Does acute normovolemic haemodilution reduce perioperative allogeneic transfusion: a meta-analysis

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Authors' objectives
To systematically review the literature, and to statistically summarise the evidence evaluating acute normovolaemic haemodilution (ANH).

Searching
The following sources were searched: MEDLINE from 1966 to 1996, Current Contents in 1996, and EMBASE from 1978 to 1996. Bibliographies of all identified RCTs were examined for additional publications.

Study selection
Study designs of evaluations included in the review
Any prospective randomised controlled trial (RCT) comparing ANH with a concurrent control group, regardless of the language or medium of publication was retrieved for further analysis.

Specific interventions included in the review
Allogeneic blood, and unspecified crystalloid or colloid solutions. ANH was defined as whole blood withdrawn on the day of surgery and replaced with crystalloid or colloid solution.

Participants included in the review
Patients undergoing cardiac, vascular, orthopaedic, thoracic, hepatic, gastrointestinal, ENT (ear, nose or throat) or urology surgery. Patients aged less than 18 years and women undergoing childbirth were excluded.

Outcomes assessed in the review
The primary outcome measure was the proportion of patients exposed to at least 1 U of allogeneic blood in the peri-operative stage. The other outcomes measured were the difference in allogeneic units transfused when ANH was used, and the difference in peri-operative blood loss with the use of ANH.

How were decisions on the relevance of primary studies made?
The titles and abstracts were reviewed to determine their eligibility for analysis.

Assessment of study quality
The quality of the trial methodology was assessed using the 3-item scale of Jadad et al. (see Other Publications of Related Interest). Trials received points for randomisation, blinding, and for accounting for all enrolled patients. The total score ranged from 0 (lowest quality) to 5 (highest quality). The authors do not state how the papers were assessed for quality, or how many of the authors performed the quality assessment.

Data extraction
Data were abstracted by two independent investigators using standardised data collection forms, and any disagreements were resolved by consensus. Non-English language papers were abstracted by one of the investigators with the assistance of a translator. When necessary, the primary authors were contacted by mail to clarify results or to provide missing data.

The reviewers were blinded to the author(s), date of publication and journal.

Methods of synthesis
How were the studies combined?
The proportion of patients transfused was analysed using the random-effects model of DerSimonian and Laird (see Other Publications of Related Interest no.2). The results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs).

The total number of units of allogeneic blood transfused, and the volume of blood lost in the peri-operative period were analysed. Results were expressed as weighted mean differences (WMD) with 95% CIs.

The authors also tested for a difference in transfusion pattern between the ANH and control groups using a stratified proportional odds model.

How were differences between studies investigated?
Heterogeneity in the results for dichotomous and continuous variables was evaluated using the Q statistic and the chi-squared statistic, respectively. Subgroup analyses were planned a priori, and were based on the type of procedure, the pre-operative volume of blood withdrawn, the post-operative volume of blood lost, and the use of a transfusion protocol.

Results of the review
Twenty-four trials with 1,218 participants (629 in the ANH groups and 589 in the control groups) were included in the meta-analysis.

The included trials received quality scores of either 1 or 2.

When all the trials were pooled, ANH reduced both the likelihood of exposure to allogeneic blood (OR 0.31, 95% CI: 0.15, 0.62) and the total number of units of allogeneic blood transfused (WMD -2.22 U, 95% CI: -3.57, -0.86).

When surgical procedures were considered individually, ANH was effective in reducing the likelihood of exposure to at least 1 U of allogeneic blood in cardiac and miscellaneous procedures, but not in orthopaedic surgery. Marked heterogeneity of results was found.

In trials in which the volume of blood withdrawn during haemodilution was less than 1000 mL, the reduction in the likelihood of transfusion failed to reach statistical significance (OR 0.43, 95% CI: 0.18, 1.02). On the other hand, studies in which at least 1000 mL of autologous blood were withdrawn before surgery showed large and statistically-significant reductions in the likelihood of transfusion (OR 0.16, 95% CI: 0.04, 0.65). Statistically-significant heterogeneity was absent in the analyses of trials with larger pre-operative phlebotomy.

The volume of peri-operative blood loss did not seem to influence the likelihood of exposure to allogeneic blood. Statistically-significant heterogeneity was absent in all analyses, bar the analysis of units transfused in trials with blood loss greater than 1000 mL.

Trials without transfusion protocols showed marked reductions in both the likelihood of exposure to allogeneic blood (OR 0.12, 95% CI: 0.04, 0.37) and the units of allogeneic blood transfused (WMD -3.01 U, 95% CI: -3.47, -2.55).

In trials using a protocol to guide peri-operative transfusion, ANH failed to reduce either the likelihood of transfusion (OR 0.64, 95% CI: 0.31, 1.31) or the units administered (WMD -0.25 U, 95% CI: -0.60, +0.10).

The results reported for the adverse events were incomplete.

Authors’ conclusions
The results of this systematic review and statistical summary of published trials of ANH were inconclusive. When all the trials of ANH were combined, it seemed that ANH was effective in reducing both the likelihood of exposure to allogeneic blood and the volume of blood transfused. However, the presence of substantial and unexplained heterogeneity suggested that the benefit of ANH was inconsistent and could not be definitively supported by this overview.
CRD commentary
The authors made an extensive search of the literature in all languages, but since no keywords were given, the search strategy could not be duplicated. There was also no mention of searching for unpublished data, so publication bias could not be excluded. They have been explicit in their inclusion and exclusion criteria, and their protocols for extracting and quality rating the data. The quality rating scale they used, however, was not comprehensive and only three aspects of validity were assessed. [A: The authors add in further correspondence that the use of Jadad's assessment was justified because it was the only validated scale available at the time of publication of this review, and updates of this systematic review are in progress.] As the authors acknowledge, the quality of the previous trials was low and heterogeneity between the included trials was significant. The conclusions of this review support the finding that the existing literature cannot support the use of ANH in surgery. It is possible that biased experimental design is, in part, responsible for the reported efficacy of this technique.

Implications of the review for practice and research
The authors state that larger trials with carefully defined indications for the transfusion of allogeneic blood are required to establish the efficacy of this technique.

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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.