Lower or higher doses for prophylactic platelet transfusions: results of a meta-analysis of randomized controlled trials

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CRD summary
This review compared the effectiveness of lower and higher doses of prophylactic platelet transfusions used to treat thrombocytopenic bleeding. The authors concluded that higher doses of platelet transfusions are associated with an increase in the transfusion interval and post transfusion platelet count increment. The reliability of these conclusions cannot be assessed because of the lack of details about the review process.

Authors' objectives
To compare the effectiveness of lower and higher doses of prophylactic platelet transfusions in the treatment of thrombocytopenic bleeding in patients with haematologic diseases.

Searching
MEDLINE, EMBASE and the Cochrane Library were searched to 2005; the search terms were not reported. The reference lists of retrieved studies and relevant reviews were also screened.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that compared transfusions of high-dose platelets (HDP) and low-dose platelets (LDP) were eligible for inclusion. The trigger to initiate transfusion ranged between 10 and <25 (x10^9) cells/L per litre in the included studies. Platelet transfusions in the included studies ranged from 3.35 to 7.7 (x10^11) for the HDP group and 2.01 to 4.6 (x10^11) for the LDP group. The majority of included studies used platelets collected by apheresis.

Participants included in the review
Studies of participants aged over 16 years with haematological disorders were eligible for inclusion. The participants in the included studies were adults with a median age range across of the studies of between 38 and 55 years. All of the included participants had chemotherapy-induced thrombocytopenia. Nearly half of the included participants had a diagnosis of acute leukemia, 7% had a diagnosis of breast cancer, and 44% required bone marrow transplantation. Three studies excluded participants with known clinical factors for platelet consumption.

Outcomes assessed in the review
The included studies needed to report on at least one of the following outcomes to be included in the review: mean difference in the transfusion interval, mean difference in the post-transfusion platelet (PLT) count increment, or the odds ratio (OR) of bleeding.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors assessed the quality of the included trials using the Jadad quality assessment score, which assesses the method of randomisation, the method of blinding, and the disclosure of withdrawals and drop-outs. The maximum possible score was 5. The authors did not state how many reviewers performed the assessment, or how any disagreements were resolved.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Means and standard deviations were extracted for the transfusion interval and PLT count increment; 2x2 data, in order to calculate ORs, were extracted for the incidence of bleeding.

Methods of synthesis
How were the studies combined?
Where no significant heterogeneity was evident, the studies were grouped according to outcome and pooled weighted mean differences (WMDs) or ORs calculated using a fixed-effect model.

How were differences between studies investigated?
Heterogeneity was assessed using the I-squared and the Q statistics, with statistical heterogeneity identified as present if the probability of homogeneity was less than 0.20. Any significant variability identified between the studies was investigated using subgroup analysis, grouping studies by: number of participants; number of transfused platelets; study design; diagnosis; mean difference between HDP and LDP transfusions; transfusion trigger; platelet type; blood type compatibility; storage duration; and study quality.

Results of the review
Five RCTs (n=442) were included in the review. Two studies used a crossover RCT design.

Only one study received a maximum Jadad quality score of 5. Four studies used adequate randomisation methods, 3 studies described withdrawals and drop-outs, and only 2 studies used double-blinding.

Four RCTs showed a statistically significant increase in transfusion interval in the HDP group compared with the LDP group (pooled WMD 1.04 days, 95% CI: 0.89, 1.19; I squared 0%; p<0.00001).

Four RCTs reported a significant increase in post-transfusion PLT count increment in the HDP group compared with the LDP group; however, significant heterogeneity was detected (I-squared 93.7%; p<0.00001). Subgroup analyses showed significant heterogeneity in all but the subgroup that guaranteed blood group compatibility. The pooled results from these studies showed a significantly higher post-transfusion PLT count in the HDP group compared with the LDP group (WMD 2.36E10 cells/L, 95% CI 18.28, 28.92; I-squared 0%; p<0.00001).

Three RCTs reported that the OR of bleeding in the HDP group compared with the LDP group varied from 0.68 to 2.06; however, significant heterogeneity was identified between the studies. Subgroup analyses showed significant heterogeneity with the exception of study design, diagnosis, mean difference between HDP and LDP, and study quality. The pooled OR from 2 homogeneous RCTs showed that the HDP group had significantly higher levels of bleeding than the LDP group (OR 2.03, 95% CI 1.06, 3.89; I-squared 0%; p=0.03).

Authors' conclusions
The transfusion of higher doses of platelets to adult thrombocytopenic patients with haematologic diseases is associated with an increase in the transfusion interval and, when blood group compatibility is guaranteed, post-transfusion PLT count increment. However, further research is required.

CRD commentary
The review question was clear in terms of the study design, participants, intervention and outcomes. The authors searched relevant databases over a reasonable timeframe, but did not state whether any language restrictions were applied and made little apparent effort to identify unpublished studies; this suggests a potential for publication and language bias. The authors did not describe how papers were selected for the review or how the data were extracted, so the potential for reviewer error and bias cannot be assessed. The validity of the studies was assessed using defined criteria and the results were summarised; the authors did not state how this process was carried out, thus introducing the potential for reviewer error and bias.
Adequate details of the included studies were reported. The statistical synthesis was well defined and appeared appropriate. The authors assessed statistical heterogeneity and carried out further investigations of its possible sources using subgroup analyses. However, the statistical power of these tests was likely to have been low given the small number of included studies. Overall, the authors' conclusions reflect the data presented, but it is unclear to what extent they are reliable given the poor reporting of review methods and the aforementioned limitations.

**Implications of the review for practice and research**  
Practice: The authors did not state any implications for practice.  
Research: The authors stated that a well-designed study of adequate power is essential to establish the most effective and efficient dose of prophylactic platelet transfusions.

**Bibliographic details**  
Cid J, Lozano M. Lower or higher doses for prophylactic platelet transfusions: results of a meta-analysis of randomized controlled trials. Transfusion 2007; 47(3): 464-470

**PubMedID**  
17319827

**DOI**  
10.1111/j.1537-2995.2006.01137.x

**Indexing Status**  
Subject indexing assigned by NLM

**MeSH**  
Adolescent; Adult; Aged; Aged, 80 and over; Blood Cell Count; Female; Hemorrhage /etiology; Humans; Male; Middle Aged; Platelet Transfusion /adverse effects /methods; Preventive Medicine /methods; Randomized Controlled Trials as Topic; Time Factors

**AccessionNumber**  
12007000811

**Date bibliographic record published**  
31/10/2007

**Date abstract record published**  
31/10/2007

**Record Status**  
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.