Unrelated umbilical cord blood transplantation and unrelated bone marrow transplantation in children with hematological disease: a meta-analysis

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CRD summary
This review concluded that unrelated umbilical cord blood transplantation was an effective option for the treatment of children with haematological disease and had equivalent survival outcomes when compared with unrelated bone marrow transplantation. In light of the poor reporting, vulnerability to various biases and uncertainty around the appropriateness of the meta-analyses, these conclusions should be regarded with caution.

Authors' objectives
To compare the outcomes of unrelated umbilical cord blood transplantation versus unrelated bone marrow transplantation as a source of haematopoietic stem cells in children with haematological disease.

Searching
The following databases were searched between January 1985 and May 2008: MEDLINE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, ACP Journal Club, and DARE. Search terms were reported. Only articles published in English or Chinese were considered for inclusion. Reference lists of retrieved studies were also searched.

Study selection
Studies were eligible for inclusion if they compared unrelated umbilical cord blood transplantation with unrelated bone marrow transplantation in children who required allogeneic haematopoietic stem cell transplantation to treat malignant or non-malignant disorders. Each study had to report one or more of the following outcomes: neutrophil and platelet engraftment, transplantation-related mortality, relapse, graft-versus-host disease, overall or event-free survival. The primary review outcome was survival.

Included trials were not clearly described in terms of baseline characteristics, but the majority of patients appear to have been diagnosed with leukaemia. Studies without comparable patient demographics were excluded.

More than one reviewer independently assessed studies for inclusion. The authors did not report how disagreements were resolved.

Assessment of study quality
Validity appears to have been assessed according to consistency, accuracy and balance between treatment groups, Jadad scores were also given in a table, but further details were not reported.

Two reviewers appear to have independently assessed study quality.

Data extraction
Odds ratios (OR) and associated 95% confidence intervals (CI) were extracted where possible for specified outcomes. Means and standard deviations (SD) also appear to have been extracted.

Data were extracted by two reviewers independently using standardised data extraction forms. The authors did not report how disagreements were resolved.

Methods of synthesis
Trials were pooled to give odds ratios and 95% confidence intervals for dichotomous outcomes and weighted mean differences (WMD) for continuous outcomes using fixed-effects models, unless significant statistical heterogeneity was
indicated by the $I^2$ test in which case a random-effects model was used. Publication bias was assessed using a funnel plot.

**Results of the review**

Seven controlled clinical trials (n=1,453 patients) were included in this review. Trials were published between 2001 and 2007. Sample sizes ranged from 24 to 791 children. Jadad scores were reported as 1 point for six out of seven trials; none were described as blinded. Significant heterogeneity was found for white blood cell and platelet engraftment, graft-versus-host disease rates and cytomegalovirus analyses. The funnel plot was relatively symmetrical indicating that publication bias was unlikely to be present.

Engraft failure rate (six trials) was significantly higher in the UCBT (unrelated umbilical cord blood transplantation) group compared to the UBMT (unrelated bone marrow transplantation) group, OR 4.96 (95% CI: 3.25 to 7.59). White blood cell engraftment times (WMD 10.25, 95% CI: 5.42 to 15.08) and platelet engraftment times (WMD 30.39, 95% CI: 10.80 to 49.99) were significantly delayed in the UCBT patients compared with UBMT patients (four trials).

Acute graft-versus-host disease rates (OR 0.54, 95% CI: 0.36 to 0.81) and chronic graft-versus-host disease rates (OR 0.36, 95% CI: 0.27 to 0.48) were significantly lower in the UCBT group.

Relapse rates (five trials) were significantly lower in the UCBT group, OR 0.66 (95% CI: 0.51 to 0.86).

Early transplant-related mortality (five trials) was significantly higher in the UCBT group, OR 2.36 (95% CI: 1.79 to 3.11).

Disease free survival (six trials) and cytomegalovirus infections rates (three trials) did not differ significantly between the two interventions.

**Authors’ conclusions**

Unrelated umbilical cord blood transplantation was an effective option for the treatment of children with haematological disease and had equivalent survival outcomes when compared with unrelated bone marrow transplantation.

**CRD commentary**

This review addressed a clear clinical question but the inclusion criteria were broad and only partially described. The searches did not include any sources of grey literature, considered only published articles in two languages and covered only a limited number of databases; so it is likely that relevant studies may have not been detected or included resulting in publication and language biases. The review processes were poorly described, making it difficult to rule out reviewer error and/or bias from the study selection, validity assessment and data extraction phases. It was not possible to assess the suitability of the primary trials for pooling as no patient characteristics or baseline data were provided; meta-analysis may or may not have been appropriate. The Jadad scores suggested that all of the included trials were relatively poor in quality; despite this the authors drew relatively strong conclusions. In light of the poor reporting, vulnerability to various biases and uncertainty around the appropriateness of the meta-analyses, these conclusions should be regarded with caution.

**Implications of the review for practice and research**

**Practice:** The authors stated that unrelated umbilical cord blood transplantation should be considered as an alternative stem cell source for children, especially when an unrelated bone marrow donor is not available.

**Research:** The authors stated that well designed trials with large samples are required.

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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.