PREDNISOLONE VERSUS COMBINATION OF PREDNISOLONE AND IVIG IN TREATMENT OF ACUTE IDIOPATHIC THROMBOCYTOPENIA AMONG CHILDREN

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ABSTRACT

Background

Immune thrombocytopenia (ITP) is a medical situation appearing from animmunological reaction, resulting in a decreased platelet count and improved susceptibility to bleeding. Intravenous immunoglobulin (IVIG) in conjunction with corticosteroids, such as prednisolone, is often used as the first medicine practice for children. Nevertheless, there needs to be more information corresponding to the effectiveness of hybrid treatment to corticosteroids alone.

Objectives

In this study we aim to compare the outcomes of treating patients with prednisoloneas a sole treatment with the combination of prednisolone and IVIG in treating acute immune thrombocytopenic purpura in children.

Patients and Methods

In this randomized controlled experiment, 42 pediatric patients interpreted with immune thrombocytopenic purpura (ITP) were comprised. These children were unsystematically allocated to two groups: one group got intravenous immunoglobulin (IVIG) in combination with prednisolone (n=21), while the other group accepted prednisolone alone (n=21). Platelet counts were measured at baseline, day 3, and week 2.

Results

The study's results demonstrate that the average baseline platelet count was 17.52±4.59 x 109/L, and no notable difference was seen between the groups. On the third day of the study, the hybrid group displayed a statistically meaningful increase in platelet recovery (113.71±26.3 x 109/L) as compared to the group receiving prednisolone alone (80.90±18.09 x 109/L, $p<0.001$). In the second week, the group acquiring the combined treatment had significantly more significant increases in platelet counts (207.71±45.26 x 109/L) compared to those receiving prednisolone alone (121.62±26.33 x 109/L, $p<0.001$).

Conclusion

the management of a combination of intravenous immunoglobulin (IVIG) and prednisolone resulted in a more immediate and considerable elevation in platelet levels as compared to the use of prednisolone alone as a monotherapy in pediatric patients recently analyzed with immune thrombocytopenic purpura (ITP). The results of this study provided proof in favor of the use of IVIG in combination with steroids as a more compelling first treatment option for reducing the risks associated with bleeding. The demographic characteristics and treatment results are consistent with previous empirical discoveries.

Keywords: *Immune thrombocytopenia, intravenous immunoglobulin, pediatrics, prednisolone.*

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INTRODUCTION

Acute idiopathic thrombocytopenia, often understood as ITP, is a frequent hematologic condition known as acute thrombocytopenia that influences children. It is described by a temporary drop in platelet counts and the possibility of bleeding symptoms [1, 2] .The body's immune system wrongly attacks the platelets in the blood, rendering an autoimmune disease, which destroys the platelets and thrombocytopenia. Though the majority of instances of acute ITP clear up on their own within a few weeks or months, some children might have severe bleeding problems, which need instantaneous and efficient remedy.

ITP in children is often a harmless disease that usually goes away on its own between 6 and 18 months following diagnosis. The International Working Group (IWG) [3] .members recently described three phases of the disease: "newly diagnosed ITP," involves the situation in all pediatric and adult people during periods of diagnosis, containing self-limited forms; "persistent ITP," which characterizes the illness in suffering patients who do not perform spontaneous remission or maintain their response after stopping therapy between 3 and 12 months after diagnosis; and "chronic ITP," which explains the illness in patients who do not execute spontaneous remission or maintain their response after stopping therapy between 3 and 12 months after a diagnosis. Despite the fact that the current therapy for ITP does not alter the typical progression of the disorder but is used to alleviate clinical signs, this is only a suggestion for a small percentage of suffering persons with a lower platelet count and significant hemorrhage [4, 5] .This is because the treatment does not impact the normal progression of the condition.

Recent studies have shown that corticosteroids are an effective initial treatment for children with ITP, intravenous immunoglobulin IVIg, or a combination of the two for specific patients [6, 7]. About eighty percent of children who have ITP will recover without therapy on their own by the eighth week. Due to the fact that both clinical severity and platelet count are prior to elucidating the danger of the acute form of ITP in children, it can be concluded that there is no demand for therapy in over 80% of children [8, 9] .Corticosteroids (Prednisolone, Methylprednisolone, and Dexamethasone) are the initial medicine option for ITP in children with a low platelet count and extreme bleeding signs. Intravenous immunoglobulin, often known as IVIg, is a prescription that should be reserved for those who struggle with using steroids and are bleeding actively. In addition, the surgical removal of the spleen, treatment with rituximab anti-D, thrombopoiesis stimulating drugs, immunoglobulin, and the watch-and-wait strategy are all forms of treatment [10].

