-mediated nature of the disease, and the absence or minimal signs of bleeding in a large proportion of cases have led to a revision of the terminology. ITP may be found in isolation (primary) or along with other autoimmune and medical conditions (secondary) like systemic lupus erythematosus, human immunodeficiency virus (HIV), hepatitis C, drugs etc. Based on duration of the disease, ITP can be further classified into three categories like newly diagnosed (diagnosis to 3 months), persistent (3-12 months), and chronic (> 12 months). [1] Current concepts regarding pathophysiologic mechanisms of thrombocytopenia in ITP have shifted from the traditional view of increased platelet destruction mediated by autoantibodies to more complex mechanisms in which both impaired platelet production and T cell–mediated effects play a role. [2]

Treatment of ITP, the most common bleeding disorder of childhood, is a controversial issue until date. Recent consensus recommend that the majority of children with newly diagnosed ITP with no bleeding or mild bleeding (defined as skin manifestations only, such as bruising and petechiae) can be treated with "observation alone" regardless of platelet count because severe bleeding events are thought be rare. Nevertheless, it is necessary to treat all children with moderate to severe bleeding symptoms or those at increased risk of bleeding. The first-line/ initial pharmacologic management can be provided with a short course of corticosteroids, intravenous immunoglobulin (IVIg), or anti-D immunoglobulin (anti-D). If a rapid increase in platelet count is desired, then a single dose of IVIg (0.8 to 1 g/kg) or anti-D are preferred based on the ability of these agents to

increase the platelet count within 24-48 hours in the majority of children. Anti-D is recommended only in patients, who are Rh positive, who have a negative direct antiglobulin test (Coombs), and who have not undergone splenectomy. Splenectomy may be indicated when there is no response to corticosteroids or immunoglobulins and the patient still have bleeding, including of the central nervous system. [3,4]

Among all the corticosteroids, the role of prednisone (PDN) as a front-line therapy for primary ITP in children has been proven in different studies with varying initial response rate. Although, adults have a standard regimen for PDN in acute ITP, but children have not. Opinion differs widely among different investigator groups, ranging from 2 mg/kg/day for 2 weeks then tapered over 21 days to 4 mg/kg/day for 3-4 day. [5-11]

High-dose dexamethasone (HD-DXM) have been used in many studies as second-line treatment option for children or adolescents with ITP who have significant ongoing bleeding despite treatment with IVIg, anti-D, or conventional doses of PDN and/or who have persistent or chronic ITP, but did not provide a uniform response. [12-19] However, the regimen used in those studies varied widely, ranging from 20-40 mg/m^2 per day (maximum 40 mg/day) for four days every 15-28 days for 4-6 cycles. Recently a short-course HD-DXM therapy has also been shown to be efficacious in both adult and childhood acute ITP. [20-27]

Recent comparative studies showed HD-DXM is more effective than conventional PDN therapy in newly diagnosed adult ITP as initial treatment with fewer incidences of relapses and toxicities. [28-31] However, even after extensive search through MEDLINE PubMed (major search engine), we did not find any study comparing the efficacy and safety between HD-DXM and oral PDN as a front-line treatment of newly diagnosed ITP in children. The aim of this prospective randomized clinical trial was to evaluate the effectiveness of single course of HD-DXM comparing conventional PDN therapy as a first-line treatment of newly diagnosed ITP in children.

II. Materials And Methods

This single-blind prospective randomized clinical trial was conducted at Pediatrics Department, NRS Medical College and Hospital, Kolkata, a tertiary care teaching institute in the state of West Bengal from the month of July 2014 to June 2017. Enrollment of patients was began from July 2014 and stopped in June 2016 but the follow-up was continuing until June 2017. The study consisted of 2 phases: the initial response phase lasted from the time of enrollment up to achievement of initial response or day 10, whichever was shorter, and an observational follow-up phase lasted from day of response to end of the study. Ethical committee of the Institute approved the study protocol and informed consent was obtained from the legal guardians of all children. All children, upto the age of 12 years, who were diagnosed with primary ITP according to the International Working Group (IWG) guidelines, were enrolled in the present study. [1,3] Our inclusion criteria were: newly diagnosed treatment-naive primary ITP with either a baseline peripheral platelet count < 30×10^9/L or with the presence of bleeding symptoms. Bleeding symptoms was classified according to the standard scoring system graded from 0 to 4 (Table 1). Bleeding symptoms were considered present if the grading of bleeding was 1 or higher. However, for safety considerations, patients with life-threatening bleeding (Grade 4) eg, massive hemorrhage with severe anemia, central nervous system bleeding was not included in our study.

