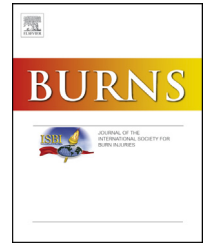


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Review

Albumin administration for fluid resuscitation in burn patients: A systematic review and meta-analysis



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ABSTRACT

Objective: The objective was to systematically review the literature summarizing the effect on mortality of albumin compared to non-albumin solutions during the fluid resuscitation phase of burn injured patients.

Data sources: We searched MEDLINE, EMBASE and CENTRAL and the content of two leading journals in burn care, *Burns* and *Journal of Burn Care and Research*.

Study selection: Two reviewers independently selected randomized controlled trials comparing albumin vs. non-albumin solutions for the acute resuscitation of patients with >20% body surface area involvement.

Data extraction: Reviewers abstracted data independently and assessed methodological quality of the included trials using predefined criteria.

Data synthesis: A random effects model was used to assess mortality. We identified 164 trials of which, 4 trials involving 140 patients met our inclusion criteria. Overall, the methodological quality of the included trials was fair. We did not find a significant benefit of albumin solutions as resuscitation fluid on mortality in burn patients (relative risk (RR) 1.6; 95% confidence interval (CI), 0.63–4.08). Total volume of fluid infusion during the phase of resuscitation was lower in patients receiving albumin containing solution -1.00ml/kg/\%TBSA (total body surface area) (95% CI, -1.42 to -0.58).

Conclusion: The pooled estimate demonstrated a neutral effect on mortality in burn patients resuscitated acutely with albumin solutions. Due to limited evidence and uncertainty, an adequately powered, high quality trial could be required to assess the impact of albumin solutions on mortality in burn patients.

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1. Introduction

The role of albumin solutions in the resuscitation of patients with acute burn remains controversial even though it could be supported by a physiologic rationale. Albumin plays a major role in maintaining oncotic pressure in the vascular space and following major burn, it is rapidly lost from the surface of the affected areas and in the interstitial space. Besides oncotic pressure, albumin has other multiple physiological effects, such as binding and transportation of various substances (for example, drugs, hormones) within the blood, antioxidant properties, nitric oxide modulation and buffer capabilities [1]. The importance of capillary leakage [2] and the impact of albumin leakage into the interstitial space resulting in increased edema are of significant concern [3]. Moreover, it is well accepted that almost all burn patients will eventually develop hypoalbuminemia and the leakage of albumin into the interstitium may not be a concern later on with restoration of capillary integrity. In fact, albumin solutions could be administered either for fluid resuscitation or for the correction of hypoalbuminemia, two clearly distinct clinical indications. Our work is concerned with the former use of albumin solutions.

Three previous meta-analyses [4–6] have compared albumin solutions in the management of burn patients. The first two [4,5] addressed its use in burn injured patients through subgroup analyses. The first meta-analysis [4] included 38 randomized controlled trials (RCTs) and explored the impact of albumin administration on mortality in critically ill patients. While the overall pooled analysis showed a trend toward benefit on mortality for non-albumin containing solutions (RR 1.05; 95% CI, 0.95–1.16), a subgroup analysis in burn patients demonstrated a significant increase in the risk of death with albumin solutions (RR 2.93; 95% CI, 1.28–6.72). Similarly, the second meta-analysis [5] including 42 RCTs demonstrated a non significant increased risk of death with albumin solutions overall (RR 1.11; 95% CI, 0.95–1.28) and in the subgroup of burn patients (RR 1.76; 95% CI, 0.97–3.17). While the summary estimates are qualitatively similar, they differ in magnitude of their effect on mortality in the subgroup of burn patients. Of importance, neither meta-analysis was designed to assess directly the impact of albumin vs. non-albumin solutions on mortality in critically ill burn patients. The third meta-analysis [6] concerned only burn patients but, it included randomized and non-randomized studies. A reduced mortality was observed (OR 0.34; 95% CI, 0.19–0.58) when two randomized studies were excluded [7,8]. Our objective was to systematically review the literature to summarize the effect of albumin, compared to non-albumin solutions, on mortality in the acute resuscitation of burn injured patients. As previously stated, the correction of hypoalbuminemia is not the topic of interest here. We hypothesize that the systematic use of albumin in the acute resuscitation of burn injured patients would not be beneficial.

2. Methods

2.1. Study identification

We sought to identify relevant studies published until July 2015 using a multifaceted strategy. We searched MEDLINE, EMBASE and CENTRAL using OVID database to identify articles fulfilling our inclusion criteria using the following search terms: burn(s) OR thermal injury AND albumin OR colloid(s) OR crystalloid(s) OR fluid resuscitation OR fluid therapy. We limited the search strategy to humans and RCTs. We also electronically searched the content of two leading journals in burn care, *Burns* and *Journal of Burn Care and Research* (previously known as *Journal of Burn Care and Rehabilitation*) to find potentially relevant abstract publications or articles. We also hand-searched the reference lists of included trials and other systematic reviews of albumin to identify additional trials. Unpublished trials were sought through trial registries (<http://www.controlled-trials.com> and <http://www.clinicaltrials.gov>). Authors of included studies could not be contacted for additional data. No language restriction was applied.

2.2. Study selection

Two reviewers (RE, MJD) independently screened abstract citations, retrieved articles and assessed trials for study inclusion. We selected parallel-group RCTs that compared albumin to non-albumin solutions in the resuscitation of burn patients admitted to a Burn Intensive Care Unit (BICU). We included studies concerned by burn (thermal, electrical or chemical) injured patients with a greater than 20% of total body surface area involvement and resuscitation occurring within 24h of injury. We excluded studies that focused on burn patients with concurrent trauma, infection or dermatologic conditions leading to BICU admission. We also excluded studies where albumin solutions were used for other indication besides resuscitation therapy (correction of hypoalbuminemia for example).

2.3. Data abstraction and assessment of methodological quality

Reviewers independently abstracted data and information pertaining to the trials methodology from each study. We abstracted information regarding the trial's methodological quality using the Cochrane's criteria [9] including method of randomization, allocation concealment, blinding, incomplete outcome data (loss of follow-up). We resolved disagreement among reviewers by consensus. We assessed agreement among the reviewers on trial inclusion and quality assessment using Cohen's kappa.

2.4. Statistical analysis

The primary outcome was all cause mortality as defined by the authors in their studies. Secondary outcomes of interest included the total volume of resuscitation fluid infusion, ICU and hospital length of stay (LOS) and organ dysfunction. We used a random-effect model to pool the results. We entered

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