Review: Albumin administration is not associated with excess mortality in acutely ill patients

QUESTION

In acutely ill patients, is albumin administration associated with excess mortality?

DATA SOURCES

Published and unpublished trials in any language were identified by searching 4 electronic databases and 4 search engines for relevant Internet resources; hand searching 4 general medicine journals from January 1990 to November 2000; contacting albumin suppliers and authors of published randomized trials; and reviewing bibliographies of previous meta-analyses, review articles, and other investigations involving albumin.

STUDY SELECTION

Studies were selected if they were randomized controlled trials comparing intravenous albumin therapy with crystalloid therapy, no purified albumin, or a lower dose of purified albumin and had available mortality data. The clinical indication for albumin administration or therapeutic intent was not restricted. Studies were not excluded if concomitant treatments were given in a similar manner to both study groups. Studies were excluded if the control group tested synthetic colloids, blood products, or plasma protein fraction.

DATA EXTRACTION

Data were extracted on clinical setting, study population, details of albumin and control regimens, study end points, study quality, and outcomes. The main outcome measure was mortality.

MAIN RESULTS

55 trials ($n = 3504$) met the inclusion criteria. Duration of follow-up was available for 49 trials; median duration of follow-up was 11 days (range 0.04 to 1096 d). 13 trials were not included in the pooled analysis because no patients died in either group. Of the remaining 42 trials, no statistically significant difference in mortality existed between the intervention and control groups (Table). The relative risk for death was lower in trials that had blinding, ≥ 100 patients, mortality as an end point, and no crossovers.

CONCLUSION

In acutely ill patients, albumin administration is not associated with a greater risk for death than crystalloid therapy, no albumin, or lower doses of albumin.

Albumin vs control for mortality in acutely ill patients at median 11-day follow-up*

Trial categories	Weighted event rates (albumin vs control)	Relative risk (95% CI)	RRI (CI)
All	19% vs 17%	1.11 (0.95 to 1.28)	11% (−5 to 28)
Surgery or trauma	12% vs 11%	1.12 (0.85 to 1.46)	12% (−15 to 46)
Burns	27% vs 15%	1.76 (0.97 to 3.17)	76% (−3 to 217)
Hypoalbuminemia	15% vs 10%	1.59 (0.91 to 2.78)	59% (−9 to 178)
High-risk neonates	24% vs 20%	1.19 (0.78 to 1.81)	19% (−22 to 81)
			RRR (CI)
Ascites	27% vs 29%	0.93 (0.67 to 1.28)	7% (−28 to 33)
Other	26% vs 29%	0.91 (0.67 to 1.22)	9% (−22 to 33)

*Abbreviations defined in Glossary; RRI, RRR, and CI calculated from data in article. All meta-analyses were done using a fixed-effects model.

COMMENTARY

The review by Wilkes and Navickis is the 13th meta-analysis evaluating the effect of fluids on mortality in seriously ill patients. The strengths of this meta-analysis are the comprehensive search strategies used to identify primary studies, which minimized publication and English-language bias; the explicit selection criteria used; the use of such methodologic quality indicators as random assignment as an inclusion criterion; extraction of data in duplicate; and rating of treatment allocation, crossovers, and blinding for each included study. However, all relevant cointerventions, such as blood products, were not well reported in the original trials. 23 of 78 potentially eligible studies were excluded because no mortality data were available, which highlighted how many trials were designed to address short-term physiologic end points.

In this meta-analysis, the relative risk (RR) for mortality for all patients was 1.11 (Table). Subgroup analyses were preplanned and included surgery or trauma patients, those with burns or hypoalbuminemia, and neonates (RRs are in the Table).

The review is relevant to all clinicians caring for seriously ill patients. Results for the overall population and for all but one of the subgroups indicate a trend toward harm associated with albumin; the RRs are > 1.

The most sanguine result is seen for patients with ascites, although the confidence interval includes the possibilities of modest benefit and modest harm, as also shown for the other subgroups (Table). In deciding on the use of albumin in critically ill patients, clinicians should consider the lack of evidence of benefit and the trend toward harm in the point estimate and in the confidence interval, including the possibility of an appreciable mortality increase, shown in this and other meta-analyses. These factors and the cost of albumin compared with that of crystalloids (1) may have contributed to the decreased use of albumin (2). Meanwhile, the international research community has embarked on additional focused physiologic studies and large, rigorous, randomized trials in diverse populations to more precisely understand the effect of albumin on morbidity and mortality.

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References
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