Platelet Transfusions in Patients with Hypoproliferative Thrombocytopenia

Conclusions from Clinical Trials and Current Controversies

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KEYWORDS

• Platelet transfusion • Thrombocytopenia • Bleeding • Acute leukemia
• Hematopoietic stem cell transplantation • Chemotherapy

KEY POINTS

- A uniform prophylactic platelet transfusion strategy for all patients with thrombocytopenia is not appropriate.
- Patients may have significant bleeding at platelet counts of greater than 10×10^9/L and should be assessed and managed on clinical grounds, not platelet count alone.
- Platelet count is not the only factor that contributes to a patient's propensity to bleed.
- Patients with acute leukemia should receive prophylactic platelet transfusions when their platelet count is less than 10×10^9/L to prevent clinical bleeding.
- Greater consistency in the assessment and documentation of bleeding across transfusion trials is essential to support comparisons of outcomes between studies.

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INTRODUCTION

Duke[1] reported the first description of bleeding in the setting of thrombocytopenia, which improved after blood transfusion and recurred when the platelet count decreased. Up to 70% of patients with hematologic malignancy will have clinically significant bleeding (World Health Organization [WHO] grade 2 or higher) and up to 10% will have severe or life-threatening bleeding.[2]

Patients have a tendency to develop bleeding symptoms as their platelet counts decrease, and major bleeding occurs more frequently at platelet counts of less than 10×10^9/L.[2,3] However, many patients with severe thrombocytopenia do not develop clinically significant bleeding.[4,5] Conversely, major and even fatal bleeding is well-recognized to occur at platelet counts of greater than 10×10^9/L.[2,4–7]

In early leukemia studies, bleeding as a result of thrombocytopenia was a major contributing factor to mortality rates.[8] Platelet transfusions helped to decrease the incidence of death attributable to bleeding[8,9] and today mortality as a result of thrombocytopenia-related bleeding is exceedingly rare[2] (**Table 1**). Platelet transfusions have become an important adjunctive therapy and led to improved patient survival. They have also supported delivery of more intensive chemotherapy regimens.[8–10]

Platelet concentrates are the second most commonly prescribed blood product after red blood cells (RBC)[11] and hematooncology patients are the largest users of platelet concentrates.[12–14] Platelet transfusion rates are increasing; in the United States, more than 2 million platelet units were transfused in 2011, a 7.3% increase compared with 2008.[14] Platelet transfusions may be given therapeutically, to treat bleeding when thrombocytopenia or abnormal platelet function are contributing factors, but are more frequently given prophylactically, in efforts to avert bleeding before a procedure or when the platelet count falls below a certain threshold.[12,15,16] Many patients with platelet counts of less than 10×10^9/L will not have clinically significant bleeding, and therefore many platelet transfusions may be being given unnecessarily.

METHODS

This review provides an update of the literature and some of the challenges raised by a very recent update of a Cochrane systematic review.[17] The methodology of this update has been described elsewhere; in brief, searching for platelet transfusion trials multiple datasets was undertaken. Eligible trials were identified and data abstracted, alongside an assessment of risk of bias. The update of an earlier Cochrane review[18] aimed to determine whether therapeutic-only platelet transfusions were as effective and safe as prophylactic platelet transfusions in patients with hematologic disorders undergoing cytotoxic chemotherapy or hematopoietic stem cell transplantation (HSCT).[17] Seven randomized controlled trials (RCTs) met the predefined selection criteria (one is still ongoing), leaving a total of 6 eligible trials and a total of 1195 participants. These trials were conducted over a 35-year time period. Five studies contained separate data for each arm and were able to be critically appraised. Only 1 study was deemed to be at low risk of bias.[4]

MAIN FINDINGS FOR REVIEW

For the systematic review's primary outcome (number of patients with $\geq$1 bleeding episode within 30 days) significant heterogeneity was noted ($I^2 = 88\%$).[17] This heterogeneity may reflect in part the different methodology and grading systems used to analyze and categorize bleeding in the individual studies. Four studies in the