Intravenous immunoglobulin (IVIg) is a blood product in the serum of numerous healthy donors. It contains microbial antigens, autoantigens, and anti-unique type antibodies [11] .and is good for children diagnosed with ITP [12]. Numerous investigations have indicated that intravenous immunoglobulin (IVIg) may raise platelet counts (PC) more rapidly than corticosteroids, with the first reaction often happening within one to two days, and may decrease the likelihood of developing chronic immune thrombocytopenia (ITP) [13,-15].

The motivation for using hybrid therapy like IVIG and steroids is to employ agents with non-overlapping toxicities to target extra pathways interested in autoantibody exhibition platelet destruction. In a number of different trials, IVIG is combined with steroids, which results in greater response rates. Most of these investigations have been carried out on adults of various ages [16, 17] .Such investigations in the pediatric age group are required to be effective.

This investigation aims to study the effect of prednisolone alone and compare it with results obtained in patients treated with the combination of prednisolone and IVIG in treating acute idiopathic thrombocytopenia among children.

METHODOLOGY

Study design and setting: the current study was designed as a randomized control trial (RCT). This study was done at the pediatric department of Raparin Teaching Hospital in Erbil City, Iraq, and carried out from the 1st of September 2020 to the 2nd of April 2023. A total of 42 children were examined in the study which was divided into 2 groups each classified into first prednisolone group and second prednisolone and IVIG group. The researchers estimated and evaluated the consequences of receiving merely prednisolone in comparison to outcomes treated with the combination of prednisolone and IVIG in acute idiopathic thrombocytopenia disease among children.

Method and data collection: The study was performed

at the department of pediatric in Erbil. The researchers reported [42] .ITP children in the category of pediatric age group patients. The research was conducted with the aid of an English questionnaire in which the data collected on clinical symptoms in the patients which were shown as petechia, purpura, epistaxis, gum and mucous membrane bleeding and hematuria in addition to pretreatment platelet account (×109/L) and hemoglobin ranges: 2-12 months Hb < 11.5 gm/dl, 12-24 months Hb <12, 2-6 year Hb <12.5 and 7-12 year Hb < 13.5 gm/dl were regarded as anemia. The treatment delivered to symptomatic case with skin manifestation or bleeding (epistaxis, hematuria, bleeding from gum etc) with platelet less than 30 × 109/L. The groups divided into first, prednisolone (1-2mg/kg/day) group, we gave prednisone 1-2mg /kg (the used dosage and why) orally after meal for 2 weeks then tapering it within few days then followed up the patients for gastric upset almost all of the patients tolerate it. The second group was IVIG (1gm/kg/day for 2 days + prednisolone receivers, IVIG (1gm/kg/day for 2 days) infused over 2-6 hours to minimize the side effects which may include headache, fever, & vomiting. The follow-up process included patients body temperature, pulse rate and blood pressure, both therapy groups conducted CBC, blood picture done at first day, 3rd day and after 2 weeks. All the medical records were documented and the condition discussed with the parents.

Data management and statistical analysis:

The data recorded on a specially designed questionnaire, collected and entered in the computer via Microsoft Excel worksheet (Excel 2016) and then analyzed using appropriate data system which is called Statistical Package for Social Sciences (SPSS) version 28 and the results were compared between patients with different variables, with a statistical significance level of ≤ 0.05. The results are presented as rates, ratios, frequencies, and percentages in tables and figures and analyzed using t-tests, and Chi-square tests.

Inclusion criteria: An ITP survey was performed enrolling all the cases admitted to Raparin Hospital who underwent receiving prednisolone and IVIG or prednisolone alone. Children of both genders were included depending on complete blood count. Exclusion criteria: The following cases were excluded from the study: cases with normal ranges of anemia and platelets but not having ITP, cases with hepato/ hepatosplenomegaly and apical cells in peripheral blood.

