Unrelated donor umbilical cord blood transplantation versus unrelated donor bone marrow transplantation in adult and pediatric patients: a meta-analysis


CRD summary
The authors concluded that unrelated donor umbilical cord blood transplantation was inferior compared to unrelated donor bone marrow transplantation in adults with haematologic disease. Given the heterogeneity and uncertain quality of the trials and potential for bias in the review, the authors' conclusions should be interpreted with caution.

Authors' objectives
To assess the safety and efficacy of unrelated donor bone marrow transplantation and unrelated donor cord blood transplantation in patients with haematological diseases.

Searching
MEDLINE, EMBASE, The Cochrane Library and Science Citation Index were searched up to June 2009 for relevant publications; search terms were reported. References of retrieved articles were searched manually.

Study selection
Studies that compared the effects of unrelated donor bone marrow transplantation (UBMT) versus unrelated donor cord blood transplantation (UCBT) for the primary treatment of adults and children with malignant and non-malignant disorders were eligible for inclusion. The primary outcome was survival. Secondary outcomes were engraftment, graft-versus-host disease, transplantation-related mortality and relapse. Studies with fewer than 20 patients per treatment group or that assessed T-cell-depleted UBMT were excluded.

The included studies were of children (age range 0.1 to 19.5 years) or adults (age range, where reported, 15 to 69 years) with acute leukaemia or haematologic diseases. Proportions of patients who were human leucocyte antigen matched and antigen mismatched differed between studies (as reported in the review). The percentage of 6/6 HLA-matched patients ranged from zero to 100% across treatment groups; in all studies the proportion of 6/6 HLA matched patients was greater in the UBMT groups.

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
Two reviewers assessed the quality of the studies based on consistency, accuracy and comparability between treatment groups. No further details were provided.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Two reviewers independently extracted data to calculate hazard ratios (HRs) for overall survival and relative risks (RRs) for other outcomes, both with their 95% confidence intervals (CIs). Where hazard ratios were not reported in the original article, they were estimated from data extracted from Kaplan-Meier curves. Primary authors were contacted for further details where necessary. Disagreements were resolved through consensus.

Methods of synthesis
A random-effects model was used to pool hazard ratios and relative risks, and their 95% CIs. Statistical heterogeneity was assessed using $T^2$, $X^2$ and $I^2$.

Subgroup analyses were performed for adults and children. For the outcome graft-versus-host disease, results were reported separately for Grades II-IV acute graft-versus-host disease and chronic graft-versus-host disease.
Results of the review

Ten controlled clinical trials (CCTs) (11 comparisons) were included in the review: six of children (750 who received UCBT and 673 who receiving UBMT) and four of adults (603 who received UCBT and 1,529 who received UBMT).

Patients who received UCBT showed worse overall survival (HR 1.28, 95% CI 1.13 to 1.44, $I^2$ not reported; eight CCTs) and a higher rate of transplantation-related mortality (RR 1.28, 95% CI 1.03 to 1.58, $I^2$=68%; 10 CCTs) compared with patients who received UBMT. By contrast, patients who received UCBT showed a significantly lower incidence of grades II-IV acute graft-versus-host disease (RR 0.73, 95% CI 0.64 to 0.82, $I^2$=30%; 10 CCTs) and chronic graft-versus-host disease (RR 0.70, 95% CI 0.51 to 0.97, $I^2$=79%; 10 CCTs) compared to patients who received UBMT. Incidence of relapse did not differ between the two treatment groups ($I^2$=59%; seven CCTs).

Subgroup analyses significantly altered the results for some outcomes. In adults, UCBT was associated with a statistically significant decrease in overall survival (HR 1.26, 95% CI 1.13 to 1.40; $I^2$=0%) and a significant decrease in risk of acute graft-versus host disease. There was no significant difference between UCBT and UBMT in chronic graft-versus host disease, relapse and transplantation-related mortality.

In children, there was no significant difference between UCBT and UBMT in overall survival or transplantation-related mortality. UCBT was associated with a statistically significant decrease in risk of acute and chronic graft-versus host disease and relapse.

Authors’ conclusions
UCBT resulted in inferior outcomes compared to UBMT in adult patients.

CRD commentary
The review question and supporting inclusion criteria were clearly stated. The literature search was adequate. But only published data were sought and it was unclear whether language restrictions were imposed, so potentially relevant data may have been missed. As highlighted by the authors, publication bias could not be assessed due to the small number of included studies. The authors stated that they assessed the quality of the included trials, but no further details or results were provided and trial quality remained uncertain. The authors reported that they undertook quality assessment and data extraction in duplicate; it was unclear whether this was also true for study selection. Few details on patients and methodological procedures were provided. There was some evidence of statistical heterogeneity, which suggested that it may not have been appropriate to pool the trials. The authors acknowledged that heterogeneity should be taken into consideration when interpreting the findings. Sample sizes were small and there was a twofold difference in the number of adult patients who received UCBT compared to UBMT.

Given the heterogeneity among the trials and their uncertain quality and potential for bias in the review, the authors’ conclusions should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors stated that UCBT could be considered as an alternative stem cell source for children, even when an unrelated marrow donor was available. They also stated that it remained unclear whether double unit grafts, expansion and better HLA-matching level influenced the outcome of UCBT in adults.

Research: The authors stated that individual patient data analysis was needed to further compare the effects of UCBT versus UBMT in adults and children.

Funding
None stated.

Bibliographic details
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.