Immunopathologia Persa
DOI:10.34172/ipp.2025.43817
http immunopathol.com

Comparative analysis of three treatment approaches for primary immune thrombocytopenic purpura; prednisolone with thrombopoietin, prednisolone alone, and pulse methylprednisolone; a randomized clinical trial

Mahmoud Dehghani-Ghorbi[1], Reyhaneh Azimi[2], Niloufar Taherpour[3], Soheila Sadeghi[2], Sina Homaee[4*], Farnaz Saberian[2*]

[1]Hematology-Oncology Department, School of Medicine, Imam Hossein Educational Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Department of Internal Medicine, School of medicine, Imam Hossein Hospital, Shahid Behehsti University of Medical Sciences, Tehran, Iran
[3]Prevention of Cardiovascular Disease Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Department of Internal Medicine, Chronic Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran

***Correspondence to**
Sina Homaee, Email: sina.homaee@gmail.com and Farnaz Saberian, Email: dr.f.saberian@gmail.com

Received 2 Jan. 2025
Revised: 4 Mar. 2025
Accepted 7 Mar. 2025
ePublished 30 Mar. 2025

Keywords: Autoimmune, Immune thrombocytopenic purpura, Glucocorticoids, Thrombopoietin, Prednisolone

Citation: Dehghani-Ghorbi M, Azimi R, Taherpour N, Sadeghi S, Homaee S, Saberian F. Comparative analysis of three treatment approaches for primary immune thrombocytopenic purpura; prednisolone with thrombopoietin, prednisolone alone, and pulse methylprednisolone; a randomized clinical trial. Immunopathol Persa. 2025;11(2):e43817. DOI:10.34172/ipp.2025.43817.

Abstract

Introduction: Idiopathic thrombocytopenic purpura (ITP) is a hematological disorder characterized by thrombocytopenia (a reduced platelet count) without an identifiable clinical etiology. Various treatment options are available, with glucocorticoids being the primary recommendation. Although recombinant human thrombopoietin (rhTPO) has shown promise in limited studies, data remain insufficient to determine the optimal treatment approach.

Objectives: This study compared the therapeutic efficacy of prednisolone+rhTPO, prednisolone alone, and pulse methylprednisolone alone in treating primary ITP.

Patients and Methods: This open-label, parallel, randomized clinical trial included 75 patients diagnosed with primary ITP. Participants were randomly assigned to one of three equal treatment groups: pulse methylprednisolone (2–3 mg/kg intravenously, n=25), oral prednisolone (1 mg/kg daily, n = 25), and rhTPO+oral prednisolone (250 µg rhTPO weekly via subcutaneous injection + 0.5 mg/kg daily, n = 25). All patients were followed for seven months, and treatment outcomes, including complete response, partial response, stable response, and adverse events, were compared across the groups.

Results: The mean age of the participants was 43.12±11.22 years, and 54.67% were female. Platelet counts showed a significant upward trend in all three groups, with the most pronounced increase observed in the prednisolone + rhTPO group ($P<0.001$). After seven months, the prednisolone + rhTPO group achieved the highest platelet count. The complete and sustained response rates were 76% and 72% in the pulse methylprednisolone group, 52% and 48% in the oral prednisolone group, and 84% and 88% in the prednisolone+rhTPO group, respectively ($P<0.05$). The relapse rate of platelet decline was 4% in the prednisolone+rhTPO group, 16% in the pulse methylprednisolone group, and 36% in the oral prednisolone group ($P=0.016$). Adverse drug events did not significantly differ between groups ($P>0.05$).

Conclusion: The combination of prednisolone+rhTPO provides superior therapeutic efficacy compared to traditional monotherapies, demonstrating higher response rates and a lower relapse rate.

Trial Registration: The trial was registered in the Iranian Clinical Trial Registry (IRCT) under the registration number IRCT20230717058813N1 (https://irct.behdasht.gov.ir/trial/71792) and was approved by the ethics committee under the ethical code IR.SBMU.MSP.REC.1402.180.

Introduction

Primary immune thrombocytopenia (ITP) is an autoimmune hematological disorder characterized by a significant reduction in platelet count (below 100×10^9/L) and an increased risk of bleeding complications (1-3). The etiology of ITP is multifactorial, and the precise mechanisms by which the immune system erroneously targets its components, leading to autoimmunity and subsequent platelet destruction, remain poorly understood (4).

