The Colloid Controversy

Are Colloids Bad and What Are the Options?

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KEYWORDS

• Albumin • Blood products • Colloids • Colloid therapy • Endothelial glycocalyx • Human serum albumin • Hydroxyethyl starch • Plasma

KEY POINTS

- Biologic and synthetic colloids have been used to increase oncotic pressure and treat shock.
- The optimal colloid product, timing, and regimen are unknown and may depend on the patient and clinical scenario.
- Human serum albumin has been associated with severe adverse effects in dogs.
- Hydroxyethyl starches have been implicated in causing higher mortality, acute kidney injury, and coagulation abnormalities in people. Studies evaluating risks of these products in veterinary patients are needed.

Maintenance of intravascular volume is vital to maintaining cardiac output and, subsequently, oxygen delivery. Classically, the Starling equation has described intravascular volume maintenance as a balance between interstitial and intravascular hydrostatic and oncotic pressures, as well as the reflectance and permeability of the capillary endothelium. Recent research suggests that interstitial oncotic pressure effects on fluid balance are negligible and the structure and function of the endothelial glycocalyx (EG) may be the key determinant of vascular barrier competence.[1–3] Damage to the EG caused by ischemia and reperfusion, sepsis, volume overload, diabetes, surgery, and trauma may also help explain some of the challenges associated with maintaining intravascular volume in critical patients.[1]

The role of the EG in vascular barrier competence has caused reexamination of fluid resuscitation practices.[1] Hypervolemia has been shown to damage the EG, increasing the albumin escape rate.[3–5] Persistence of a positive daily fluid balance has been

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associated with higher mortality in septic patients.[6] Studies investigating conservative fluid strategies have revealed an association with lower mortality in certain disease populations, such as patients with acute respiratory distress syndrome and trauma.[7,8]

Colloids, large hydrophilic molecules (>10,000 Da) that do not readily cross the vascular endothelium, are often considered as part of the fluid plan in critical patients. Colloid fluids are thought to have a volume-sparing effect by increasing intravascular colloid osmotic pressure (COP). With an intact vascular barrier, colloids have a more sustained, high-volume effect compared with crystalloids.[1] This article reviews currently available colloids and their potential risks and benefits in veterinary medicine.

BLOOD PRODUCTS

Albumin

Albumin serves as the reference colloid for synthetic products. It is the most abundant protein in the body, accounting for 60% of the plasma proteins and 80% of the COP of plasma.[9] Albumin has a low isoelectric point, and hence has a net negative charge at physiologic pH. This negative charge accounts for an additional 30% of the pressure provided by albumin, which arises from the Gibbs-Donnan effect.[9] Albumin has additional important functions, which include binding and transporting drugs, free fatty acids, and bilirubin; acid-base effects; antioxidant and free radical scavenging; positive and negative effects on vascular integrity; and antiapoptotic, anticoagulant, and antithrombotic effects.[10]

Hypoalbuminemia is common in critical illness and has been associated with poor clinical outcomes in humans and animals with various disease states.[11–14] Complications associated with hypoalbuminemia include pulmonary edema, delayed wound healing, hypercoagulability, and multiple organ dysfunction.[15] The use of albumin supplementation is appealing given its ancillary effects, and its potential to increase intravascular volume and treat hypoalbuminemia simultaneously. In humans, albumin has been used clinically in several disease states, but evidence to support a benefit of albumin administration is lacking except in liver disease and failure.[10,16]

Studies in critically ill humans comparing human serum albumin (HSA) and crystalloids have not consistently identified a significant volume-sparing effect. In a double-blind, randomized controlled trial of 6045 human patients in the Saline versus Albumin Fluid Evaluation (SAFE) study, outcomes of resuscitation with albumin and saline were similar regardless of baseline serum albumin concentrations.[17] A minor increase in central venous pressure was observed in the albumin group with an albumin/saline ratio of 1:1.4.[17] Although a significant volume-sparing effect was not observed in this population, a decrease in adjusted risk of death at 28 days was shown among patients diagnosed with sepsis who received albumin compared with those treated with saline. In another study, the Albumin Italian Outcome Sepsis (ALBIOS) study, use of albumin solely to maintain a target serum concentration of 3 g/dL or more until discharge in humans with severe sepsis did not improve survival at 28 and 90 days.[18] In contrast, a recent meta-analysis of randomized controlled clinical trials comparing effects of albumin and crystalloid on mortality in adults with sepsis and septic shock revealed a trend toward decreased 90-day mortality in patients with sepsis receiving albumin. The 90-day mortality of patients with septic shock receiving albumin decreased significantly.[19]

Species-specific Albumin

Lyophilized canine albumin has recently been rereleased through Animal Blood Resources International (ABRI). There is a paucity of data regarding potential benefits and outcomes of dogs receiving canine albumin. In a study of 14 dogs with septic