Patients with previously treated ITP or had received corticosteroids or immunosuppression therapy for non-ITP diseases within 3 months before enrollment, diabetes, hypertension, cardiovascular diseases, liver and kidney dysfunction, serologically positive for acquired immunodeficiency syndrome, hepatitis C, and hepatitis B, active infection, autoimmune hemolytic anemia, malignancy, and connective tissue diseases were excluded. Diagnosis of ITP was done by thorough medical history, physical examination, and complete blood cell counts with cytomorphologic examination of peripheral blood smear, in which no alterations of erythrocytic and leukocytic series should be present. Relevant laboratory investigations were performed to exclude the secondary causes of thrombocytopenia as mentioned in the exclusion criteria. We did not perform bone marrow aspiration routinely but done it before starting additional ITP-modifying treatment in all patients who did not have a response on day 10 following initiation of therapy.

Patients were randomly divided into two groups: Group A received oral HD-DXM 20 mg/m^2/day in two divided doses for four consecutive days followed by abrupt stoppage. Group B was treated with oral PDN 2 mg/kg/day for 10 day followed by gradual tapering over 2-3 weeks. Continuation of low dose oral PDN for another 2-3 weeks were aimed to maintain platelet count above 30×10^9/L with an absence of bleeding symptoms. Among the study population, patients who had failed to achieve the response within 10 days following initiation of therapy had received rescue therapy with a single course of 1 g/kg IVIG and /or corticosteroids at the minimum effective dose. Among the initial responders, who had a loss of response at any time during the study period were treated according to the standard practice of the study center. Complete blood count and peripheral blood smear were checked daily for initial 10 days or until patient achieved complete remission following initiation of treatment, whichever was shorter. We counted duration of follow-up from the

time of initial response. We repeated the platelet counts among the initial responders monthly during initial follow-up visits for the first six months, subsequently every three months until the end of study. Blood counts were repeated at any time during follow-up period if patient turned back with bleeding manifestations.

Outcome was measured by parameters like response, time to response, duration of response, sustained response (SR), loss of complete response, loss of response, clinical improvement of bleeding symptoms and adverse effect. We described initial response into three categories like complete response (CR), response (R) and no response (NR) as per criteria proposed by an International Working Group (IWG). [1] Complete response (CR) was defined as platelet count $\geq 100\times10^9$/L measured on two occasions >7 days apart and absence of bleeding, whereas response (R) as platelet counts between 30 and 100×10^9/L and at least doubling of the baseline count measured on two occasions >7 days apart and absence of bleeding. No response (NR) was defined as platelet count $< 30\times10^9$/L or less than doubling of the baseline count measured on two occasions more than a day apart or presence of bleeding.

Time to response (TTR) was defined as the duration from initiation of treatment to achievement of R or CR. Duration of response (DOR) was measured from the achievement of CR or R to loss of response (platelet count dropped below 30×10^9/L or presence of bleeding) or to the last follow-up visit. We defined sustained response (SR) as platelet count maintained $> 30\times10^9$/L with an absence of bleeding symptoms or no requirement for additional ITP-modifying treatment for six consecutive months following achievement of initial response. [20,24] Loss of CR was defined as a CR patient whose platelet count later fell $< 100\times10^9$/L measured on two occasions more than a day apart and/or the presence of bleeding. Loss of response was defined when platelet count dropped later $< 30\times10^9$/L measured on two occasions more than a day apart or experienced bleeding in a patient who had achieved either CR or R earlier. Adverse events were evaluated according to Common Terminology Criteria for Adverse Events published by US National Cancer Institute. [32]

Results were analyzed according to the intention to treat (ITT) population, which included all randomized patients who received the first dose of either HD-DXM or PDN. Statistical analysis was performed using SPSS version 16 (SPSS Inc, Chicago, IL, USA). Continuous variables were compared using Student's t test for independent sample whereas categorical variables were compared using the Fisher's exact test. Two-sided P value < 0.05 was considered significant.