Recent research suggests that a key factor in this disease is the imbalance between

Key point

In an open-label, parallel, randomized clinical trial on 75 primary idiopathic thrombocytopenic purpura (ITP) patients, who were randomly assigned to one of three equal treatment groups: pulse methylprednisolone, oral prednisolone, and rhTPO (recombinant human thrombopoietin) +oral prednisolone, we found:

- The prednisolone + rhTPO group demonstrated a significantly higher complete and sustained response rate at six months than the other treatment groups.
- The relapse rate due to serum platelet decline was significantly lower in the prednisolone + rhTPO group (4%) than in the pulse methylprednisolone (16%) and oral prednisolone (36%) groups ($P = 0.016$).
- Adverse drug events were observed in 42.67% of patients, with no statistically significant differences in their distribution across treatment groups, indicating comparable safety profiles.

effector and regulatory immune cells, leading to immune dysregulation and a loss of immune tolerance. This disruption enhances platelet clearance by immune cells and interferes with thrombopoiesis. Historically, ITP was thought to result primarily from anti-platelet antibodies, which promote opsonization and subsequent platelet destruction. However, recent studies have identified a significant role for cytotoxic T cells in ITP pathophysiology, particularly in their deleterious effects on megakaryopoiesis (5,6).

The standard treatment for ITP has remained largely unchanged, consisting of corticosteroids, intravenous immunoglobulin, and anti-D antibody therapy. Corticosteroids typically increase platelet counts in approximately 75% of patients within one to two days; however, only 25% achieve a sustained response. These treatments are associated with predictable adverse effects, including hypertension, fatigue, hyperglycemia, and adrenal insufficiency (7-9). Despite their widespread use, the efficacy and long-term response rates of different therapeutic agents are not fully understood, highlighting the need for further research (10,11).

Objectives

This study compared the therapeutic effects of prednisolone combined with recombinant human thrombopoietin (rhTPO), prednisolone alone, and pulse methylprednisolone alone in patients with ITP.

Patients and Methods

Study design

This open-label, parallel, randomized clinical trial evaluated the efficacy of three treatment protocols in patients with ITP; prednisolone combined with rhTPO, prednisolone alone, and pulse methylprednisolone alone. The study was carried out at the internal medicine clinic of Imam Hossein educational hospital in Tehran, Iran, between 2023 and 2024.

The inclusion criteria required patients to be between 18 and 60 years old, have a normal spleen size, and be diagnosed with ITP according to the working group criteria based on bleeding symptom scores (12). The exclusion criteria included any prior ITP treatment, use of corticosteroids or immunosuppressive therapy for non-ITP conditions within the last three months, malignancy, connective tissue diseases, seroconversion to HIV, hepatitis B virus or hepatitis C virus, pregnancy or lactation, active infection, hepatic or renal dysfunction, psychosis, pregnancy-induced osteoporosis, and secondary ITP associated with myelodysplastic syndrome, antiphospholipid syndrome or collagen disease.

Blinding

As physicians, researchers, and patients were aware of the assigned treatment, this study was conducted as an open-label (non-blinded) trial.

Interventions

- Group 1: Pulse methylprednisolone (2–3 mg/kg intravenously) administered for three days every two weeks over four weeks, followed by re-evaluation.
- Group 2: Oral prednisolone (1 mg/kg daily) administered for 4–6 weeks, followed by re-evaluation.
- Group 3: Human synthetic analogue (250 µg weekly subcutaneously for four weeks) combined with oral prednisolone (0.5 mg/kg daily) until re-evaluation.

All medications taken by the patients were recorded using a researcher-designed checklist. Additionally, platelet counts were assessed monthly.

Data collection tools

Data were collected using a researcher-designed checklist tailored to the study's objectives. This checklist comprised two sections: (a) general information, including age, gender, body mass index (BMI), and medical history, and (b) clinical information, which recorded platelet counts and any adverse drug reactions observed during the study. Additionally, the ITP bleeding assessment tool (ITP-BAT) was utilized to assess bleeding incidents. This tool assigns grades to bleeding symptoms on a scale from 0 to 3 or 4, with a grade of 5 indicating fatal bleeding cases (13).

Outcomes

The primary outcome measures of drug therapy included response, sustained response, complete response, and non-response within six months.

- Complete response was defined as a platelet count $\geq 100\times10^9$/L with no bleeding (11).
- The response was defined as a platelet count $\geq 50\times10^9$/L, at least a two-fold increase from baseline, and no bleeding (11).
- Non-response was defined as a platelet count $<50\times10^9$/L, a less than two-fold increase from baseline, or the presence of bleeding (11).
- A sustained response was defined as a response lasting at least six consecutive months (11).
- Relapse was defined as a platelet count $<50\times10^9$/L

or the recurrence of bleeding symptoms after achieving a response (11).

