

PLASMA ALBUMIN (Commentary)

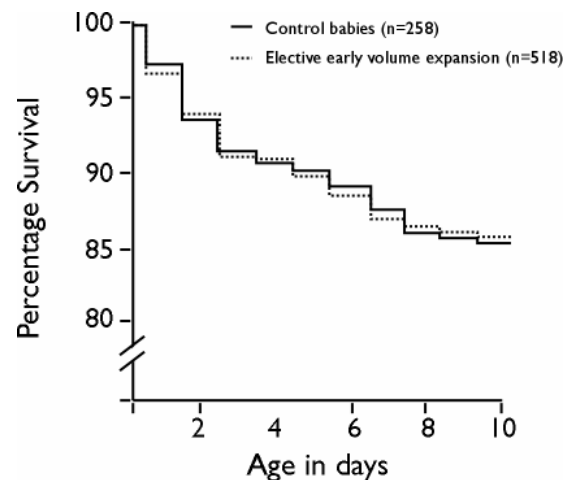
Controversy over the use of plasma albumin

Whether it is better to use a colloid rather than a crystalloid solution when trying to promote intravascular fluid retention in the shocked, hypovolaemic, patient has been debated for the best part of a century. Indeed the physiologist EH Starling was among the first to suggest that albumin might be useful in this situation. When the protein chemist EJ Cohn perfected plasma fractionation and made stable supplies of relatively pure dried albumin available to the sailors injured at Pearl Harbour in December 1941 news of its apparent beneficial effect soon spread (Silverman, 1999), and military surgeons were soon using it very widely, especially in situations where a ready supply of fresh blood was not immediately available. Unfortunately no controlled trials were ever undertaken before it came into very widespread use. Indications for its use also grew over time.

Albumin soon became one of those medicines that had already “stood the test of time.” Its use was therefore taken on trust by the licensing authorities when they started evaluating new drugs more critically in the 1970s. Albumin became one of the products “nodded through” thanks to this “grandfather clause”. That this “received wisdom” might have been misplaced only came to light when the Cochrane Injuries Group undertook a systematic review of the thirty small studies that had been undertaken into its use and published this in the BMJ in July 1998. The product had, by then, been in widespread use for 50 years.

The 1998 systematic review seemed to suggest that 0.9% sodium chloride might be just as good as plasma albumin at reducing the risk of death in shocked and hypotensive patients. Indeed there was even a suggestion that albumin use might be associated with a small **increase** in the risk of death. The review soon generated an increasingly heated and polarised debate between those who thought that the product was flawed and dangerous and those who thought that it was the review that was flawed. Few stopped to think that there might, of course, be a further possibility. It might be that there was nothing inherently dangerous about the product – it might just be the way in which it was being used that was potentially dangerous. Poor workmen frequently blame their tools.

Paediatricians, in particular, were initially reluctant to give up the use of a popular product, pointing out that few of the studies in the review related to children, and that those that did were small. In fact the only sizable trial that had ever been done in the neonate in an attempt to prevent, rather than correct, early supposed hypovolaemia (using Fresh Frozen Plasma or gelatin rather than plasma albumin) suggested that such use was not hazardous – it was just totally ineffective (NNNI Trial Group, 1996). An early, prophylactic, 20 mg/kg infusion had no effect on blood pressure, no positive or negative impact on survival (see fig), and no effect on the incidence of intraventricular haemorrhage or later neuro-developmental disability either. Indeed recent observational data have suggested that over-enthusiastic ‘volume expansion’ with any fluid during early neonatal ‘resuscitation’ may actually be harmful.



In fact what the Cochrane collaborators thought they had shown was not that the use of Albumin was necessarily dangerous, but that there was “a dearth of properly controlled evaluations on which to base current intensive care.” Those who criticised the review, saying that it was based on a haphazard collection of small disparate trials, missed the point. If that was true the logical response was not to criticise the review, but to set to and do the trial that should have been done 50 years ago.

That is, in fact what the Australia and New Zealand Intensive Care Society did, backed by the Australian and New Zealand Medical Research Councils. In a quite amazing collaborative exercise they managed to recruit 6,997 critically adults into a formal randomised controlled trial (SAFE, or Saline versus Albumin Fluid Evaluation) in just 18 months. The outcome was announced at the meeting of the Society of Critical Care Medicine in Orlando, Florida in February 2004. Albumin was no better than saline – mortality was 20.9% and 21.1% respectively. Indeed in patients with trauma, including head trauma, the outcome favored saline over albumin (relative risk 1.36).

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