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Consideration of Colloids and Crystalloids in Fluid Management

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Introduction

Fluid resuscitation for critically-ill patients has been a staple of treatment since the induction of the first crystalloid in 1830 for treatment of cholera.[1] Colloid solutions, the first being gelatins, were later created in the 1930s for shock treatment. Albumin was fractionated from whole blood and extensively used during World War II.[2] It was not until after World War II the pathophysiology behind these two solutions was well studied and debated for effectiveness.

There has been a heated debate on how to appropriately manage fluid dynamics in critically-ill patients, in particular using crystalloids vs colloid fluids. Using crystalloids to replenish volume within the vascular system through hydrostatic pressure leads to fluid accumulation in the extracellular space. Administration of fluids in a healthy individual has shown that crystalloids expand the intravascular space by 20% of infused volume; however, under physiological stress efficacy can increase up to 60%.[3]

The average adult is roughly comprised of 50-60% water that embodies the intracellular and extracellular space.[1] Extracellular space is further broken into the interstitial, intravascular, and transcellular spaces. Because crystalloids are small molecules, most providers are concerned about the interstitial edema associated with revascularization. Critical illness causes inflammatory states that leads to endothelial dysfunction associated with interstitial edema. Since one significant downside of crystalloid administration is fluids crossing the permeable membrane, colloids can complete resuscitation without changing oncotic pressure and avoiding edema while increasing intravascular expansion. Due to the increased molecular weight and larger molecules associated with colloids, it is relatively impermeable to an intact capillary membrane.[2]

Now that there are over sixty years of research on the topic, is there a consensus on what is more successful for fluid resuscitation? The goal of this literature review is to consider when colloid use is appropriate, and if so, is there any significant benefit that cannot be accomplished with crystalloid therapy alone.

Hemodynamics

One area of discussion is whether crystalloids achieves a better hemodynamic response when compared to colloids. A study by Nicholas et al. compared 220 patients with a pulmonary artery catheterization based on the CRISTAL trail evaluating demographics, heart rate, stroke volume, blood pressure, and central venous pressure (CVP) measured by pulmonary artery catheter (PAC). Out of the 220 patients studied 103 received crystalloids while 117 were administered colloids. All patients were administered no more than 30ml/kg for resuscitation. Overall, administration of colloids was associated with lower heart rates and volume administration when resuscitating patients 3500 vs. 2500 ml when comparing hydroxy starches to normal saline. To achieve similar treatment goals, crystalloids should be administered using 20-50% more volume than colloids.

The SAFE study evaluated the use of 4% albumin when compared to 9% saline and was found to show statistical significance with lower heart rate on the first day of treatment.[4] Alternative studies such as the Albumin Italian Outcome Sepsis (ALBIOS) and Crystalloid Versus Hydroxyethyl Starches Trial (CHEST) found decreased heart rate, lower use of vasopressor therapy, and higher CVP respectively when comparing starches, albumin, and saline.

Some argue that by retaining a negative fluid balance, respiratory distress syndrome can be avoided in the septic patient. Negative fluid balance is accomplished when colloids remain in the intravascular space from oncotic pressure. In the sepsis subgroup, the first six hours it was

noted that approximately 69% of patients during the study reach mean arterial pressure and urine output goals for resuscitation. This is in contrast to the colloid group, where 66% of patients reached the same outcomes.[4] The conclusion of the study was there is zero difference between the management of patients with sepsis for achieving hemodynamic goals set by the 6-hour campaign of surviving sepsis. There was no difference in any other hemodynamic endpoint other than the HR, and rate pressure product.[4]

Complications

Colloids, particularly starches, have an extensive complication profile including kidney injury, which requires renal replacement treatment. The CHEST trial compared Hydroxyethyl starch (HES) 6% vs. 0.9% saline and found renal replacement therapy to be significantly increased.[5] The Scandinavian Starch Study and Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis Study found that use of starches have an increased association of acute kidney injury (AKI) when compared to crystalloids.[6-8] Hydroxyethyl starches can accumulate in the skin, liver, and kidney causing Hydrops Lysosomalis Generalisatus which is associated with pruritus, coagulopathy, AKI, and potential hyperbilirubinemia.[5]

In 2012, a prospective open-label pilot study was accomplished in Australia that restricted use of fluids to specialist approval only under standard fluid therapy with a 6-month phase-out period. Since implementation, there has been a significant decrease in the incidence of AKI and renal replacement treatment,[9] though it has yet to be proven on a large scale. New generation 6% HES with a lower molecular weight were produced for an improved safety profile, but there is increased mortality based on systematic reviews.