As a secondary outcome, the adverse effects of corticosteroid use, including hypertension, hyperglycemia, avascular necrosis, Cushingoid features, infection, and edema, were assessed and compared monthly over six months.

Follow-up duration

The total study duration was seven months. Treatment was administered for six months, during which blood cell counts and adverse drug events were evaluated every four weeks (monthly) to assess treatment response. Following the treatment course, all patients were monitored for 30 days to detect platelet decline (relapse).

Randomization

Eligible participants were randomly assigned to one of three treatment groups in a 1:1:1 ratio: prednisolone alone, prednisolone+rhTPO, and pulse methylprednisolone alone. Randomization was performed using a permuted block randomization method, with 7 blocks in sizes 6, 9, 12, and 15 generated via the "ralloc" package in STATA software (version 17). Patients were allocated to groups according to the randomized subject list, with each participant assigned a unique research code.

Sample size estimation

Based on the study by Yang Li et al (14), the complete response (CR) rate at 14 days post-treatment was 82.4% in the group receiving corticosteroids+rhTPO, compared to 42.9% in the group receiving corticosteroids alone. Using a type I error rate of 5% ($\alpha = 0.05$) and a power of 80% ($\beta = 0.2$), along with an estimated dropout rate of 20%, the required sample size was calculated to be 75 patients (25 patients per group). The calculation was performed using PASS software 2021, version 21.0.3.

Statistical analysis

This study employed an intention-to-treat approach for data analysis. The normality of quantitative data was initially assessed using a histogram. Quantitative variables were summarized using mean and standard deviation, while qualitative variables were presented as frequency and percentage.

To compare the mean values of quantitative variables across the three treatment groups, either a one-way analysis of variance (ANOVA) (parametric test) or a Kruskal-Wallis test (non-parametric test) was applied, depending on the distribution of the data. The assumption of homogeneity of variance for normally distributed data was evaluated using Bartlett's test following one-way ANOVA. Differences in the distribution of categorical variables were examined using either the chi-square test or Fisher's exact test.

A linear generalized estimating equations (GEE) regression model was conducted to analyze the trend of platelet changes over time, with the correlation structure in the GEE model set as exchangeable. All statistical analysis were performed using STATA version 17 (StataCorp LLC, College Station, TX 77845, USA), with a significance level of $P < 0.05$.

Results

General information

A total of 75 patients diagnosed with ITP were randomly assigned in a 1:1:1 ratio to one of three treatment groups: pulse methylprednisolone (n = 25), oral prednisolone (n = 25), and prednisolone combined with rhTPO (n = 25) (Figure 1).

The mean age of the study participants was 43.12 ± 11.22 years, with 56% under 45. Females comprised 54.67% of the patient population. There were no statistically significant differences in mean age or gender distribution among the three treatment groups (Table 1).

The most common underlying diseases among patients with thrombocytopenia were hypertension (17.3%), diabetes (13.3%), and chronic respiratory disease (8%). No significant differences were observed in the distribution of these conditions across the three treatment groups ($P > 0.05$).

The overall mean initial platelet count was $21.25 \pm 9.78 \times 10^9$/L. According to the ITP-BAT, 62.67% of participants had no bleeding, 17.33% had a bleeding risk score of 1, 18.67% had a risk score of 2, and 1.33% had a risk score of 3. The skin was the most common bleeding site, occurring in 25.33% of affected individuals.

Statistical analysis revealed no significant differences in mean initial platelet count ($P = 0.203$) or the distribution of bleeding risk scores ($P = 0.149$) across the three treatment regimens. Patient details are summarized in Table 1.

Serum platelet changes during the study

Figure 2 presents the platelet count trends over the six-month treatment period and the 30-day follow-up (seventh month) across the three treatment groups. Over the seven-month duration, the mean serum platelet count was $131.65 \pm 89.65 \times 10^9$/L in the pulse methylprednisolone group, $87.89 \pm 74.24 \times 10^9$/L in the oral prednisolone group, and $127.14 \pm 80.44 \times 10^9$/L in the prednisolone + rhTPO group ($P < 0.001$).

According to the GEE analysis, the platelet count change trend over time was statistically significant across all three treatment groups ($P < 0.001$). The interaction effect between treatment groups and time was also statistically significant ($P < 0.001$), indicating that mean platelet counts changes over the seven-month period varied depending on the treatment regimen.