III. Results

Between July 2014 to June 2016, 131 children with age group between 1-12 years were diagnosed to have primary ITP and were screened for eligibility. However, ultimately 96 cases were fulfilled the inclusion criteria and enrolled for the study. Forty nine children were randomly assigned to the group A and 47 to group B. Children belong to group A received HD-DXN 20 mg/m^2/day in two divided doses for consecutive four days followed by abrupt stoppage, whereas group B received PDN 2 mg/kg/day for 10 day followed by gradual tapering over 2-3 weeks. No significant difference was noted between different baseline variables like mean age (P = 0.336), gender (P = 0.834) and platelet count (P = 0.756) of the two groups. Among the study population, majority were presented with skin (55.21%) and mucus bleeding (26.04%) in both the group. Although 18 cases (18.75%) presented with Grade 3 bleeding but no significant statistical difference was noted regarding mean baseline platelet count (6860 ± 713 vs. 8287 ± 642; P = 0.096) between both the groups. Children who came with Grade 4 bleeding means severe life threatening bleeding were excluded from our study. We did not get any such case with grade 0 bleeding as no child came to us for routine screening test. Maximum number of children were with grade 1 bleeding 53.06% (n=26) and 57.45% (n=27) in both the groups respectively (Table 2).

Initial response:

We assessed initial overall responses (OR) (CR+R) on day 10 following initiation of therapy in both the groups. As shown in Table 3, single courses of HD-DXN resulted in a significantly higher incidence of overall response (CR+R) compared with PDN (P = 0.049). HD-DXN also resulted in a significantly higher incidence of CR (34 vs 16; P = 0.001) and a shorter median time to response [4 day (1-6) vs 6 day (2-9); P = <0.0001] (Table 3). We observed disappearance of different types of bleeding among all the responders in both Groups. One child in Group A and five children in Group B were also showed disappearance of bleeding manifestations among the non-responders. Following initiation of treatment, bleeding was effectively controlled early in Group A as compared to Group B. Statistically significant response in terms of improvement of bleeding manifestations was seen on day 3 (n=27, P = 0.009) among the children in Group A (Table 4).

Long-term outcome:

After three months following initial response, in Group A, 13 patients were NR; four cases showed R and 32 cases revealed CR and loss of CR and R occurred in this period. In Group B, NR, R and CR were observed in 23, 10 and 14 patients, respectively (P = 0.0345). At 6 months' follow-up after initial response, the

number of patients with NR, R and CR were 14 versus 27, three versus 6 and 32 versus 14 respectively in both the groups. The incidence of SR and sustained CR showed significant difference (*P* = 0.007 and 0.0006 respectively) between the two Groups. Subsequently, loss of response was noted in one patient in each Group (P = 0.0006) until the end of study. Median time to loss of response among the initial responders in both the groups was 65 days (33-197) and 52.5 days (33-190). Median duration of response among initial responders was 615 days (33-1078) and 190 days (23-1062) respectively between both the groups (Table 3).

Both the drugs were well tolerated by children. Three children in Group A developed gastritis. Whereas, in Group B, five cases experienced gastritis, one gained weight, one developed hypertension and one developed glucose intolerance. The incidence of these different types of treatment related toxicities showed no significant difference between the two Groups (Table 5).

IV. Figures and Tables

Table 1: Grade and type of bleeding symptom:

Grade	Type of bleeding
0	Absent
1	Petechiae
2	Ecchymoses and/or dripping with moderate blood loss
3	Major mucous hemorrhage with copious loss of blood without sequelae
4	Major mucous and/or parenchymal hemorrhage with copious loss of blood with sequelae and/or life-threatening

Table 2: General characteristics of patients:

Variables	Group A	Group B	*P* value
Gender	18/31	19/28	0.834
Median age in years (range)	6.5 (2-11)	7 (2.5-10.5)	0.336
Median platelet count, $\times 10^9$/L (range)	12.5 (7.7-14.75)	12.75 (7.3-14.65)	0.756
Grade of bleeding (No.):			
0	0	0	
1	26(53.06%)	27(57.45%)	
2	13(26.53%)	12(25.53%)	
3	10(20.41%)	08(17.02%)	
4	Excluded	Excluded	

Table 3: Comparison of outcome between the two groups:

Short-term outcome			
Initial response	Group A (n=49)	Group B (n=47)	*P value*
Complete response (CR), n (%)	34 (69.39)	16 (34.04)	0.001
Overall response, n (%)	47 (95.92)	39 (82.98)	0.049
Median time to response, day (range)	4 (1-6)	6 (2-9)	<0.0001
Long-term outcome			
Follow-up	Group A (n=49)	Group B (n=47)	*P value*
Follow-up at three months			
Complete response (CR), n (%)	32 (65.31)	14 (29.79)	0.0006
Overall response, n (%)	36 (73.47)	24 (51.06)	0.0345
Follow-up at six months			
Complete response (CR), n (%)	32 (65.31)	14 (29.79)	0.0006
Overall response, n (%)	35 (71.43)	20 (42.55)	0.0070
Follow-up till the end of study			
Complete response (CR), n (%)	32 (65.31)	14 (29.79)	0.0006
Overall response, n (%)	34 (69.39)	19 (40.43)	0.0073
Median time to loss of response among initial responders	65 days (33-197)	52.5 days (33-190)	0.9037
Median duration of response among initial responders	615 days (33-1078)	190 days (23-1062)	0.0326

