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RESEARCH ARTICLE

Efficacy of oral versus intravenous steroids in the treatment of pediatric immune thrombocytopenic purpura: A single center experience

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Objectives: This study conducted to assess the response rate to steroid in children with acute primary ITP and compare the relative effectiveness of oral steroid to intravenous dexamethasone.

Methods: A retrospective study involves children with primary ITP and treated by steroids with age below 15 years who were consulted the outpatient hematology clinic at central teaching hospital of pediatric from 1st of January 2024 to 31 December 2024. Patient were divided into two groups based on treatment modality: (1) children treated by oral prednisolone; (2) children treated by intravenous dexamethasone. For each patient recruited in the study, two set of data were collected: clinical data (presentation, severity of bleeding) , demographical data (age, gender), and laboratory data: which included platelets count that obtained from complete blood counts (baseline at presentation, on day 14th, and on day 28th of establishment of either mode of therapy).

Results: A total of 135 children diagnosed with primary ITP was treated by steroid with age range 2 months to 15 years. The severity of ITP was mild –moderate in 71% of patients and those was treated by oral prednisolone, while 29% were presented with severe bleeding and were treated by intravenous dexamethasone. The means of platelet count significantly elevated after the initiation of therapy in both oral prednisolone (P value = 0.03) and intravenous dexamethasone group (P value = 0.001) during 1st and 2nd evaluation. During the first evaluation, children on intravenous steroids show a significantly higher response than those treated by oral steroids P value = 0.001 and this difference maintained in the second evaluation visit with P value =0.021

Conclusion: Intravenous dexamethasone demonstrates greater efficacy than oral prednisolone in managing children with primary ITP, suggesting its preference as the optimal steroid regimen for treatment.

Keywords: thrombocytopenia, steroids, purpura, pediatrics

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Introduction

Immune thrombocytopenic purpura (ITP) is an acquired autoimmune hematological disorder with an estimated annual incidence of 5-10 per 100.000 in children[1]. The condition characterized by formation of autoantibody against platelets antigen which results in premature removal of platelets from circulation and resultant thrombocytopenia [2]. Presentation is variable ranging from asymptomatic thrombocytopenia to bleeding including life threating cerebral hemorrhage [3] .

It is divided into primary or secondary according to the presence of underlying cause that trigger the immune thrombocytopenia [3]. Primary ITP characterized by significant reduction in platelet count with bleeding in the absence of other causes or disorders that associated with thrombocytopenia [4]. Since there is no specific diagnostic test for primary ITP, the diagnosis usually made only after excluding possible secondary causes [5–7].

The management of primary ITP had been a subject of debate; however, it depends mainly on the severity of bleeding to include one or more of the following treatment modalities that is observation, steroids, anti-D, and intravenous immunoglobulins. Treatment approach must be tailored to accommodate presentation of each case to maximize the response and reduce possible drug toxicity [8]. When steroids are chosen as first line of therapy, studies recommend either high-dose dexamethasone or standard-dose prednisone as first-line therapy; however, there is debate about which regimen of corticosteroid to be used [9,10]. A comparable long-term rise in platelets count were linked to both strategies but the short-term response was studied inadequately [11].

Guidelines for treating patients with ITP in other parts of the world cannot be applied to developing countries like Iraq who face a shortage in high-cost treatment modalities, so a local guideline that adapt to the status of each country is mandatory[12,13]. These guidelines will most probably be established based on comparing results obtained by different available treatment regimens[5]. Steroid is widely available and low in cost compared to other treatment modality make it the first line therapy for children with ITP in Iraq [14], this study was conducted to assess the response rate to steroid in children with acute ITP and compare the relative effectiveness of oral steroid to intravenous dexamethasone in the treatment of pediatric patients diagnosed with ITP.

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Methods:

A retrospective study involves children diagnosed with primary ITP and treated by steroids with age below 15 years who were consulted the outpatient hematology clinic at central teaching hospital of pediatric from 1st of January 2024 to 31 of December 2024. Patients were diagnosed as case of primary ITP after excluding the secondary causes of immune thrombocytopenia including hepatitis (A-E), cytomegalovirus, human immunodeficiency virus, and/or *H pylori* [15,16]. So, all patients in this study had negative bone marrow examination and serological test for systemic lupus erythematosus and Coombs test and retic count for Evan syndrome.