Ethical considerations: This study was submitted to the Research Protocol Ethics and Scientific committees of the Pediatrics program at Kurdistan Higher Council of Medical Specialties for scientific and ethical approval which was granted. This study was explained to each patient's parents and verbal consent was obtained from each parent. Confidentiality and anonymity of data were ensured.

RESULTS

A total of 42 cases were enrolled in our study, Table 1, Figure 1 shows that most (66.7%) of patients were male, one-third (33.3%) of them were female, most (64.3%) of them had petechiae and purpura, 16.3% of cases faced petechiae, purpura, and epistaxis and finally, only 4.8% of them had petechiae, purpura, and hematuria. Table 2 reveals that mean age std. deviation of participants was 47.52 ± 28.28 months, mean platelet before treatment of cases was 17.52 ± 4.59 ×109/L, mean platelet after three days of treatment of cases was 97.31 ± 27.8 ×109/L, average platelet after two weeks of treatment of them was 164.67 ± 56.88 ×109/L and finally mean hemoglobin of participants was 11.39 ± 1.03 gm/dl. Findings of Table 3 indicate that, there was a non-significant statistical difference between treatment groups with hemoglobin and platelet before treatment. p-values were > 0.05. There was significant statistical difference between treatment groups and platelet after two weeks of treatment, platelet counts highly increased in ITP patients who received the combination therapy with (mean of 207.71 ×109/L) compared to those who were taking prednisolone alone (mean of 121.62 ×109/L). There was a significant statistical difference between treatment groups and platelet after three days of treatment, platelet number increased highly after three days of taking combination therapy with (mean of 113.71 ×109/L) compared to prednisolone alone treatment had lower platelets with (mean of 80.9 ×109/L). t-test was highly significant and p-value was < 0. 001.

Table 1. Gender and clinical symptoms of participants.

Variables	Categories	Frequency	Percent
gender	male	28	66.7
	female	14	33.3
clinical symptoms	Petechiae and purpura	27	64.3
	Petechiae, purpura and epistaxis	7	16.7
	Petechiae, purpura, gum and mucous membrane bleeding	6	14.3
	Petechiae, purpura and hematuria	2	4.8
Total		**42**	**100%**

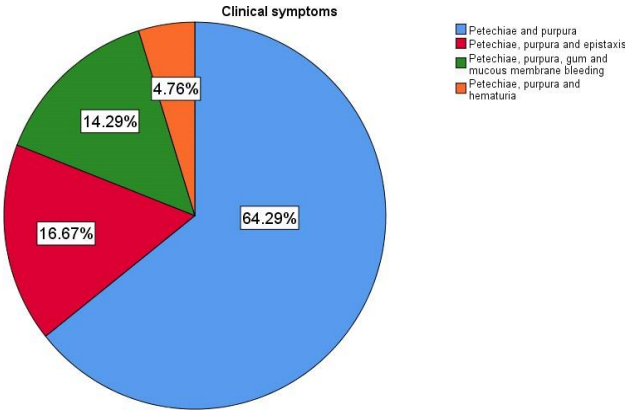

Figure 1. clinical symptoms of ITP disease.

Table 2. Average age, platelet treatments, and hemoglobin of participants.

	N	Range	Minimum	Maximum	Mean	Std. Deviation
Age (months)	42	120	8	128	47.50	28.28
Platelet before treatment (×109/L)	42	18	8	26	17.52	4.59
Platelet after three days of treatment (×109/L)	42	111	49	160	97.31	27.80
Platelet after two weeks of treatment (×109/L)	42	220	80	300	164.67	56.88
Hb gm/dl	42	4.2	8.8	13.0	11.39	1.03

Table 3. Difference between treatment groups regarding platelet counts on various timings.

Platelet and Hb	Treatment	N	Mean	Std. Deviation	p-value	t-test
Hemoglobin (gm/dl)	Prednisolone	21	11.571	1.08	0.261	Non-significant
	Combination therapy	21	11.210	0.96		
Platelet before treatment (×109/L)	Prednisolone	21	17.33	5.51	0.792	Non-significant
	Combination therapy	21	17.71	3.56		
Platelet after three days of treatment (×109/L)	Prednisolone	21	80.90	18.09	< 0. 001	Highly significant
	Combination therapy	21	113.71	26.30		
Platelet after two weeks of treatment (×109/L)	Prednisolone	21	121.62	26.33	< 0. 001	Highly significant
	Combination therapy	21	207.71	45.26		

DISCUSSION

The carefully designed and meticulously conducted randomized controlled trial aimed to compare the effectiveness of a treatment regimen involving the spontaneous use of IVIG and prednisolone instead of prednisolone alone. The current study was conducted within the framework of the first therapy for pediatric patients newly diagnosed with ITP, a medical condition explained by decreasing platelet levels. The outcomes from this study contribute to the growing body of evidence that advocates for using combination therapy as a preferred strategy. This method enables improved restoration of platelet counts and effectively mitigates the potential hazards linked to bleeding difficulties.

