

A brief history of colloids for fluid therapy

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Fluid therapy with water and salts was probably first given in the 1830s for treatment of patients suffering from Blue Cholera.¹ Although case reports from the time describe a significant improvement in clinical symptoms outcomes were poor, attributed in part to the lack of a sustained effect. Over the next 70 years the use of IV crystalloid solutions became more widespread however the frequently observed short term effects lead clinicians to try and develop new solutions that would “remain in the circulation longer”.² Gelatin, was the first fully artificial plasma substitute to be used extensively for shock treatment, in a large part due to the large number of casualties with hypovolaemic shock treated close to the battlefield during World War 1.³ It is interesting to note that in his first case series Hogan commented on the relative lack of benefit of colloid fluid in non-haemorrhagic causes of shock.

By the end of world war II use of colloid for resuscitation was well established and dextrans as well as Gelatins used as a substitute to plasma for resuscitation. Hydroxyethyl starch (HES) solutions, derived from waxy-maize derivatives were introduced in the 1970s as a further attempt to more closely mimic the volume expanding effect and duration of action seen with albumin solutions. From the 1980s onwards there was rapid increase in the amount of synthetic colloids used, in particular HES, driven in part by the popular belief that colloids produced better resuscitation than crystalloids⁴ and were safer and more cost-effective than donated blood derived products, especially albumin solutions.

By 1985 it was being suggested that the end of routine use of crystalloid solutions as volume expanders was approaching,⁵ however over the following 13 years a number of systematic reviews and meta-analysis suggested that there may be adverse events and worse outcomes associated with the use of synthetic and natural colloids^{6,7}. A landmark paper by the Cochrane collaboration in 1998 that implicated the use of human albumin in excess mortality sparked immediate publicity and the call for a ban on albumin use.⁸

In response to this controversy, the recently formed Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS-CTG) proposed the SAFE study – a double blind evaluation of 4% albumin vs saline for volume resuscitation in intensive care. Published in 2004⁹ the SAFE study represented the largest RCT performed in intensive care patients (n=6999) and demonstrated that the use of albumin was safe (with the exception of patients with TBI), however no clinical benefits could be shown over saline.

Although the use of albumin decreased significantly following the Cochrane publication in 1998 the use of artificial colloids continued to increase, and this was demonstrated by the same group of investigators with an international observational study of iv fluid use in intensive care.¹⁰ The increased use of synthetic colloids in general and of HES solutions in particular prompted the design of a trial comparing the effects of HES and Saline on clinical outcomes in the intensive care unit. The CHEST study,¹¹ published in 2012 demonstrated that the use of HES solutions was not associated with any improvement in outcomes and was actually associated with an increase in the use of renal replacement therapy and other adverse effects such as pruritus.

CHEST was published shortly after two other similar but smaller studies in patients with sepsis demonstrated higher mortality in patients who received HES solutions instead of crystalloid solutions.^{12,13} Following the publication of these landmark papers there was an initial reaction from regulatory authorities around the world that ranged from a complete ban on HES use to less restrictive warnings and guidance. The CRISTAL study¹⁴ suggested a possible benefit to colloids over crystalloids; however it has significant methodological limitations.

Recent consensus guidelines have attempted to distil the evidence from these large studies,^{15,16} however the mobilisation of a significant industry promotional machine and the large amount of money involved in the IV fluid business worldwide suggest that the colloid story still has a few chapters left.

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