Table 4: Response in terms of disappearance of bleeding manifestations between the two groups:

Day of disappearance of bleeding	Group A (n=49)	Group B (n=47)	*P value*
Day 2, n (%)	8 (16.33)	2 (4.26)	0.092
Day 3, n (%)	27 (55.10)	16 (34.04)	0.009
Day 4, n (%)	11 (22.45)	20 (42.55)	0.720

Day 5-10, n (%)	2 (4.08)	6 (12.77)	1.000
Persistence of bleeding >Day 10	1 (2.04)	3 (6.38)	
Total, n (%)	49 (100)	47 (100)	

Table 5: Distribution of different categories of responses between the two groups:

Complications	Group A (n=49)	Group B (n=47)	*P value*
Gastritis, n (%)	3	5	0.4593
Weight gain, n (%)	Nil	1	0.4535
Hypertension, n (%)	Nil	1	0.4535
Glucose intolerance, n (%)	Nil	1	0.4535
Overall complications	3	8	0.0604

V. Discussion

It is well known that, until now, prednisone or prednisolone is considered the most largely used therapeutic approach as first-line treatment for newly diagnosed primary ITP patients, especially children. [3,4] Although, adults have a standard regimen, but best dosage are missing in children. Variable response was observed in children with the conventional dose of prednisone (1-2 mg/kg/day for a maximum 14 days). [33,34] Higher doses (4 mg/kg/day) for 3 to 4 days have been shown to be effective in up to 72% to 88% of children (platelet count $>50\times10^9$/L) within 72 hours. [7-9] Moving from the Andersen experience, concerning the use of pulsed HD-DXN given in resistant/refractory ITP with very satisfactory results, we planned a first prospective randomized monocenter study with the aim to compare the efficacy and safety between HD-DXN and PDN as first-line therapy in previously untreated pediatric ITP patients. [35]

The overall initial response rate (CR+R) in HD-DXN group in our study was very encouraging (47/49; 95.92%), whereas that in PDN group was 82.98% (39/47). More or less similar efficacy of HD-DXM was observed in the previous studies done by Yadav D et al, Cheng Y et al, Borst F et al, Gómez-Almaguer D et al, Mazzucini MG et al, Mashhadi MA et al, Masanao Teramura et al and Wei Y et al. [19,20,21,25,27,28,29,31] HD-DXN also resulted in a higher incidence of CR when compared with PDN (34/49, 69.39% vs 16/47, 34.04%) which is statistically significant (P = 0.001). Our results were comparable with the observations made by Mashhadi MA et al and Wei Y et al. [28,31] However, nearly identical initial response and CR rates were observed in the study done by Masanao Teramura et al. [29] Median time to response was shorter in HD-DXN group when compared with that of PDN group [4 days (1-6) vs 6 day (2-9)], which was also statistically significant (P = <0.0001). Wei Y et al also noted similar observation in their study. [31] Bleeding was more effectively controlled in the HD-DXN group as compared with PDN group. Statistically significant improvement was observed in Group A on day 3 (P = 0.009).

The incidence of SR and sustained CR showed significant difference between the two groups (P = 0.0070 and 0.0006 respectively). In Group A, among the 35 SR, 34 (97.1%) were from initial CR category, whereas, in Group B, out of 20 SR, 16 (80%) from initial CR. This concludes that initial CR was the definite positive indicator associated with an increased incidence of SR in the initial responders of both groups. Our observation coincides with the observation made by Wei Y et al. [31] In our study, in Group A, among the 13 patients who showed loss of response within the study period, 11 (84.6%) had developed it within 3 months. In contrast, among the 20 patients in Group B, who showed loss of response within the study period, 15 (75%) had had developed it within 3 months. No statistically significant difference was observed regarding median time to loss of response among the initial responders in both the groups [65 days (33-197) and 52.5 days (33-190); P = 0.9037].

