Is albumin administration beneficial in patients with sepsis?

In 1998, a Cochrane meta-analysis reported increased mortality in patients receiving human albumin solution compared to those receiving crystalloids. This reduced the use of human albumin solution in the UK by 40–45% (Vincent et al, 2014).

Subsequent research refuted this finding, and use of human albumin solution in the intensive care unit (as a volume expander or to correct hypoalbuminaemia) is now thought to be safe, although trials have often failed to show a statistically significant positive impact on outcome. Does evidence support the use of human albumin solution in sepsis and what should current practice be?

Evidence for use of albumin in sepsis

Albumin has many physiological properties, most significant its ability to maintain 70–80% of colloid oncotic pressure. It also acts as a free radical scavenger, removing nitric oxide. Albumin is a cotransporter of many substances and acts as a buffer, which may be beneficial in acidotic patients. Sepsis generally leads to a hypoalbuminaemic state, and albumin replacement may reduce morbidity and mortality (Vincent et al, 2014).

In 2004 the Saline *vs* Albumin Fluid Evaluation (SAFE) study showed that 4% human albumin solution was as safe as normal saline for resuscitation of patients with sepsis. This study suggested that human albumin solution should be considered as resuscitation fluid in patients with severe sepsis, particularly if they are not responding to crystalloid infusions (Vincent et al, 2014). The Surviving Sepsis Campaign echoed this, suggesting that crystalloids should be the initial fluid of choice, and human albumin solution used when patients require substantial amounts of crystalloids (Dellinger et al, 2013).

In the Albumin Italian Outcome Sepsis (ALBIOS) randomized controlled study in 100 intensive care units (Wiedermann and Joannidis, 2014), addition of 20% human albumin solution to crystalloids during the first 28 days of treatment to maintain a serum albumin level of 30 g/litre or more was safe but did not give a survival advantage over crystalloids alone in patients with severe sepsis. This was seen over a follow-up period of 28 and 90 days. Human albumin solution produced higher targeted mean arterial pressure within 6 hours of administration, as well as a lower heart rate and lower net fluid balance over 7 days. Time to suspension of inotropic or vasopressor agents was shorter in the human albumin solution group. Eight different meta-analyses published since this trial show that human albumin solution has a better safety profile than other colloid solutions.

Evidence against use of albumin in sepsis

The Early Albumin Resuscitation during Septic Shock (EARSS) study (Caironi et al, 2015) showed no significant difference in mortality rates in 798 patients with septic shock who received human albumin solution or normal saline. Irrespective of human albumin solution administration, the study found no difference in time for duration of mechanical ventilation or need for renal replacement therapy in patients with severe sepsis.

A meta-analysis showed a trend towards reduced 90-day mortality in patients with severe sepsis who were resuscitated with human albumin solution compared with crystalloid, but this was not statistically significant. Although hypoalbuminaemia is statistically associated with poor outcome in severe sepsis, correcting this does not appear to improve outcome (Vincent et al, 2014). Other considerations are the risk of transmission of microorganisms and allergic effects.

In theory administration of human albumin solution could exacerbate pulmonary extravascular water accumulation by transcapillary leak, although there are no clinical data to confirm this. Human albumin solution is safer than other colloids. Its higher cost may be outweighed by reduced long-term morbidity and mortality in patients with severe sepsis or septic shock (Vincent et al, 2014).

Conclusions

Use of human albumin solution probably does not do any harm, but may show benefit. There is still no conclusion as to which concentration to use, what dose to give and when administration should start. Most studies have looked at mortality as a primary outcome, although secondary morbidity-related outcomes and costs may be clinically relevant.

Crystalloids remain the first choice of fluid resuscitation in patients with sepsis and septic shock. When colloids are indicated, use of human albumin solution in patients with septic shock may be beneficial and should be considered early. In other patients, use of human albumin solution is probably safe and may have advantages over other colloids but more research is needed before routine use is recommended. **BJHM**

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