In the early months of treatment, platelet counts increased in all three groups before stabilizing in patients receiving pulse methylprednisolone and oral prednisolone. However, in the prednisolone+ rhTPO group, the

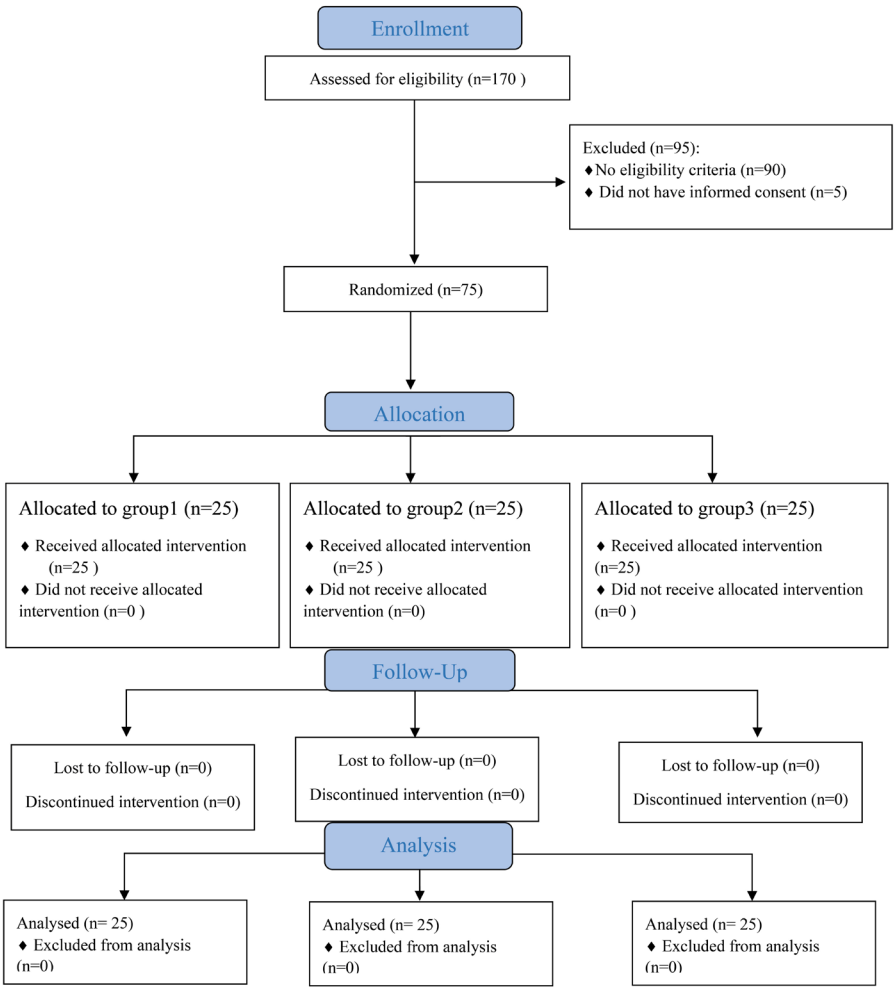

Figure 1. CONSORT flowchart of the study.

platelet count continued to increase over time without reaching a plateau. Notably, during the 30-day follow-up period after six months of treatment, patients in the prednisolone+rhTPO group continued to show an upward trend in mean serum platelet levels, unlike the other two groups, where platelet counts remained stable (Figure 2).

Response to treatment

Table 2 presents the treatment response rates at six months and the relapse rates 30 days post-treatment (seventh month of the study). The complete response rate ($P=0.035$) and sustained response rate ($P=0.009$) were significantly higher in the prednisolone+rhTPO group compared to the other treatment groups.

Following the 30-day post-treatment follow-up, the relapse rate of serum platelet decline was 4% in the prednisolone + rhTPO group, 16% in the pulse methylprednisolone group, and 36% in the oral prednisolone group ($P=0.016$; Table 2).

Adverse events related/unrelated to glucocorticoid use

As shown in Table 2, adverse events reported during the study included limb edema (22.67%), hyperglycemia (8%), sepsis (5.33%), avascular necrosis (4%), and hypertension (2.67%). Although adverse events were more frequently observed in the oral prednisolone group compared to the other treatment groups, the differences in adverse event distribution were not statistically significant (Table 2).

Discussion

This study assessed the therapeutic efficacy of different treatment regimens, prednisolone, rhTPO, pulse methylprednisolone, and a combination of prednisolone+rhTPO, in patients with ITP. A total of 75 patients were analyzed, providing valuable insights into the effectiveness and safety of these therapeutic approaches.