Out of total 53 relapse cases, 50 had a relapse within first three month following initial response and overall median time to relapse was 45 days (range, 14 to 129 days) as noted by Cheng Y et al which was almost similar with our observations. [20] Among the initial responders, median duration of response was significantly higher in HD-DXN group when compared with that of PDN group (P = 0.0326). This concludes that effect was more sustained with HD-DXN therapy when compared with that of PDN. Our treatment protocol was well tolerated by patients of both the groups. No statistically significant difference of overall treatment related toxicities were observed between among the patients of both the groups (P = 0.0604).

VI. Conclusion

In conclusion, treatment involving steroid therapy for ITP is used to obtain not only a high initial response rate but also a sustainable response that avoids the need for any further treatment. Based on our findings, HD-DXN could be used as a first-line treatment for pediatric patients with newly diagnosed primary

ITP because it accomplishes both of these. Our analysis showed that initial treatment with HD-DXN produced longer response duration compared to a conventional dose of prednisone.

However, multicenter prospective randomized clinical trials on a large pediatric cohort are warranted to establish the optimal initial steroid therapy for newly diagnosed primary pediatric ITP.

References

[1]. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. Blood. 2009;113(11):2386-2393.

[2]. Stasi R, Evangelista ML, Stipa E, Buccisano F, Venditti A, Amadori S. Idiopathic thrombocytopenic purpura: current concepts in pathophysiology and management. Thromb Haemost. 2008 Jan;99(1):4-13.

[3]. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010;115(2):168-186.

[4]. Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;117(16):4190-4207.

[5]. Buchanan GR, Holtkamp CA. Prednisone therapy for children with newly diagnosed idiopathic thrombocytopenic purpura. A randomized clinical trial. Am J Pediatr Hematol Oncol. 1984 Winter;6(4):355-61.

[6]. Bellucci S, Charpak Y, Chastang C, Tobelem G. Low doses v conventional doses of corticoids in immune thrombocytopenic purpura (ITP): results of a randomized clinical trial in 160 children, 223 adults. Blood. 1988 Apr;71(4):1165-9.

[7]. Blanchette VS, Luke B, Andrew M, et al. A prospective, randomized trial of high-dose intravenous immune globulin G therapy, oral prednisone therapy, and no therapy in childhood acute immune thrombocytopenic purpura. J Pediatr. 1993;123(6):989-995.

[8]. Blanchette V, 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):703-707.

[9]. Carcao MD, Zipursky A, Butchart S, Leaker M, Blanchette VS. Short-course oral prednisone therapy in children presenting with acute immune thrombocytopenic purpura (ITP). Acta Paediatr Suppl. 1998 Jun;424:71-4.

[10]. Fujisawa K, Iyori H, Ohkawa H, et al. A prospective, randomized trial of conventional, dose-accelerated corticosteroids and intravenous immunoglobulin in children with newly diagnosed idiopathic thrombocytopenic purpura. Int J Hematol 2000;72(3):376-383.

[11]. Ou CY, Hsieh KS, Chiou YH, Chang YH, Ger LP. A comparative study of initial use of intravenous immunoglobulin and prednisolone treatments in childhood idiopathic thrombocytopenic purpura. Acta Paediatr Taiwan. 2006 Sep-Oct;47(5):226-31.

[12]. Adams DM, Kinney TR, O'Branski-Rupp E, Ware RE. High-dose oral dexamethasone therapy for chronic childhood idiopathic thrombocytopenic purpura. J Pediatr. 1996 Feb;128(2):281-3.

[13]. Chen JS, Wu JM, Chen YJ, Yeh TF. Pulsed high-dose dexamethasone therapy in children with chronic idiopathic thrombocytopenic purpura. J Pediatr Hematol Oncol. 1997 Nov-Dec;19(6):526-9.

[14]. Ku¨hne T, Freedman J, Semple JW, Doyle J, Butchart S, Blanchette VS. Platelet and immune responses to oral cyclic dexamethasone therapy in childhood chronic immune thrombocytopenic purpura. J Pediatr. 1997;130(1):17-24.

[15]. Borgna-Pignatti C, Rugolotto S, Nobili B, et al. A trial of high-dose dexamethasone therapy for chronic idiopathic thrombocytopenic purpura in childhood. J Pediatr. 1997;130(1):13-16.

[16]. Wali YA, A Lamki Z, Shah W, Zacharia M, Hassan A. Pulsed high-dose dexamethasone therapy in children with chronic idiopathic thrombocytopenic purpura. Pediatr Hematol Oncol. 2002;19(5):329-335.

