Small-volume resuscitation with hyperoncotic albumin: a systematic review of randomized clinical trials
Jacob M, Chappell D, Conzen P, Wilkes M M, Becker B F, Rehm M

CRD summary
The authors concluded that hyperoncotic albumin for volume expansion was associated with reductions in morbidity, renal impairment and oedema in some clinical conditions, but further research was required. The evidence appeared to support the authors’ conclusions, but the lack of reporting of review methods made it difficult to comment on the reliability of these conclusions.

Authors' objectives
To compare the effects of hyperoncotic albumin (20 to 25 per cent) with other volume expansion regimens in clinically important outcomes.

Searching
MEDLINE, EMBASE and The Cochrane Library were searched without time period restrictions. Search terms were reported. No language restrictions were applied. In addition, reference lists were examined and the Index Medicus and speciality journals were handsearched.

Study selection
Parallel-group and cross-over randomised controlled trials (RCTs) that compared the effects of hyperoncotic albumin (20 to 25 per cent) for volume expansion with other volume expansion regimes on clinically relevant outcomes in acutely ill patients were eligible for inclusion. Studies evaluating other uses of albumin or albumin as an adjunct to paracentesis were excluded. The primary quantitative outcome was mortality.

The included studies were in patients with a variety of conditions including surgery (cardiac and non-cardiac), trauma, sepsis, liver disease, high-risk neonates, brain injury, intradialytic hypotension and nephritic syndrome. Most studies used hydroxyethyl starch as the control; other studies used crystalloid, no albumin or lower-dose albumin. Some studies used more than one control regimen.

Studies assessed a variety of outcomes including survival, morbidity, major organ function, haemodynamics, major organ oedema, coagulation, colloid oncotic pressure, diuretic responsiveness and inflammatory markers. The median duration of follow-up in studies used in the survival analysis was five days.

The authors stated neither how papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Validity was assessed using blinding and allocation concealment. The authors did not state how the validity assessment was performed.

Data extraction
For each study, major finding and the number of deaths (on an intention-to-treat basis) were extracted; the relative risk (RR) of death with the 95% confidence interval (CI) was calculated where possible. Authors were contacted if required for unpublished survival data and clarification of study design. The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
The studies were grouped by condition of patient and combined in narrative synthesis. Pooled RRs of survival were calculated using a fixed-effect model; data from cross-over RCTs were excluded from the meta-analysis. Heterogeneity was assessed, but methods were not reported. Publication bias, based on mortality data, was assessed using the test of Egger. The statistical power of the meta-analysis was calculated (methods were reported).
Results of the review
Twenty-five RCTs were included (n=1,485). These included 21 parallel-group and four cross-over RCTs. Blinding was used in four RCTs and allocation concealment was adequate in four RCTs.

Surgery (five RCTs): Hyperoncotic albumin was associated with better preservation of renal function compared with hydroxyethyl starch (one study) and reduced intestinal oedema compared with hydroxyethyl starch and crystalloid (one study).

Trauma (five RCTs, all conducted by the same researcher): Three studies reported no apparent benefits for hyperoncotic albumin compared with hydroxyethyl starch. Two studies reported that hydroxyethyl starch was associated with increased cardiac index and oxygenation.

Sepsis (seven RCTs, including six by the same researcher): Hydroxyethyl starch was associated with a higher cardiac index and oxygenation than hyperoncotic albumin (three studies).

Liver disease (three RCTs): Hyperoncotic albumin was associated with an improved treatment response and renal function and shorter hospital stay in patients with refractory ascites (one study).

High-risk neonates (three RCTs): Hyperoncotic albumin was associated with a reduction in illness frequency, improved respiratory function and less whole-body oedema in high-risk premature infants (two studies) and higher Apgar scores, lower risk of cerebral oedema and shorter hospital stay in newborns with asphyxia (one study).

Brain injury (two RCTs): Hyperoncotic albumin was associated with a reduction in disability in patients with acute ischaemic stroke (one study) and more favourable neurological outcomes in patients with closed head injury (one study).

Intradialytic hypotension (two cross-over RCTs): Hyperoncotic albumin was associated with a greater avoidance of blood volume reduction than saline (one study) or hypertonic saline (one study).

Nephrotic syndrome (three RCTs): Hyperoncotic albumin in combination with furosemide was associated with an accelerated diuresis and increased weight loss (one study) and aiding the diuretic and naturetic effects of furosemide (one study).

Survival: There was no statistically significant difference in survival between hyperoncotic albumin and control regimens, RR 0.95 (95% CI: 0.78, 1.17; 20 RCTs). No significant heterogeneity was found (p=0.86). Egger’s test showed no evidence of publication bias (p=0.87). The analysis had a 98 per cent power of detecting a 35 per cent reduction in RR of mortality and an 82 per cent power of detecting a 35 per cent increase in RR of mortality.

Other results were reported.

Cost information
Hyperoncotic albumin was associated with lower costs of care in patients with liver disease (one study).

Authors’ conclusions
Hyperoncotic albumin for volume expansion was associated with reductions in morbidity, renal impairment and oedema in some clinical conditions, but further research is required.

CRD commentary
The review question was clearly stated. Inclusion criteria were defined for intervention and study design. Criteria for outcomes were broad and could have resulted in selective reporting of positive results, but the primary quantitative outcome was clearly stated. Several relevant sources were searched and attempts were made to minimise language bias. It was not clear if attempts were made to minimise publication bias, but no evidence of publication bias was found. Only RCTs were included, but the validity assessment was limited to two criteria and that made it difficult to determine the overall quality of studies. Studies were appropriately grouped by clinical condition of patients and principally combined in a narrative synthesis. The authors discussed some of the limitations of the review, including the diversity...
among studies with respect to patients groups and control regimens. Evidence appeared to support the authors’ conclusions but the lack of reporting of review methods made it difficult to comment on the reliability of these conclusions.

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

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further research with longer follow-up was required to evaluate the effects of hyperoncotic albumin in surgery, trauma and sepsis and to compare its effects with standardised and well-specified control regimens. There was also a need to examine whether the reduction in oedema influenced clinical outcomes.

**Funding**

CSL Behring, Marburg, Germany.

**Bibliographic details**


**PubMedID**

18318896

**DOI**

10.1186/cc6812

**Original Paper URL**

http://ccforum.com/content/12/2/R34

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Albumins /therapeutic use; Edema /prevention & control; Humans; Hypovolemia /therapy; Plasma Substitutes /therapeutic use; Randomized Controlled Trials as Topic; Resuscitation /methods; Solutions

**AccessionNumber**

12008106381

**Date bibliographic record published**

03/02/2009

**Date abstract record published**

08/07/2009

**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.