The results revealed significant differences in platelet count trends across the treatment groups. The prednisolone+rhTPO combination demonstrated the most favorable outcomes, achieving the highest platelet counts after seven months. These findings are consistent with previous studies suggesting that rhTPO improves corticosteroid efficacy, likely due to its role in stimulating megakaryocyte production and promoting platelet

Table 1. General and baseline clinical characteristics of patients with ITP across different treatment groups

Variables	Methylprednisolone pulse (n=25)	Oral prednisolone (n=25)	Prednisolone + rhTPO (n=25)	Total (n=75)	*P* value
General characteristics					
Age (y)	42.40 ± 9.99	44.72 ± 12.20	42.24 ± 11.66	43.12 ± 11.22	0.688[a]
≤45 years	16 (64.0)	12 (48.0)	14 (56.0)	42 (56.0)	0.522[b]
>45 years	9 (36.0)	13 (52.0)	11 (44.0)	33 (44.0)	
Gender					
Female	14 (56.0)	12 (48.0)	15 (60.0)	41 (54.67)	0.686[b]
Male	11 (44.0)	13 (52.0)	10 (40.0)	34 (45.53)	
BMI (kg/m^2)	25.59 ± 2.63	26.15 ± 2.51	25.24 ± 3.09	25.66 ± 2.74	0.505[a]
Underlying diseases (yes)					
Diabetes	1 (4.0)	4 (16.0)	5 (20.0)	10 (13.33)	0.319[c]
Hypertension	4 (16.0)	4 (16.0)	5 (20.0)	13 (17.33)	1.000[c]
Dyslipidemia	3 (12.0)	0 (0.0)	0 (0.0)	3 (4.0)	0.102[c]
COPD/Asthma	1 (4.0)	2 (8.0)	3 (12.0)	6 (8.0)	0.866[c]
Hypothyroidism	1 (4.0)	0 (0.0)	0 (0.0)	1 (1.33)	1.000[c]
Medical information					
Basic platelet (10^9/L)	23.36 ± 8.94	19.24 ± 11.15	21.16 ± 9.05	21.25 ± 9.78	0.203[d]
Basic bleeding risk score					
0	16 (64.0)	12 (48.0)	19 (76.0)	47 (62.67)	0.149[c]
1	6 (24.0)	5 (20.0)	2 (8.0)	13 (17.33)	
2	3 (12.0)	8 (32.0)	3 (12.0)	14 (18.67)	
3	0 (0.0)	0 (0.0)	1 (4.0)	1 (1.33)	
Major domain of bleeding					
No bleeding	16 (64.0)	12 (48.0)	19 (76.0)	47 (62.67)	0.130[c]
Skin	4 (16.0)	10 (40.0)	5 (20.0)	19 (25.33)	
Visible mucosae	5 (20.0)	3 (12.0)	1 (4.0)	9 (12.0)	

BMI, Body mass index; COPD, Chronic obstructive pulmonary disease.
Data described as mean ± standard deviation and frequency and percentages (%).
[a] based on one-way ANOVA test; [b] based on chi-square's test; [c] based on Fisher's exact test; [d] based on Kruskal-Walli's test.

generation (15,16).

The partial treatment response rates were notably higher in the prednisolone + rhTPO group (92%) compared to pulse methylprednisolone (84%) and oral prednisolone (68%). However, while these findings suggest a trend toward improved efficacy with combination therapy, the differences did not reach statistical significance. Although clinical benefits may exist, further large-scale studies are needed to confirm these observations. Nonetheless, the findings of this study align with previous research, indicating that combination therapy, particularly corticosteroids with human immunoglobulin, is more effective than monotherapy in eliciting a treatment response in ITP patients (17).

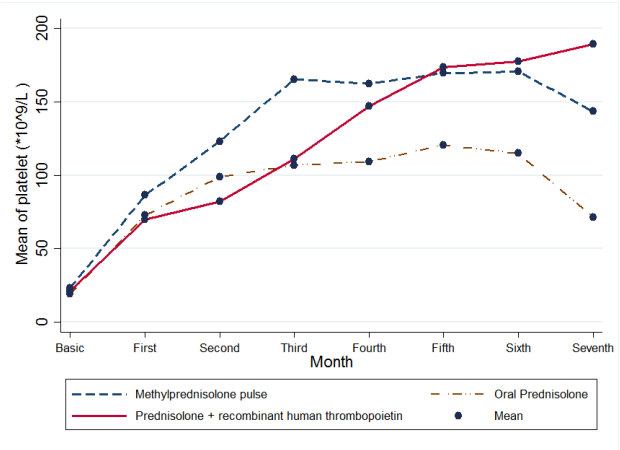

Figure 2. The trend of platelet counts changes in patients with ITP across different treatment approaches over six months and the 30-day follow-up period.