Children incorporated in the present study after matching the following inclusion criteria: (1) age less then 15 years, (2) diagnosed as primary ITP, (3) steroid was the only treatment received by the patients. On the other hand, children were excluded from the study if matched any of the following exclusion criteria :(1) cases with secondary ITP, (2) presence of other associated disease that cause bleeding tendency such as liver failure, chronic renal failure, and inherited disorders that cause bleeding diatheses, (3) age 15 years or more, (4) children received alternative or additional therapy beside steroids, and (4) incomplete or missing data.

Patient were divided into two groups based on treatment modality: first group include children treated by oral prednisolone 1-2 mg /kg/day over 2 weeks then tapering, second group included children treated by intravenous dexamethasone 24 mg /m^2 / day for 4 days for 3 cycles every 2 weeks regardless of the response.

For each patient recruited in the study, two set of data were collected: First the clinical data (presentation, severity of bleeding) and demographical data (age, gender). Second the laboratory data: which included platelets count that obtained from complete blood counts (baseline at presentation, on day 14th, and on day 28th of establishment of either mode of therapy). Severity of bleeding were divided into two grads only as distinguishing between mild and moderate grades of bleeding based on the Buchanan and Adix score[17] proved challenging, as data were collected retrospectively. Consequently, we categorized any patient presenting with exclusively cutaneous bleeding as having a mild-to-moderate grade of bleeding, while those with mucosal bleeding were classified as severe.

The response to treatment were assessed by two evaluation visits: the first evaluation visits at day 14th, the 2nd evaluation visits at day 28th after the commencement of therapy. During these visits, platelet counts, and clinical condition of the patient (presence of bleeding and its type) is documented. Accordingly, the patient's response will fill into one of following three outcomes: Complete response (CR): when platelet count more than 100 $\times 10^9$/L and absence of bleeding. Partial response (PR); platelet count 30 -100 $\times 10^9$/L and at least 2-fold increase the baseline count and absence of bleeding. No response (NR); platelet count < 30 $\times \mathbf{10^9/L}$ or less than 2-fold increase of baseline platelet count or bleeding.

Statistical analysis

The data analyzed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Independent t-test (two tailed) was used to compare the continuous variables accordingly. Paired t-test was used to compare the continuous variables before treatment and after responses. A level of P – value less than 0.05 was considered significant.

Ethical approval

The ethical committee at Mustansiriyah university-college of medicine approved the study with approval number (37) dated on 27-11-2024.

Results

A total of 135 children diagnosed with primary ITP during the study period was treated by steroid with age range (2 months to 15 years) with a mean of 4.83 ± 2.6 years. Female predominated the studied sample with female to male ratio of 1.5:1. The most common type of bleeding was cutaneous (70%). The severity of ITP was mild –moderate in 71% of patients and those was treated by oral prednisolone, while 29% were presented with severe bleeding and were treated by intravenous dexamethasone, as seen in Table 1, Figure 1.

On presentation, the mean platelet counts in children with ITP treated by intravenous dexamethasone (16.53 ± 14.77) $\times 10^9$/L was significantly lower than platelet count in children treated by oral prednisolone (23.56 ± 10.02) $\times 10^9$/L with (p value < 0.0001).

The mean platelet counts among patients treated with intravenous dexamethasone (1st and 2nd evaluation) were significantly higher than that before treatment (71.0 versus 16.53) $\times 10^9$/L, P= 0.001; 76.0 versus 16.53 $\times 10^9$/L, P= 0.001, respectively). Also, the mean of platelet counts in patients who received oral prednisolone (1st and 2nd evaluation) the response was significantly higher than that before

Table 1. The demographic and clinical characteristics of the studied children with ITP.

