CRD summary
This review evaluated the effects of granulocyte transfusions in children with neutropenia and evidence of fungal or bacterial infections. As all the available evidence came from observational studies, the authors decision not to draw a firm conclusion and recommend further research is appropriate.

Authors' objectives
To evaluate any favourable effects and side effects of granulocyte transfusions in paediatric oncology patients with neutropenia.

Searching
MEDLINE, EMBASE and LILACS were searched from inception to August 2006. Cochrane Central Register of Controlled Trials (issue 4, 2006), Web of Science (to August 2006) and the Internet were also searched. There were no language or publication status restrictions.

Study selection
Randomised and quasi-randomised controlled trials (RCTs), phase II trials, cohort studies, case-control studies, case reports and data from abstracts were eligible for inclusion. Studies had to be of children (aged one to 18) with a malignancy or immunological disorder, neutropenia and evidence of infection (proven bacteraemia, fungal sepsis or strong clinical suspicion) or an increased chance of infection. Studies of adults were eligible if data for children could be analysed separately. Studies could evaluate granulocyte transfusions from any source of granulocytes and with any method of collection, for both therapeutic or prophylactic purposes.

Most included studies were case reports or cohort studies, including only one un-controlled RCT and two early phase trials. Studies included oncology patients (66.7%), patients with a granulocyte dysfunction (24.3%), and a combination of patients (9%). Most patients (74.5%) were haematological; the remainder were allogeneic bone marrow transplant patients. Where reported, the mean age was 8.9 years (range two to 17 years).

The authors did not state how studies were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The number of days with neutropenia (granulocytes ≤500cells/μL), mean number of granulocytes transfused, the response of the infectious episode (survival or death) and details of side effects were extracted. Data extracted about the donor were: stimulation using granulocyte colony-stimulating factor, corticosteroids or both; side effects; and the method of granulocyte collection.

Two reviewers independently extracted data and disagreements were resolved by discussion.

Methods of synthesis
Study results were presented in tables, grouped by year of publication (before or after 1984) and type of disorder (immune, oncological, or both). Results in the text were presented as a narrative, grouped by outcome or treatment method.

Results of the review
Sixty-six studies were included (510 patients): 38 case reports; 23 cohort studies; one uncontrolled trial of prophylactic granulocyte transfusions; two abstracts; and two phase I/II studies. There were 456 patients with oncology disorders and 54 patients with a granulocyte dysfunction.
Infections: In 59 studies of therapeutic granulocyte transfusions, a proven sepsis was reported in 55. Fifty-three patients received granulocytes due to a Gram-positive infection, 103 patients received granulocytes for a Gram-negative infection, and 141 patients received granulocytes for a fungal infection. In seven studies of prophylactic granulocyte transfusions, there were four studies reporting a proven sepsis, five patients had a previous Gram-negative infection and four patients had a previous fungal infection.

Granulocyte transfusions: For therapeutic granulocyte transfusions the mean number of granulocyte concentrates transfused was 8.7 (range 1 to 46). For prophylactic granulocyte transfusions the mean number of granulocyte concentrates transfused was 4.8 (range 2 to 8). For paediatric oncology patients receiving therapeutic granulocyte transfusions the mean number of granulocyte concentrates transfused was 5.4 (range 1 to 21). Mean numbers of granulocytes transfused was $32 \times 10^9$/L (range 2 to $82 \times 10^9$/L) for therapeutic granulocyte transfusions and $33 \times 10^9$/L (range 22 to $46 \times 10^9$/L) for prophylactic granulocyte transfusions.

Donor: Fifty-one studies reported data on the donor. For therapeutic studies 20 used related donors, 24 unrelated donors and one used both. For prophylactic studies, six reported data on the donor, with three studies using related donors and three studies using unrelated donors.

Clinical outcomes: In 31 case reports, 53 patients died and 81 patients survived. In 21 cohort studies, there were 50 deaths and 168 patients who survived. Over all studies, 30% of patients died and 70% survived. The death rate in patients where donors were stimulated with granulocyte colony-stimulating factor and steroids was 50% lower than for the unstimulated group (43 compared with 20 deaths).

Side effects: Seven studies reported pulmonary complications. Nine studies reported allergic reactions, all of which were resolved without complications. Three studies reported transmission of infections. Three studies reported flu-like symptoms in donors who were stimulated with granulocyte colony-stimulating factor.

Authors’ conclusions
The review found no randomised evidence that showed a positive benefit of granulocyte transfusions. The available observational evidence showed that paediatric neutropaenic patients with a bacterial or fungal infection could benefit from granulocyte transfusion, but a well-designed clinical trial is needed to establish the timing and dose needed.

CRD commentary
This review had clear inclusion and exclusion criteria. There was an adequate search of the literature, with no language restrictions, but searching for unpublished literature was limited. Data were extracted by two reviewers independently, but it was not reported if studies were selected in the same way, which may have increased the risk of error and bias in the process.

A formal quality assessment was not performed. The authors did discuss the weaknesses of the study designs and decided that a conclusion on the efficacy of granulocyte transfusions could not be drawn from the available evidence. It would have been useful if the text/tables of the review had reported the design of each study, so that studies with stronger designs (such as the few prospective trials) could have been evaluated. Further individual study details, such as the patient age and duration of neutropenia, would also have been helpful.

Given the observational nature of the evidence, the authors’ decision not to draw a firm conclusion but recommend further research is appropriate.

Implications of the review for practice and research
Practice: The authors recommended that granulocyte transfusions should be only be given as part of a well-designed clinical trial.

Research: A well-designed clinical trial in neutropenic children was needed to establish a standardised protocol, and evaluate the optimum timing and dose of granulocyte transfusions.

Funding
Not stated.
Bibliographic details

DOI
10.1016/j.ejca.2007.07.018

Original Paper URL
http://www.ejcancer.info/article/S0959-8049(07)00557-6/abstract

Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Child; Child, Preschool; Epidemiologic Methods; Granulocytes /transplantation; Hematologic Neoplasms /therapy; Humans; Immune System Diseases /therapy; Infant; Infection /therapy; Leukocyte Transfusion /methods; Neutropenia /therapy

AccessionNumber
12008103164

Date bibliographic record published
01/09/2008

Date abstract record published
07/10/2009

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.