The complete and maintenance response rates highlight the potential advantages of combining prednisolone with rhTPO (15). This study's maintenance response rate in the prednisolone+rhTPO group (88%) was substantially higher than in the other treatment groups. This finding is particularly significant, as achieving sustained remission is a key objective in ITP management, with long-term treatment strategies playing a crucial role in improving patient quality of life (18,19).

The significant differences in complete response rates between groups emphasize the importance of tailoring treatment strategies based on individual patient profiles. This study's results are consistent with existing evidence (15-17,20), which supports the beneficial effects of adding rhTPO to glucocorticoids in treating primary ITP.

Table 2. Comparison of treatment responses and adverse drug events in patients with primary immune thrombocytopenia across different treatment approaches over the study period

Variables	Methylprednisolone pulse (n=25)	Oral prednisolone (n=25)	Prednisolone +rhTPO (n=25)	Total (n=75)	*P* value
Partial responses					
No	4 (16.0)	8 (32.0)	2 (8.0)	14 (18.67)	0.086[a]
Yes	21 (84.0)	17 (68.0)	23 (92.0)	61 (81.33)	
Completed responses					
No	6 (24.0)	12 (48.0)	4 (16.0)	22 (29.33)	**0.035*[b]**
Yes	19 (76.0)	13 (52.0)	21 (84.0)	53 (70.67)	
Maintenance responses					
No	7 (28.0)	13 (52.0)	3 (12.0)	23 (30.67)	**0.009*[b]**
Yes	18 (72.0)	12 (48.0)	22 (88.0)	52 (69.33)	
Relapse of thrombocytopenia[c]					
No	21 (84.0)	16 (64.0)	24 (96.0)	61 (81.33)	**0.016*[a]**
Yes	4 (16.0)	9 (36.0)	1 (4.0)	14 (18.67)	
Bleeding risk score[c]					
0	23 (92.0)	21 (84.0)	23 (92.0)	67 (89.33)	0.761[a]
1	1 (4.0)	2 (8.0)	2 (8.0)	5 (6.67)	
2	1 (4.0)	2 (8.0)	0 (0.0)	3 (4.0)	
3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Major domain of bleeding[c]					
No bleeding	23 (92.0)	21 (84.0)	23 (92.0)	67 (89.33)	0.855[a]
Skin	1 (4.0)	2 (8.0)	1 (4.0)	4 (5.33)	
Visible mucosae	1 (4.0)	2 (8.0)	1 (4.0)	4 (5.33)	
Adverse drug events (yes)					
Expired	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Glucocorticoid-induced hypertension	0 (0.0)	2 (8.0)	0 (0.0)	2 (2.67)	0.324[a]
Glucocorticoid-induced hyperglycemia	2 (8.0)	3 (12.0)	1 (4.0)	6 (8.0)	0.866[a]
Glucocorticoid-induced avascular necrosis	0 (0.0)	3 (12.0)	0 (0.0)	3 (4.0)	0.102[a]
Glucocorticoid-induced cushing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	N/A
Glucocorticoid-induced sepsis	2 (8.0)	2 (8.0)	0 (0.0)	4 (5.33)	0.537[a]
Glucocorticoid-induced edema	4 (16.0)	10 (40.0)	3 (12.0)	17 (22.67)	0.050[a]

N/A: Not applicable.
Data described as frequency and percentages (%).
[a]based on Fisher's exact test; [b]based on chi-square's test.
[c]Occurrence during the 30 days after six months of treatment.

The relapse rate of thrombocytopenia was significantly lower in the prednisolone+rhTPO group (4%) compared to the pulse methylprednisolone group (16%) and the oral prednisolone group (36%). This finding suggests that combination therapy may be more effective and durable in maintaining platelet counts over time.

However, adverse events were reported across all treatment groups, with a higher incidence in the oral prednisolone group. While these differences were not statistically significant, they emphasize the importance of closely monitoring corticosteroid-related side effects, given their potential long-term implications (21).