Variables	Number (n=135)	Percentage (%)
Age		
Up to 5 years	59	44
6-10	58	43
11-15	18	13
Gender		
Female	85	63
Male	50	37
Bleeding type		
Epistaxis only	5	4
Menorrhagia only	3	2
Gum bleeding only	4	3
Mucocutaneous	27	20
Cutaneous	96	71
Severity		
Mild-moderate	96	71
Severe	39	29

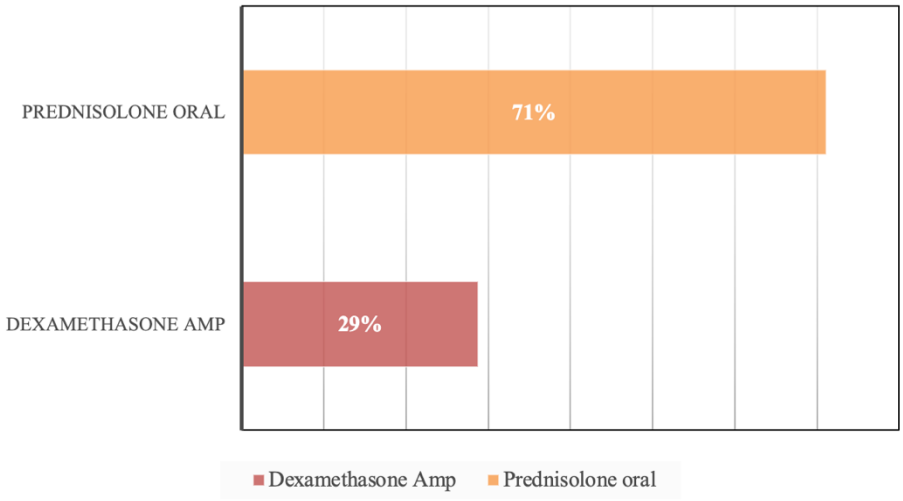

Fig. 1. Distribution of study patients by modality of treatment

treatment (42.09 versus 23.56 $\times 10^9$/L, P= 0.03; 50.81 versus 23.56 $\times 10^9$/L, P= 0.03respectively) as seen in Table 2.

During the first evaluation, all children (100%) treated by iv steroid show a response, while only (46.9%) of children responded to oral steroid with statistical significance P value =0.001. This difference was still maintained during the second evaluation visit, with a statistical significance P value =0.021, as shown in Table 3.

Discussion

Treatment of children with ITP usually follows a personalized treatment plan to address presentation and characteristics of each case and minimize the use of unnecessary therapy [8]. In this study, steroid was used in two different regimens (oral prednisolone vs intravenous dexamethasone) and the response of the children with acute ITP was compared between the two groups. Patients on intravenous dexamethasone show a higher trend of response and specifically a significantly higher rate of complete response, so these findings support the use of intravenous dexamethasone as an initial steroid regimen in the treatment of children with acute ITP.

In the pediatric age group, studies considered steroids either in high-dose dexamethasone or standard-dose prednisone as first-line therapy for children with ITP in whom therapy is needed; however, there is debate about the type and dose of corticosteroid to be used [9]. Prednisone is the standard initial treatment of ITP, usually given at 0.5 to 2 mg/kg bodyweight daily for 4 weeks to a maximum and then tapered[18]. Because of the side effects of this prolonged steroid regimen, physicians were interested in short courses and alternative steroid regimens. Oral prednisolone in 2-4 mg/kg/day for 7 days or high-dose dexamethasone in short courses had been used initially in refractory ITP[19] , but subsequently proved to be effective in adult patients with acute ITP[20,21]. With time, high dose dexamethasone became the preferred type of steroid in adult patient with acute ITP [22].

The need to achieve rapid and sustained rise in the platelets is not the only determinant of the steroid regi-

Table 2. Comparison of the mean platelet counts after 1st and 2nd responses with baseline count according to steroid type

Treatment option	Platelet count ($\times 10^9$/L)				
	Baseline Mean ± SD ($\times 10^9$/L)	1st evaluation Mean ± SD ($\times 10^9$/L)	P-Value*	2nd evaluation Mean ± SD ($\times 10^9$/L)	P-Value*
I.V. Dexamethasone	16.53±14.77	71.0 ± 37.08	0.001	76.0 ± 24.73	0.001
Oral Prednisolone	23.56 ± 10.02	42.09 ± 47.39	0.03	50.81 ± 38.22	0.03

*P value significant <0.05

Table 3. The outcome according to treatment options in the 1st and 2nd evaluation.

