Review: Albumin does not reduce death in critically ill patients with hypovolemia, burns, or hypoalbuminemia


Question
Does human albumin or plasma protein fraction reduce mortality in patients who are critically ill (hypovolemia, burns, or hypoalbuminemia)?

Data sources
Studies were identified using the Cochrane Controlled Trials Register, MEDLINE, EMBASE/Excerpta Medica, BIDS Index to Scientific and Technical Meetings, and the register of the Medical Editors' Trial Registry; hand searches of 29 journals and proceedings of several conferences; bibliographies of relevant papers; and contact with authors and manufacturers.

Study selection
Randomized controlled trials were selected if they enrolled critically ill patients who had hypovolemia from surgery or trauma, burns, or hypoalbuminemia; studied human albumin or plasma protein fraction; compared interventions with no albumin or plasma protein fraction or with a crystalloid solution; and measured mortality.

Data extraction
Data were extracted on patient illness and numbers, interventions and controls, duration of follow-up, mortality, and allocation concealment. Data were extracted in duplicate, and disagreements were resolved by discussion.

Main results
30 trials (1419 patients) met the inclusion criteria, and 24 had ≥1 death in any study group (total of 1204 patients). Albumin administration in these trials varied widely with respect to volume and concentration. Control groups included various crystalloids. No significant heterogeneity was found between or within the groups of trials or overall (P<0.2). Albumin was associated with higher mortality in the albumin groups for critically ill patients, patients with hypoalbuminemia, and patients with burns; a trend toward increased mortality was shown for patients with hypovolemia (Table).

Conclusion
Human albumin given to critically ill adults is associated with increased mortality.


Mortality associated with albumin vs control in critically ill patients (hypovolemia, burns, or hypoalbuminemia)*

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Number of studies</th>
<th>Weighted event rate</th>
<th>RRI (95% CI)</th>
<th>NNH (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>24</td>
<td>14.2%</td>
<td>9.5%</td>
<td>68 (26 to 123)</td>
</tr>
<tr>
<td>Burns</td>
<td>3</td>
<td>23.8%</td>
<td>9.8%</td>
<td>140% (11 to 419)</td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>8</td>
<td>15.0%</td>
<td>9.7%</td>
<td>69% (7 to 167)</td>
</tr>
<tr>
<td>Hypovolemia</td>
<td>13</td>
<td>12.4%</td>
<td>9.4%</td>
<td>46% (-3 to 122)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary; RRI, NNH, and CI calculated from data in article. Duration of follow-up was from 1 day to 2 weeks.

Commentary
The debate about whether to use colloids or crystalloids for fluid resuscitation in seriously ill patients is old but not tired. This meta-analysis by the Cochrane Injuries Group Albumin Reviewers summarizes 30 randomized trials comparing albumin or plasma protein fraction with either no colloid administration or with crystalloids. The article highlights the need to critically appraise both the validity of the review methods and the validity of the primary studies summarized in the review.

Trial reports were sought comprehensively, minimizing the chance of publication and language bias. Explicit selection and validity criteria were reported, although the latter focused primarily on allocation concealment and follow-up. Close inspection of the primary studies is necessary before drawing firm conclusions about increased mortality associated with albumin because of other important influences on mortality in critical illness that are not clearly reported in the primary studies or in this review. Understanding these issues and the handling of the persons who withdrew or crossed over from one treatment to the other would help to better interpret these small trials and may lead to a more conservative interpretation of the results of this meta-analysis. Another issue limiting the generalizability of these findings is that intensivists today rarely use the albumin dosing schedules studied in some of these trials.

This meta-analysis raises useful, fundamental, and challenging questions about daily practice and appropriately encourages us to conduct large, rigorous, randomized trials to generate more accurate and precise estimates of the benefits and harms of albumin administration. The colloid-crystalloid debate may then be informed by more and better evidence generated in the coming years.

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