The patient demographics are consistent with the standard epidemiology of children's immune thrombocytopenia (ITP). The observed male prevalence of 66.7% aligns with prior determinations showing a male bias or an equal distribution of genders [18] .The average age of 4 years is associated with the most elevated rate, often seen between the ages of 2 and 6 years, when most children prolong ITP after viral infections that may encourage the creation of autoantibodies [19].

The average platelet counts at first diagnosis, recorded as 17.52 ± 4.59 x 109/L, aligns with the expected range of 10-30 x 109/L seen in several studies [20, 21] .No significant difference was seen between the groups in the severity of baseline thrombocytopenia. Following a therapy period of three days, it was seen that the hybrid group displayed a particularly more substantial increase in platelet count, counting at 113.71 ± 26.3 x 109/L, in comparison to the platelet count of 80.90 ± 18.09 x 109/L observed in the group obtaining steroids alone. According to a comprehensive analysis conducted in 2013, the median time needed for platelet recovery to reach a level more than 50 x 109/L was discovered to be 2-3 days when using a mixture of intravenous immunoglobulin (IVIG) and steroids, compared to 5-7 days when using steroids alone [22].

After two weeks, the class acquiring the combined medicine indicated a significant elevation in platelet counts, acquiring a mean value of 207.71 ± 45.26 x 109/L. This value is roughly twice as high as the mean platelet count of 121.62 ± 26.33 x 109/L in the class treated with steroids. This observation is consistent with the findings of a meta-analysis, which proposes that the combination of IVIG and steroids results in much higher plateau platelet levels than the use of steroids alone. The rate of obtaining a platelet count of more than 150 x 109/L is about twice as high when IVIG is administered in conjunction with steroids as compared to using steroids alone [23]. The integrated outcomes of intravenous immunoglobulin (IVIG) and steroids work together to increase platelet destruction and construction inhibition.

It is worth mentioning that 16.7% of the patients had epistaxis at presentation, suggesting clinically substantial bleeding. Combination treatment led to an immediate restoration of normal or safe platelet count of platelet levels, expediting the cessation of bleeding. The approaches recommend initiating treatment for counts below 30 x 109/L in cases with considerable bleeding, as was done in the research referenced [24] .Hemoglobin levels remained stable, as anticipated since anemia is special to ITP. This randomized trial supports upfront combined IVIG and steroids as standard therapy for newly diagnosed pediatric ITP patients to maximize platelet increases, minimize bleeding risk, and improve outcomes.

Conclusions

This study follows a randomized controlled trial format and presents compelling data supporting combination treatment, including intravenous immunoglobulin (IVIG) and prednisolone. The findings suggest that this combined treatment approach leads to faster and more productive platelet count improvements than prednisolone alone as a monotherapy. The study specifically focuses on children who have newly diagnosed with immune thrombocytopenia. The patient population's demographic composition and illness featuresareconsistent withtheestablished epidemiology of juvenile immune thrombocytopenia (ITP). Platelet recovery showed a statistically significant increase in the group receiving intravenous immunoglobulin (IVIG) in conjunction with prednisolone compared to the group alone administered prednisolone after a three-day and two-week therapy course. The conclusion contributes to the expanding corpus of data that substantiates the efficacy of IVIG plus steroids as a more effective first treatment than steroids alone. Combination therapy has resulted in prompt increases in platelet counts, reducing the potential for bleeding complications in individuals who have just been diagnosed with immune thrombocytopenia (ITP). This work also depicts the synergistic impact of using immunomodulators with distinct modes of action, such

as intravenous immunoglobulin (IVIG) and steroids, to manage the autoantibody-induced degradation in immune thrombocytopenia (ITP) from several perspectives.

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