Outcome	Treatment modality		Total (%) n= 135	P-value
	Iv Steroid (%) n= 39	Oral steroid (%) n= 96		
1st evaluation				
Complete response	12 (30.8)	6 (6.3)	18(29)	
Partial Response	27 (69.2)	39 (40.6)	66 (52)	0.001
No response	0 (0)	51 (53.1)	51 (19)	
2nd evaluation				
Complete response	6 (15.4)	3 (3.1)	9 (26)	
Partial Response	30 (76.9)	75 (78.1)	105 (53)	0.021
No response	3 (7.7)	18 (18.8)	21 (21)	

men use, as serious side effect of steroids had been reported in children during ITP treatment with steroids[23] . The American Society of Hematology guideline panel suggest prednisone (2-4 mg/kg per day; maximum, 120 mg daily, for 5-7 days) rather than dexamethasone (0.6 mg/kg per day; maximum, 40 mg per day for 4 days)[24] . However, this guideline was lacking evidence to support strong recommendations for this type of steroid regimen[22].

In this study, the majority of children (71%) treated with steroids as an initial therapeutic choice were received oral prednisolone and only (29%) treated with intravenous dexamethasone which match result in a previous adult study in iraq in which oral prednisolone was the preferred initial treatment in primary ITP [12]. Since no guidelines for treating ITP in children are available in our institution, the choice of the steroid regimen was based on the choice of the treating physician. The preference of pediatrician to choose oral prednisolone is attributed to the ease of administration at home with no need for hospital visits, in comparison to intravenous dexamethasone, which needs hospital care for 4 days every 2 weeks for a total of 3 cycles. The US Food and Drug Administration (FDA) approved for ITP in adults, but its use in pediatric cases of ITP is still considered off-label, which may contribute to lower frequency use this regimen by pediatricians [5].

Children treated with intravenous dexamethasone had lower mean platelet count on presentation than those treated with oral prednisolone, which indicate that pediatric hematologiest tend to choose intravenous dexamethasone regimen in children with lower plateletes count at diagnosis and this goes with previous results[5] . Mithoowani et al recommennd High-dose dexamethasone to be used preferably over the oral prednisone for children with severe immune thrombocytopenia who require a rapid rise in platelet count [11].

In the current study, both regimens were effective in the management of children with ITP as both oral prednisolone and intravenous dexamethasone resulted in significant elevation of platelet counts from baseline levels during 1st and second evaluations, that consistent with previous studies[25] . When comparing the response between both regimens, during first evaluation the response of ITP children treated with intravenous dexamethasone was significantly higher than children treated with oral steroid P value=0.001 and this difference was maintained in the second evaluation.

Although these results are going with the published reports but the response during the first evaluation in this study is the highest reported as all pediatric patients treated with intravenous dexamethasone showed a complete or partial response which match adult study by Mazzucconi et al who did also report a 100% response rate to intravenous dexamethasone[19]while previous pediatric reports expected a 75%-90% respond rate in children treated by to intravenous dexamethasone [26] , this could be attributed to different clinical and laboratory criteria of recruited patients from patients involved in the current study.

The study had multiple limitations to be declared: First, the small sample size and single-center setting will limit the ability to generalize the results[27]. Second, the side effects of steroids in both dexamethasone and prednisolone had not been included in this study. However, this represents the first study to compare the effectiveness of the two most used steroid regimens for children with ITP in Iraq in the absence of local guidelines. So, the result of this study can guide to large-scale multicentric studies that incorporate the short- and long-term adverse effects of both regimens. This all will contribute to adopting a tailored guideline for treatment of children with acute ITP that aligned to the available resources and capabilities and accommodate with institutional limitations.

Conclusion

In the absence of international guidelines for the treatment of pediatric ITP, oral prednisolone remains the commonly used steroid regimen among pediatric hematologists. Intravenous dexamethasone demonstrated a higher and a more sustained response in comparison to oral prednisolone, thereby supporting its potential role as a preferred steroid regimen over the conventional oral therapy.

Authors' contribution

EAA (Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Validation; Visualization)

NNA (Conceptualization; Formal analysis; Investigation; Project administration Writing – original draft; Writing – review & editing)

Conflict of interest

None to declare.

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