International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Immune thrombocytopenia: Dexamethasone versus prednisolone- systematic review and metanalysis

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Algariri, N; Almutairi.N; Alnawfal.B.

Corresponding author:
najla ALGARIRI

najlaalgariri@gmail.com

Author Affiliation:
King Saud Medical City.

ADMINISTRATIVE INFORMATION

Support - No financial support.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 January 2025 and was last updated on 19 January 2025.

INTRODUCTION

Review question / Objective Objective: To evaluate the effectiveness and safety of Dexamethasone in compare with prednisolone in treatment of ITP.
PICO:
P (Population): People of all age groups whose diagnosed with primary ITP, regardless of severity levels of thrombocytopenia and bleeding symptoms.
I (Intervention): Administration of dexamethasone.
C (Comparison): prednisolone
O (Outcomes):1. Response Rate: the percentage of patients who achieve a significant increase in platelet count (as each study defined this significance) recorded at 6 months. 2. Side Effects: hyperglycemia or glucose intolerance, as well as hypertension.

Rationale The use of dexamethasone versus predinsolone in managing ITP is still debatable. Dexamethasone has a more potent anti-inflammatory effect than all other steroids and has a longer half-life. Understanding the implications of these pharmacokinetic differences on treatment effectiveness and safety will help clinicians to make decisions, it is important to evaluate the sustainability of such responses. Moreover, comparing side effects associated with each medication is a crucial factor in any patient. Consistent patterns can be demonstrated by systematic review and aggregating safety data will form a clearer picture regarding risks associated with each treatment. The results of this review will be disseminated among clinicians through local conferences to help them in making informed decisions.

Condition being studied Since many years, the standard therapy is prednisone at 1 mg/kg/day for 2-4 weeks, followed by tapering it; this approach was based on results from a randomized controlled trial conducted in ITP patients in 2002 and showing that longer steroid treatment improved platelet counts4. Some experts propose using

higher-dose prednisone for shorter duration to minimize side effects, while others prefer dexamethasone, which is more potent, for longer duration. It is reported that high-dose dexamethasone (HDD) modifies T-cell function effectively.5 HDD has been used as daily dose of 40 mg/kg/day (24 mg/m2) orally for four days given every 14 days for three cycles; this approach has been shown to have an initial response rate of 85% in adults and children but durable response is not nearly as good6.

One study showed comparable long-term effect of HDD and standard prednisone. However, HDD may result in quicker increases in platelet counts, particularly in acute cases.7 To determine whether HDD is more likely to result in a sustained response, a trial involved 192 adults with newly diagnosed ITP who were randomly assigned to receive 1–2 cycles of HDD or four weeks of prednisone. Individuals who received two cycles of HDD experienced a faster rise in platelet counts, but the 6-month sustained response rates were similar in both groups.8 Mithoowani et al. expanded on this information with a systematic review and meta-analysis that encompassed nine randomized trials comparing different steroid regimens. Among these, five studies (n = 533) compared one to three cycles of HDD to standard prednisone dosing. Results showed that 14 days after treatment initiation, the platelet count was higher in adults treated with HDD regimens, but 6-month durable response rates were found to be similar across all groups.9

METHODS

Search strategy Bibliographic databases and additional resources to be searched:

Embase database searched through Ovid interface from 1946 to 24/September/2024

Search strategy and restrictions:

The main search concepts are covering diagnosis (immune thrombocytopenia), intervention (steroids), with relevant synonyms for both concepts, and the RCTs filters. There were no restrictions on language, date of publication, or any other restrictions.

Millions of hits (for intervention and RCTs filters) were identified, so one filter was added to involve non animals' studies, the number of hits of RCTs filters was decreased, however still in millions. Then the search combined filters together ran again, and 4611 hits were identified.

Consultation for librarian was done through emails, to figure out the problems in this search strategy as the famous articles that are eligible for the project did not show within the search strategy attempts which were done before. Although, the previous similar systemic review's terms were applied. Advice from the librarian was followed, particularly, in Cochrane RCTs filters, and Mesh terms were applied, and formal errors were corrected. Famous articles appeared after that.

Additional Resources: The Last 10 years of the following conferences and meetings will be searched manually to capture eligible articles:

The European Hematology Association congress EHA .

The American Society of Hematology Annual Meeting and Exposition ASH.

Since unpublished studies was excluded, YODA project and clinical trail.gov were not searched.

Appendix (1): search strategy https://libaccess.mcmaster.ca/login?url=http://ovidsp.ovid.com/ovidweb.cgi?T=JS&NEWS=N&PAGE=main&SHAREDSEARCHID=2nkG4T0M2AW7DR3ITkXgbF7bqTfybx2Y0tivPdWLZn9EyV3dr4LRuF935AUpNzwSQ

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

1 Purpura, Thrombocytopenic, Idiopathic/ 8046

2 (ITP or THROMBOCYTOP*).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 90299

3 Thrombocytopenia/ 31246

4 or/1-3 90299

5 (Corticosteroid or steroids or glucocorticosteroids or dexamethasone or prednisolone or prednisone).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 355338

6 Dexamethasone/ 56891

7 Dexamethazone/ 0

8 exp Adrenal Cortex Hormones/ 432541

9 or/5-8 603975

10 4 and 9 8204

11 randomized controlled trial.pt. 622160

12 controlled clinical trial.pt. 95610

13 randomi?ed.ab. 789697

14 placebo.ab. 252123

15 drug therapy.fs. 2737926
16 randomly.ab. 442798
17 trial.ab. 716431
18 groups.ab. 2739845
19 or/11-18 6100022
20 exp animals/ not humans.sh. 5262023
21 19 not 20 5342662
22 10 and 21 4611.