Our findings align with Fang et al (17), who reported that combination therapy resulted in a significantly higher complete response rate (71.83%) than monotherapy, suggesting greater durability in maintaining platelet counts. Although that study did not specifically address relapse rates, it emphasized the effectiveness of combination therapy in relapsed ITP patients, supporting our observation that prednisolone+rhTPO was associated with lower relapse rates compared to other treatments. Additionally, adverse events were observed across all treatment groups, reinforcing the need to monitor corticosteroid-associated side effects carefully (15,18).

Regarding the risk of bleeding, 92% of patients in both the prednisolone + rhTPO and pulse methylprednisolone groups experienced no bleeding, compared to 84% in the oral prednisolone-only group. Notably, in the prednisolone+rhTPO group, all instances of bleeding were classified as mild (grade 1). These findings are consistent with the study by Yu et al (22), which reported that the bleeding score in the dexamethasone+rhTPO group was lower than in the dexamethasone-only group. This further supports the beneficial effects of rhTPO in reducing bleeding risk (22).

Conclusion

This study provides valuable insights into managing primary ITP, highlighting the therapeutic advantages of combining prednisolone with rhTPO over traditional monotherapies. The findings suggest that rhTPO is an effective adjunct to glucocorticoid therapy, significantly enhancing treatment response rates while maintaining a favorable safety profile.

The prednisolone+rhTPO combination was associated with minimal adverse effects and a lower risk of bleeding, with fewer adverse events compared to glucocorticoid monotherapy. These results highlight the potential of combination therapy as a more effective and safer approach to ITP treatment. Further research and clinical trials are warranted to optimize treatment protocols and improve long-term patient outcomes in ITP management.

Limitations of the study

This study's single-center design limited patient recruitment, potentially affecting the generalizability of findings. Additionally, the short-term follow-up and open-label design may introduce biases, which should be addressed in future research. Further studies should explore the mechanisms underlying the enhanced efficacy of rhTPO when combined with corticosteroids and assess long-term outcomes associated with this treatment strategy. Additionally, incorporating patient-reported outcomes in future research could provide valuable insights into the impact of these treatments on quality of life.

Authors' contribution

Conceptualization: Mahmoud Dehghani-Ghorbi.
Data curation: Reyhaneh Azimi.
Formal analysis: Niloufar Taherpour.
Funding acquisition: Mahmoud Dehghani-Ghorbi.
Investigation: Reyhaneh Azimi.
Methodology: Farnaz Saberian, Niloufar Taherpour.
Project administration: Reyhaneh Azimi.
Resources: Sina Homaee.
Software: Niloufar Taherpour.
Supervision: Mahmoud Dehghani-Ghorbi.
Validation: Farnaz Saberian.
Visualization: Sina Homaee.
Writing–original draft: Reyhaneh Azimi, Niloufar Taherpour.
Writing–review & editing: Mahmoud Dehghani-Ghorbi, Sina Homaee, Farnaz Saberian, Soheila Sadeghi.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research was conducted in accordance with the tents of the Declaration of Helsinki. The Ethics Committee of medicine school, Shahid Behehshti University of Medical Sciences approved this study (Ethical code#IR.SBMU.MSP.REC.1402.180). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from the internal medicine residency thesis of Reyhaneh Azimi at this university (thesis #43005821). The trial protocol was approved by the Iranian registry of clinical trial (identifier: IRCT20230717058813N1; https://irct.behdasht.gov.ir/trial/71792). Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

No specific grants from funding agencies, commercial, and non-profit sectors were received for the research, authorship or publication of this study.

