Neuroanesthesia and Intensive Care

Best evidence in critical care medicine

Fluid resuscitation among the critically ill: more water under the bridge

Article appraised

Finfer S, Bellomo R, Boyce N, French J, Myburgh J, Norton R; SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med 2004; 350: 2247–56.[1]

Structured abstract

Background: Critically ill patients require supplementary *iv* fluids to support vital functions. Crystalloids and colloids (naturally-occurring and synthetic) are frequently used for fluid support. The choice of the type of fluid used on mortality among the critically ill remains controversial, as the effect of this choice remains unknown.

Design: Multicentre prospective blinded randomized controlled trial.

Patients: 6,997 critically ill patients requiring fluid supplementation because of hemodynamic abnormalities including any of: tachycardia (heart rate > 90), hypotension (systolic pressure < 100 or mean arterial pressure < 75), need for vasoactive medications, oliguria, or delayed capillary refill. The study size had 90% power to detect a 3% difference in mortality between groups.

Intervention: Patients received fluid boluses of either 500 mL of 4% albumin or 0.9% saline, contained in identical opaque glass bottles, until resolution of the hemodynamic abnormality.

Primary endpoint: Mortality, single and multiple organ failures, days of ventilation, days of renal support, days in intensive care, and days in hospital were compared between groups.

Results: No differences were detected between groups in any outcome.

Conclusion: Among the critically ill, outcomes are no different when comparing 4% albumin and normal saline for fluid resuscitation to treatment hemodynamic abnormalities.

Commentary

Bedside controversy about the selection of fluid for hemodynamic support and resuscitation of the critically ill and perioperative patient has smouldered intermittently for decades. Advocates of colloid resuscitation, or mixed colloid-crystalloid resuscitation, hypothesize that the higher oncotic pressure of naturally-occurring and synthetic colloids might facilitate intravascular distribution, which might facilitate organ perfusion pressure, which might then improve definitive outcomes. Advocates of crystalloid resuscitation point to the ready availability, ease of administration, and historical absence of outcome data supporting non-crystalloid resuscitation. Health care analysts have raised concerns about increased mortality associated with the use of colloid-based resuscitation.[2] Finally, the high cost of naturally-occurring and synthetic colloids must be considered in the context of outcome evidence.

The large randomized blinded and controlled clinical trial discussed in this commentary makes substantial progress in addressing the question as to fluid selection in resuscitation. In this study, 6,997 patients were enrolled, with absolutely no significant difference noted in any of the outcomes considered. Close examination of the study design and methods leads the reader to conclude that the studied patients were extremely comparable, and hence the study results can be generalized to the average patient requiring resuscitation in the average critical care unit. Noteworthy from the study methods was the use of delayed consent, in which some patients requiring resuscitation were enrolled at the time of hemodynamic need, followed by informed consent. This process markedly enhanced the ability to generalize results.

In the sub-group analyses of the study, three interesting and concerning findings emerged. First, among the trauma patients with head injury, mortality was alarmingly higher in the albumin group (25% *vs* 15%,

$P = 0.009$). Next, after excluding the head-injured, overall mortality was still higher among trauma patients treated with albumin (14% *vs* 10%, $P = 0.06$). Finally, patients with sepsis in the crystalloid group had a slightly higher mortality than in the colloid group (35% *vs* 31%, $P = 0.06$).

As a rule, sub-group analyses raise hypotheses rather than providing answers. Nonetheless, the increased mortality seen among trauma patients in this study, and particularly among the head-injured, is very consistent with pre-existing and well-conducted meta-analyses.[3] An investigator would find the ethical defense of any proposed further study of trauma patients to be very challenging. The finding of the non-significant decrease in mortality among septic patients treated with colloids may be a result of an underpowered sample size, or may simply be spurious. Further investigation of the effect of fluid choice on the survival of the septic patient may be warranted. Nonetheless, until such data are available (if ever), the bedside clinician should be aware that hypothetical advantages are balanced with hypothetical disadvantages, and the absence of survival effect seen here is paramount.

Despite its large size, consistent results, and exemplary methods, this study had some limitations. Patients excluded were those undergoing cardiac surgery (because of low expected mortality), those with major surface burns, and patients with concurrent severe hypoalbuminemia and liver failure. The application of study results to the synthetic colloids is uncertain.

In conclusion, this large randomized trial has shown that the use of either crystalloid or colloid for hemodynamic support of patients in the intensive care unit is associated with equivalent outcomes. Given the demonstrated equivalent clinical effect, the bedside clinician would be wise to base the decision of fluid selection for resuscitation with a grain of salt.

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References

1 *Finfer S, Bellomo R, Boyce N, French J, Myburgh J, Norton R; SAFE Study Investigators.* A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med 2004; 350: 2247–56.

2 *Anonymous.* Human albumin administration in critically ill patients: systematic review of randomised controlled trials. Cochrane Injuries Group Albumin Reviewers. BMJ 1998; 317: 235–40.

3 *Choi PT, Yip G, Quinonez LG, Cook DJ.* Crystalloids vs. colloids in fluid resuscitation: a systematic review. Crit Care Med 1999; 27: 200–10.