Participant or population P (Population): People of all age groups whose diagnosed with primary ITP, regardless of severity levels of thrombocytopenia and bleeding symptoms.

Intervention I (Intervention): Administration of dexamethasone.

Comparator C (Comparison): prednisolone.

Study designs to be included RCTs.

Eligibility criteria A. Study types: 1. Study Design: Randomized controlled trials that compare dexamethasone to other steroids in the treatment of primary ITP were included.
3. publication status: Only published studies were included to ensure the data is complete.
B. Intervention and control types: All forms of dexamethasone versus prednisolone/ prednisone, (intervenous, oral) were used as a single agent, or in combination with other first-line pharmaceutical agents like intravenous immunoglobulin, or anti-D immunoglobulin were included.
C. Participants: Adults and pediatric patients with primary ITP.
Exclusion Criteria:
A. Study types: 1. Premature Termination: Trials that were stopped prematurely will be excluded to ensure the integrity of the data. 2. No enough data for response rate. 3. Pilot studies
B. Intervention types: Combination of assigned intervention with the second or third line of ITP treatment (rituximab, thrombopoietin receptor agonists, or splenectomy) was excluded, to avoid bias in the outcome.

Information sources Bibliographic databases and additional resources to be searched:
Embase database searched through Ovid interface from 1946 to 24/September/2024
Search strategy and restrictions:
The main search concepts are covering diagnosis (immune thrombocytopenia), intervention (steroids), with relevant synonyms for both concepts, and the RCTs filters. There were no restrictions on language, date of publication, or any other restrictions.
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Main outcome(s) Platelets response rate at 6 month.

Additional outcome(s) hypertension; glucos intolerance/ hyperglycemia.

Data management Data extraction and management: excel sheet was prepared for extracting data from the included articles, and two reviewers independently extracted data into her own sheet for the listed outcomes. Differences between the reviewers regarding the data were resolved by discussion. The gathered data were described in the attached excel sheet.
The collected variables were studies' baseline characteristics (see table 2 for more details), platelet count /mean at 6 months, people response rate number and percentage at 6 months, hyperglycemia/ glucose intolerance percentage, hypertension percentage.

Quality assessment / Risk of bias analysis Assessment of risk of bias: To assess the risk of bias across all outcomes, two authors conducted an independent evaluation of the studies in accordance with the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions. Any disagreements that arose during this process were resolved through consensus. The evaluation employed the RoB2 tool developed by Cochrane, concentrating on specific domains to identify potential biases: biases stemming from the

randomization process (including sequence generation and allocation concealment), biases resulting from deviations from the intended intervention (such as participant and personnel blinding), biases associated with missing outcome data, biases in outcome measurement, and biases related to selective reporting. Each item and subitem was assessed using signaling questions from the tool, facilitating responses categorized as “Yes,” “No,” “Probably Yes,” “Probably No,” and “No Information.” Subsequently, an overall bias assessment was reported. " The overall trial was classified as follows: • “Low risk of bias” if all domains were assessed as low risk; • “Some concerns of bias” if there were concerns in one domain but no high risk in any domain; and • “High risk of bias” if at least one domain was rated as high risk or if multiple domains presented concerns. Figure 1 illustrates the summary of risk of bias judgements for each of the five domains, along with the overall risk of bias assessment for the Response Rate, defined as the percentage of patients achieving a significant increase in platelet count (as defined by the study) recorded at 6 months post-treatment.

Strategy of data synthesis We pooled the results of trials using random-effects model.

Subgroup analysis Subgroup analysis and investigation of heterogeneity: We planned to perform subgroup analyses of studies that were done on adults versus children with ITP. In case of detecting any heterogeneity, we planned to perform sensitivity analysis for studies with a high risk of bias, however we ended up with few studies and all have same level of bias risk.

Sensitivity analysis We planned to perform sensitivity analysis for studies with a high risk of bias, however we ended up with few studies and all have same level of bias risk.

Language restriction No.

Country(ies) involved Saudi Arabia.

Keywords ITP, IMMUNE THROMBOCYTOPENIA, CORTICOSTEROID, DEXAMETHASONE, PREDINSOLONE.

Contributions of each author

Author 1 - Najla Algariri - reviewer in studies and data collector; writing manuscript.
Email: najlaalgariri@gmail.com
Author 2 - Nour Almutairi - reviewer and data collector.
Email: nooralmutairimd@gmail.com
Author 3 - Bedah Alnawfal - reviewer and data collector.
Email: bedah.alnawfal@gmail.com