[17]. Chandra J, Dua T, Narayan S, Jain V, Sharma S, Dutta AK. Dexamethasone therapy in chronic ITP. Indian Pediatr. 2000 Jun;37(6):647-50.

[18]. Hedlund-Treutiger I, Henter JI, Elinder G. Randomized study of IVIg and high-dose dexamethasone therapy for children with chronic idiopathic thrombocytopenic purpura. J Pediatr Hematol Oncol. 2003 Feb;25(2):139-44.

[19]. Yadav D, Chandra J, Sharma S, Singh V. Short-course high-dose dexamethasone therapy for chronic idiopathic thrombocytopenic purpura in children. J Trop Pediatr. 2010 Dec;56(6):446-7.

[20]. Cheng Y, Wong RS, Soo YO et al. Initial treatment of immune thrombocytopenic purpura with high-dose dexamethasone. N Engl J Med. 2003 Aug 28;349(9):831-6.

[21]. Borst F, Keuning JJ, van Hulsteijn H, Sinnige H, Vreugdenhil G. High-dose dexamethasone as a first- and second-line treatment of idiopathic thrombocytopenic purpura in adults. Ann Hematol. 2004 Dec;83(12):764-8. Epub 2004 Aug 10.

[22]. Naithani R, Mahapatra M, Kumar R, Mishra P, Saxena R. High dose dexamethasone therapy shows better responses in acute immune thrombocytopenia than in chronic immune thrombocytopenia. Platelets. 2010;21(4):270-3.

[23]. Zaja F, Baccarani M, Mazza P, et al. Dexamethasone plus rituximab yields higher sustained response rates than dexamethasone monotherapy in adults with primary immune thrombocytopenia. Blood. 2010;115(14):2755-2762.

[24]. Gudbrandsdottir S, Birgens HS, Frederiksen H et al. Rituximab and dexamethasone vs dexamethasone monotherapy in newly diagnosed patients with primary immune thrombocytopenia. Blood. 2013 Mar 14;121(11):1976-81.

[25]. Gómez-Almaguer D, Herrera-Rojas MA, Jaime-Pérez JC et al. Eltrombopag and high-dose dexamethasone as frontline treatment of newly diagnosed immune thrombocytopenia in adults. Blood. 2014 Jun 19;123(25):3906-8.

[26]. Su Y, Xu H, Xu Y, Yu J, Dai B, Xian Y, Xiao J. A retrospective analysis of therapeutic responses to two distinct corticosteroids in 259 children with acute primary idiopathic thrombocytopenic purpura. Hematology. 2009 Oct;14(5):286-9.

[27]. Mazzucini MG, Fazi P, Bernasconi S, et al. Therapy with high dose dexamethasone (HD-DXM) in previously untreated patients affected by idiopathic thrombocytopenic purpura: a GIMEMA experience. Blood 2007;109:1401–7.

[28]. Mashhadi MA, Kaykhaei MA, Sepehri Z, Miri-Moghaddam E. Single course of high dose dexamethasone is more effective than conventional prednisolone therapy in the treatment of primary newly diagnosed immune thrombocytopenia. Daru. 2012 Aug 28;20(1):7.

[29]. Masanao Teramura, Midori Ishiyama, Hiroshi Kazama et al. Comparison of High-Dose Dexamethasone and Prednisone for Initial Treatment of Adult Primary Immune Thrombocytopenia. Open Journal of Blood Diseases, 2012, 85-89.

[30]. Sakamoto K, Nakasone H, Tsurumi Set al. Prednisone versus high-dose dexamethasone for untreated primary immune thrombocytopenia. A retrospective study of the Japan Hematology & Oncology Clinical Study Group. J Thromb Thrombolysis. (Abstract) 2014 Apr;37(3):279-86.

[31]. Wei Y, Ji XB, Wang YW, Wang JX et al. High-dose dexamethasone vs prednisone for treatment of adult immune thrombocytopenia: a prospective multicenter randomized trial. Blood. 2016 Jan 21;127(3):296-302; quiz 370.

[32]. National Cancer Institute. DCTD, NCI, NIH and DHHS. Cancer therapy. Evaluation program, Common terminology Criteria for adverse event. Version 3.0. http://Ctep.Cancer.gov.2.2003.

[33]. George JN, Woolf SH, Raskob GE, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood. 1996;
[34]. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. Br J Haematol. 2003; 120(4):574-596.
[35]. Andersen JC. Response of resistant idiopathic thrombocytopenic purpura to pulsed high-dose dexamethasone therapy. N Engl J Med. 1994; 330:1560-1564.

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