Meta-analysis of autologous bone marrow transplantation versus chemotherapy in adult patients with acute myeloid leukemia in first remission
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CRD summary
This review compared autologous bone marrow transplantation (ABMT) with chemotherapy or no further treatment in adult acute myeloid leukaemia patients in first remission. ABMT prolonged event-free survival but did not improve overall survival. This conclusion may be unreliable as it was based on the pooling of clinically diverse studies.

Authors' objectives
To compare autologous bone marrow transplantation (ABMT) with other treatment regimens in adult patients with acute myeloid leukaemia (AML) in first remission.

Searching
MEDLINE was searched from January 1966 to March 2003, first with the reported search terms and then with authors' names obtained from the retrieved studies and their reference lists.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials were eligible for inclusion.

Specific interventions included in the review
Studies of ABMT compared with either chemotherapy or no further treatment were eligible for inclusion. Of the included studies, one compared ABMT with no further treatment while all the other studies had a chemotherapy regimen as the control. Both ABMT and chemotherapy protocols varied between the studies. Most stem cells used for ABMT were of bone marrow origin, and these were purged in only one of the included studies.

Participants included in the review
Participants aged 15 to 56 years with AML in first remission were eligible for inclusion. Studies with broader age ranges were eligible provided the required age group could be analysed separately. One of the included studies had an age range of 0 to 56, but data from patients aged 15 to 34 years were available for a separate analysis. Another included study had a stated age range of 11 to 59 years. The participants in all other studies fell within the age range of the inclusion criteria. The participants had achieved remission via a variety of chemotherapy regimens.

Outcomes assessed in the review
No particular outcomes were specified in the inclusion criteria, although the studies were required to present intention-to-treat data. The outcomes included in the review were death and relapse.

How were decisions on the relevance of primary studies made?
Two reviewers, one of whom was blinded to the author names, journal name, date and site of each study, made decisions independently. Any disagreements were resolved by discussion with all other authors.

Assessment of study quality
The studies were judged on the basis of several criteria: the number of participants; definition of remission; the exclusion of participants with background disease or complications; description of randomisation; drugs used to induce remission; and availability of time data. These criteria were based on those described by Chalmers et al. (see Other Publications of Related Interest). An overall score was obtained for each study and the studies were then ranked in score order. Two reviewers, one of whom was blinded to the author names, journal name, date and site of each study,
made judgements independently. Any disagreements were resolved by discussion with all other authors.

**Data extraction**
Two reviewers extracted the data using a computerised form. For each study and from both ABMT and control groups, the following data were extracted: the number of participants randomised, the number who received the allocated treatment, the number of deaths and the number of participants who relapsed. These were then used to calculate the death rate and event (death or relapse) rate for each group. Where data were presented for each follow-up year, the rates were calculated with person-years as the denominator. Rate ratios (RR) and 95% confidence intervals (CIs) for ABMT compared with the control group were then calculated for death and event rates for each study.

**Methods of synthesis**
How were the studies combined?
The studies were combined using a meta-analysis to give summary RRs and 95% CIs. Each analysis was performed using a fixed-effect model and/or a random-effects model.

How were differences between studies investigated?
Chi-squared tests were used to assess statistical heterogeneity between the studies. Where no significant heterogeneity was detected, a fixed-effect model was used for further analysis. A series of sensitivity analyses was performed to investigate influences on the pooled estimates. First, each individual study was removed separately, then the two studies with the lowest quality score were excluded, and third, only studies providing yearly information were retained in the analysis.

**Results of the review**
Six studies were included in the review. The reported, total number of participants randomised was 1,044. From one study only the participants aged 15 to 44 were included in this total, although data from all participants (age: 0 to 56) were included in some parts of the review.

**Death rate.**
The death rate was not significantly different in the ABMT and control groups. The RR was 0.94 (95% CI: 0.84, 1.09) using a fixed-effect model and 0.95 (95% CI: 0.79, 1.13) using a random-effects model. Significant statistical heterogeneity was not detected. The sensitivity analyses had no significant effect on the overall measure or on heterogeneity.

**Event (death or relapse) rate.**
The event rate was significantly lower in the ABMT group than in the control group (RR 0.85, 95% CI: 0.75, 0.97). A fixed-effect model was used as significant statistical heterogeneity was not detected. The exclusion of one study yielded an overall estimate with CIs including 1.0, but all other sensitivity analyses showed no effect on the overall measure or on heterogeneity.

**Authors’ conclusions**
ABMT in adult patients with AML in first remission prolonged event-free survival but did not improve overall survival.

**CRD commentary**
The review question was clear and the inclusion criteria were reasonably well defined. Only one database was searched and no attempt was made to locate unpublished studies, thus relevant studies might have been missed. Two reviewers carried out the study selection, quality assessment and data extraction independently, which should have minimised the introduction of errors and bias at these stages of the review process. A validity assessment was carried out, and a sensitivity analysis was performed to assess the impact on the overall result of removing low-quality studies.
Some details of the primary studies were tabulated. The studies were combined in a meta-analysis, which may not have been appropriate given the clinical diversity of the studies. Statistical heterogeneity was assessed and sensitivity analyses were used to investigate the influence of a number of factors on the overall result. The review appears generally to have been well conducted. However, the conclusion may be unreliable as it was based on the pooling of clinically heterogeneous studies.

Implications of the review for practice and research
Practice: The authors stated that they recommended stem cell collection and ABMT to every AML patient in first remission without a suitable allogeneic donor.

Research: The authors stated that trials should be performed to evaluate the survival advantage of ABMT according to different prognostic subgroups.

Bibliographic details

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Other publications of related interest

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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.