Review: Albumin increases mortality in critically ill patients

Alderson P, Bunn F, Lefebvre C, et al. **Human albumin solution for resuscitation and volume expansion in critically ill patients.** Cochrane Database Syst Rev. 2002;(1):CD001208 (latest version 26 Nov 2001).

QUESTION

In critically ill patients with hypovolemia, burns, or hypoalbuminemia, does human albumin or plasma protein fraction reduce mortality?

DATA SOURCES

Studies were identified by searching CENTRAL, the Cochrane Controlled Trials Register, MEDLINE, EMBASE/Excerpta Medica, BIDS Index to Scientific and Technical Proceedings, the register of the Medical Editors' Trial Amnesty, and bibliographies of relevant studies. 29 journals and proceedings of several conferences were hand searched, and authors and manufacturers were contacted.

STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) that enrolled critically ill patients who had hypovolemia, burns, or hypoalbuminemia; studied the use of human albumin or plasma protein fraction; compared interventions with no albumin or plasma protein fraction or with a crystalloid solution; and assessed mortality.

DATA EXTRACTION

Data were extracted on patient characteristics, fluid interventions, duration of follow-up, mortality, and methodologic quality. Data were extracted in duplicate, and disagreements were resolved by discussion.

MAIN RESULTS

31 RCTs met the inclusion criteria and reported death as an outcome. Among 1519 patients, 177 deaths occurred. Albumin administration varied widely with respect to volume and concentration. Control therapy included various crystalloids. No heterogeneity was found between the trials in the various categories ($P > 0.2$). Albumin resuscitation was associated with higher mortality for all critically ill patients and those with burns; a trend toward increased mortality was shown for patients with hypovolemia and hypoalbuminemia (Table).

CONCLUSION

In critically ill patients, human albumin may increase mortality.

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

Conditions	Number of trials	Weighted event rates		RRI (95% CI)	NNH (CI)
		Albumin	Control		
All	25	14%	9.2%	52 (17 to 99)	20 (13 to 53)
Burns	3	23%	9.8%	140 (11 to 419)	8 (5 to 40)
Hypoalbuminemia	9	16%	12%	38 (–6 to 103)	Not significant
Hypovolemia	13	11%	7.0%	46 (–3 to 122)	Not significant

*Abbreviations defined in Glossary; RRI, NNH, and CI calculated from data in article using a fixed-effects model. Duration of follow-up was 1 day to 2.5 weeks.

COMMENTARY

The debate about the safety of albumin continues. The updated meta-analysis by Alderson and colleagues concludes that albumin increases mortality in patients with hypovolemia, burns, or hypoalbuminemia. In contrast, another recent meta-analysis by Wilkes and Navickis (1) did not find an increase in mortality. That review included other types of critically ill patients, different concentrations of albumin, and different subgroups. These differences partly explain the discrepancy in the conclusions drawn by the 2 meta-analyses.

A few points are worth highlighting. First, to date, all meta-analyses of albumin yield estimates that favor lower mortality using fluids without albumin (1, 2). The statistical significance of the results depends on the studies included in the meta-analysis and the statistics used. At this time, Alderson and colleagues recommend that the use of albumin be restricted to clinical trials. At best, albumin does not reduce mortality; at worst, it increases mortality. Given the availability of cheaper alternatives, other benefits must be shown before the use of albumin can be justified.

Second, although systematic reviews provide excellent syntheses of evidence, multiple reviews of the same topic can be repetitive and potentially confusing. The discordance between the 2 recent meta-analyses on albumin underscores this problem. In the future, registration of systematic reviews with the Cochrane Collaboration, or at least searching the Cochrane Library, may avoid duplication of work. Conversely, including other study populations (e.g., high-risk surgical patients) may increase the generalizability of this Cochrane review.

Third, critical care has evolved over the time spanned by the studies in the meta-analysis by Alderson and colleagues, and the management used in these studies may not reflect current practice. Ultimately, the role of albumin in fluid therapy, if any, requires ≥ 1 large multicenter, randomized, controlled trial that uses current management strategies, enrolls broad patient populations, and measures mortality and other clinical and economic outcomes.

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References

1. **Wilkes MM, Navickis RJ.** Patient survival after human albumin administration. A meta-analysis of randomized, controlled trials. Ann Intern Med. 2001;135:149-64.
2. **Cochrane Injuries Group Albumin Reviewers.** Human albumin administration in critically ill patients: systematic review of randomised controlled trials. BMJ. 1998;317:235-40.