References

1. 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. doi: 10.1182/blood-2009-06-225565.
2. Neunert C, Lim W, Crowther M, Cohen A, Solberg Jr L, Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011;117:4190-207. doi: 10.1182/blood-2010-08-302984.
3. Neunert C, Terrell DR, Arnold DM, Buchanan G, Cines DB, Cooper N, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019;3:3829-66. doi: 10.1182/bloodadvances.2019000966.
4. McKenzie CG, Guo L, Freedman J, Semple JW. Cellular immune dysfunction in immune thrombocytopenia (ITP). Br J Haematol. 2013;163:10-23. doi: 10.1111/bjh.12480.
5. Ku FC, Tsai CR, Der Wang J, Wang CH, Chang TK, Hwang WL. Stromal-derived factor-1 gene variations in pediatric patients with primary immune thrombocytopenia. Eur J Haematol. 2013;90:25-30. doi: 10.1111/ejh.12025.
6. Rank A, Weigert O, Ostermann H. Management of chronic immune thrombocytopenic purpura: targeting insufficient megakaryopoiesis as a novel therapeutic principle. Biologics. 2010 May 25;4:139-45. doi: 10.2147/btt.s3436.
7. McGrath LJ, Kilpatrick K, Overman RA, Reams D, Sharma A, Altomare I, et al. Treatment patterns among adults with primary immune thrombocytopenia diagnosed in hematology clinics in the United States. Clin Epidemiol. 2020:435-45. doi: 10.2147/CLEP.S229266.
8. Zhou Z, Qiao Z, Li H, Luo N, Zhang X, Xue F, et al. Different dosages of intravenous immunoglobulin (IVIg) in treating immune thrombocytopenia with long-term follow-up of three years: Results of a prospective study including 167 cases. Autoimmunity. 2016;49:50-7. doi: 10.3109/08916934.2015.1104671.
9. Singh A, Uzun G, Bakchoul T. Primary immune thrombocytopenia: novel insights into pathophysiology and disease management. J Clin Med. 2021;10:789. doi: 10.3390/jcm10040789.
10. Provan D, Newland AC. Current management of primary immune thrombocytopenia. Advances in therapy. 2015;32:875-87. doi: 10.1007/s12325-015-0251-z.
11. Martínez-Carballeira D, Bernardo Á, Caro A, Soto I, Gutiérrez L. Treatment of Immune Thrombocytopenia: Contextualization from a Historical Perspective. Hematol Rep. 2024 Jun 26;16:390-412. doi: 10.3390/hematolrep16030039.
12. Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM, 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;113:2386-93. doi: 10.1182/blood-2008-07-162503.
13. Rodeghiero F, Michel M, Gernsheimer T, Ruggeri M, Blanchette V, Bussel JB, et al. Standardization of bleeding assessment in immune thrombocytopenia: report from the International

Working Group. Blood. 2013;121:2596-606. doi: 10.1182/blood-2012-07-442392.
14. Li Y, Sun L, Li F, Li Y, Hou Y, Meng Y, et al. Recombinant Thrombopoietin Effectively Shortens the Time to Response and Increases Platelet Counts in Elderly Patients with Severe Immune Thrombocytopenia. J Clin Med. 2022;11:5763. doi: 10.3390/jcm11195763.
15. Arai Y, Jo T, Matsui H, Kondo T, Takaori-Kondo A. Comparison of up-front treatments for newly diagnosed immune thrombocytopenia-a systematic review and network meta-analysis. Haematologica. 2017;103:163. doi: 10.3324/haematol.2017.174615.
16. Zhu XL, Feng R, Huang QS, Liang MY, Jiang M, Liu H, et al. Prednisone plus IVIg compared with prednisone or IVIg for immune thrombocytopenia in pregnancy: a national retrospective cohort study. Ther Adv Hematol. 2022;13:20406207221095226. doi: 10.1177/20406207221095226.
17. Fang L, Sun J, Zhao Y, Hou M, Wu D, Chen Y, et al. Efficacy and Safety Analysis of Combination Therapy Consisting of Intravenous Immunoglobulin and Corticosteroids versus Respective Monotherapies in the Treatment of Relapsed ITP in Adults. Glob Med Genet. 2023;10:87-96. doi: 10.1055/s-0043-1769087.
18. Palau J, Jarque I, Sanz MA. Long-term management of chronic immune thrombocytopenic purpura in adults. Int J Gen Med. 2010 5;3:305-11. doi: 10.2147/IJGM.S4722.
19. Liu XG, Hou Y, Hou M. How we treat primary immune thrombocytopenia in adults. J Hematol Oncol. 2023;16:4. doi: 10.1186/s13045-023-01401-z.
20. Zhou J-x, Gao L, Hu N, Yan Z-L, Tian C-y, Su J, et al. Clinical efficacy of recombinant human thrombopoietin combined with glucocorticoids in the treatment of immune thrombocytopenia. Hematology. 2022;27:1062-8. doi: 10.1080/16078454.2022.2121103.
21. Cuker A, Liebman HA. Corticosteroid overuse in adults with immune thrombocytopenia: Cause for concern. Research and Practice in Thrombosis and Haemostasis. 2021;5:e12592. doi: 10.1002/rth2.12592.
22. Yu Y, Wang M, Hou Y, Qin P, Zeng Q, Yu W, et al. High-dose dexamethasone plus recombinant human thrombopoietin vs high-dose dexamethasone alone as frontline treatment for newly diagnosed adult primary immune thrombocytopenia: a prospective, multicenter, randomized trial. Am J Hematol. 2020;95:1542-52. doi: 10.1002/ajh.25989.