Granulocyte transfusions for treating infections in patients with neutropenia or neutrophil dysfunction

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Abstract

Background
Transfusions of granulocytes have a long history of usage in clinical practice to support and treat severe infection in high risk groups of patients with neutropenia or neutrophil dysfunction. However, there is considerable current variability in therapeutic granulocyte transfusion practice, and uncertainty about the beneficial effect of transfusions given as an adjunct to antibiotics on mortality.

Objectives
To determine the effectiveness of granulocyte transfusions compared to no granulocyte transfusions for treating infections in patients with neutropenia or disorders of neutrophil function in reducing mortality.

Search strategy
Randomised controlled trials (RCTs) were searched for in the Cochrane Central Register of Controlled Trials (CENTRAL) in 2003. Searching was also undertaken on the OVID versions of Medline and Embase using an RCT search filter strategy.

Selection criteria
RCTs involving transfusions of granulocytes, given therapeutically, to patients with neutropenia or disorders of neutrophil dysfunction.

Data collection and analysis
Two reviewers completed data extraction independently. Relative risk (RR) with 95% confidence intervals (CI) using the random effects model were reported for dichotomous outcomes. Pre-specified subgroup analyses were done and reported eg granulocyte dose.

Main results
Eight parallel RCTs were included with 310 total analysed patient episodes. Different policies were applied for the schedule of transfusion, method of granulocyte procurement and process of donor selection including leucocyte compatibility. Each study used different criteria for neutropenia (range < 0.1 to < 1.0 x 10(9)/L) and definition of infection requiring treatment. For mortality, which was extracted from six trials, the summary RR = 0.64 in favour of transfusion (95% CI 0.33, 1.26), but with evidence of significant statistical heterogeneity (Chi-square 11.3 and I(2) = 56%). The data for the combined RR for mortality for the four studies transfusing higher granulocyte doses greater than 1x10(10) indicated a significant summary RR= 0.37 (95% CI 0.17, 0.82); Chi-square 3.9, I(2) 23%. Data on rates of reversal of infection could be extracted from four studies, and the combined RR was 0.94 (95% CI 0.71, 1.26), again with evidence of heterogeneity. In addition to the observed clinical diversity between all studies, uncertainty about the quantitative and qualitative analyses for these studies is compounded by methodological deficiencies.

Authors' conclusions

Currently, there is inconclusive evidence from RCTs to support or refute the generalised use of granulocyte transfusion therapy in the most common neutropenic patient populations, that is caused by myeloablative chemotherapy with or without haematopoietic stem cell support. Contemporary well designed prospective trials are required to evaluate the efficacy of this intervention in these patient populations and to establish definitively whether it has clinical benefit. In such studies, average numbers of collected granulocytes for adults should be (at least) greater than 1x10(10).