Albumin versus hydroxyethyl starch in cardiopulmonary bypass surgery: a meta-analysis of postoperative bleeding
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Authors' objectives
To assess whether cumulative blood loss during the first 24 hours after cardiopulmonary bypass is lower in patients exposed to albumin than hydroxyethyl starch (HES).

Searching
MEDLINE, EMBASE, the Cochrane Controlled Trials Register and the Cochrane Medical Editors Trial Amnesty of unpublished clinical trials were searched. In addition, conference reports, abstracts, compilations of references, and full-text journal articles available on the Internet (identified using AltaVista, Northern Light, HotBot and Excite search engines) were examined, and the authors of published trial reports on colloid administration were consulted. The New England Journal of Medicine, JAMA, BMJ and the Lancet were handsearched from January 1990 to December 2000. Reference citations in colloid-related published meta-analyses were also reviewed, as were completed reviews and protocols on the Cochrane Database of Systematic Reviews, review articles, randomised trials and non-randomised clinical studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Patients were administered a colloid regime of exogenous purified albumin or HES, in various dosages. No restrictions were placed on the type of colloid used, e.g. pre-operative, intra-operative or post-operative administration, or incorporation in the priming fluid. Some patients were administered lactated Ringer's solution, Ringer's solution or dextrose in addition to the albumin or HES, again in various dosages. Details of the full dosages were provided in the paper.

Participants included in the review
Adults and paediatric patients undergoing cardiopulmonary bypass were included. The mean age of the patients in the adult trials was 59 plus or minus 9 years.

Outcomes assessed in the review
The following were assessed: the cumulative volume of mediastinal blood loss over the first 24 hours of cardiopulmonary bypass; reoperation caused by bleeding; the duration of intubation; the length of stay in the intensive care unit; and blood product usage.

How were decisions on the relevance of primary studies made?
Two investigators independently assessed whether the trials conformed to the inclusion criteria of the meta-analyses. Any discrepancies were resolved by discussion.

Assessment of study quality
The methodological quality of the trials was evaluated on the basis of the randomisation method, exclusions after trial entry, and blinding. The randomisation method was classified as adequate, inadequate or unclear. The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
Two investigators independently extracted the data from the included trials, and any discrepancies were resolved by discussion.

**Methods of synthesis**

**How were the studies combined?**

For continuous data such as the volume of post-operative blood loss, the standardised mean difference between the randomised groups was calculated (see Other Publications of Related Interest no.1). To provide a clinical frame of reference, the patient-weighted pooled within-group blood loss was calculated for trials of adults, and corresponding z-scores were used to estimate the percentages of patients in the albumin and HES groups with post-operative blood loss exceeding 1,000 mL. In the case of reoperation because of bleeding, the relative risk and risk difference were calculated. In the absence of significant heterogeneity, pooled standardised mean differences, relative risk, risk differences, and 95% confidence intervals (CIs) were derived using fixed-effect models (see Other Publications of Related Interest no.2). Publication bias was evaluated by Egger's test.

**How were differences between studies investigated?**

The authors do not state which test was used to investigate the differences between the studies.

**Results of the review**

Sixteen RCTs (n=653) were examined.

In 88% of randomised comparisons, post-operative bleeding was lower in the albumin group, and the standardised mean difference in bleeding favouring albumin across all trials (-0.24, 95% CI: -0.40, -0.08) was statistically significant. Bleeding differences between albumin and either high or medium molecular weight HES were similar. In trials of adults the pooled mean blood loss in the albumin group was 693 mL (plus or minus 350 mL) compared with 789 mL (plus or minus 489 mL) in the HES group. The estimated proportion of adult albumin group patients with blood loss of more than 1,000 mL was 19%, compared with 33% of the adult HES patients. There was no significant heterogeneity with respect to post-operative bleeding among all trials (p=0.40).

The rate of reoperation (n=9) for albumin and HES was 5.8% (26 out of 448 patients). The pooled risk of reoperation was lower in albumin than in HES patients (-3.7%, 95% CI: -8.4, -1.0), although the difference was not statistically significant.

For ventilatory support data (n=4), the duration of intubation was shorter in albumin recipients. The pooled standardised mean difference was -0.17 (95% CI: -0.43, 0.08).

The length of stay in the intensive care unit (n=3) was briefer in the albumin group. The pooled standardised mean difference was -0.21 (95% CI: -0.45, 0.03), indicating that the difference was not statistically significant.

**Cost information**

The authors state that the investigation of HES in cardiopulmonary bypass patients has received its primary impetus from the desire for cost-savings. However, with greater potential for bleeding taken into account, albumin rather than HES might offer the lower overall costs of care in these patients.

**Authors' conclusions**

Post-operative blood loss was significantly lower in cardiopulmonary bypass patients exposed to albumin than HES.

**CRD commentary**

This review was clearly presented and readable. It contained a comprehensive search strategy without any language restrictions, although the search terms were not listed and the authors did not state the dates over which the electronic searches were conducted. There was no information on how differences between the studies were investigated, although
the results of the heterogeneity tests were reported. Overall, the methods used in this review were thorough and the primary outcome results were statistically significant.

**Implications of the review for practice and research**
Practice: The authors state that post-operative blood loss is significantly lower in cardiopulmonary bypass patients exposed to albumin than HES.

Research: The authors did not state any implications for research.

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**Other publications of related interest**


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**Record Status**
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