High molecular weight HES and medium molecular weight can cause adverse effects on coagulation. Colloids can be challenging to break down, which impairs coagulation through an

accumulation of large molecules reducing factor VIII and Von Willebrand Factor complex.[10] Ultimately, this accumulation of molecules can lead to a hemorrhagic complication. Other side effects are increased plasma viscosity and erythrocyte aggregation. Starches are also linked with a potential need for blood transfusion.[9] However, coagulation complications are not seen in the low molecular weight starches.

Another side effect that has commonly been associated with colloids is potential for a severe allergic reaction upon infusion of dextrans, starches, gelatins, or albumin. Little to no difference between rates of allergic reactions was found between crystalloids and colloids when compared.[9] Itching and rashes appeared to be connected to the use of colloids. A retrospective study from the SAFE trial linked albumin to increasing intercranial pressure with fluid resuscitation.[11]

Use of normal saline (0.9%) has concerns due to hyperchloremic metabolic acidosis induced from large volumes of administration requiring treatment with bicarb. Volunteer studies have shown the development of AKI, and reduction in glomerular filtration from vasoconstriction due to eicosanoid release in renal tissue.[5,12] Acidosis can be viewed as poor tissue perfusion, cardiac function, and may prompt application of additional fluid boluses exacerbating the acidosis. Saline has also been linked to the use of renal replacement therapy, poor outcomes with use in ICU patients, sepsis, and complications with patients who undergo surgery.[13-14]

Outcomes

In 1998 a systematic review was completed by the Cochrane Injury Group Albumin Reviewers to compare the effects of albumin on a patient with hypovolemia: burns, and hypo-albuminemia on mortality. It was found that albumin had a 6% increase in mortality, which

created a drastic change in patient management in the UK.[2] Since Australia and New Zealand were widely using albumin at this time, a larger blind study named the SAFE study demonstrated there was no associated increase in mortality with the use of albumin when compared to 0.9% saline at 28 days.[2] The findings refuted the initial findings from the Cochrane study. Two years later, an increase in mortality was observed in patients who had experienced a severe traumatic brain injury with colloids compared to saline (34.4% vs 17.4%).[11] Currently, the increase in mortality is being attributed to the development of intracranial hypertension during the first seven days due to extravasation of albumin across the blood-brain barrier.[2] In the same study, there was found to be a significant reduction in adjusted risk of death at 28 days for those who received albumin therapy. The ALBIOS trial also suggested a reduction in mortality with patients that received albumin with septic shock.

Mortality rate over 90 days was observed to be lower in the colloid population (30.7%) when compared to the crystalloid (34.2%) in the CRISTAL trial.[4] It has been explained to be exploratory as it may have some explanation toward the long-term effects of colloid resuscitation. The colloid group was observed to experience more days alive without mechanical ventilation required. It was also observed that survival without vasopressor therapy was increased in the colloid population at seven days and 28 days respectively.

Additional studies have had similar findings. A meta-analysis concluded the use of albumin-based therapy for individuals with severe sepsis or septic shock improved mortality rate over 90 days.[15] There was also a slight improvement in outcome when compared to normal saline although it was not statistically significant. More extensive studies comparing starches, dextrans, gelatins, or albumin looked at 90-day mortality rates in trauma, burns, and sepsis found little to no difference without limiting research to severe sepsis or septic shock.[9] Trauma patients

have been associated with an increased in mortality with the used of colloid therapy when compared to crystalloid resuscitation.[1]

In surgery, there have been multiple studies on perioperative fluid management. A large multi-center study found no difference between mortality, although colloids under individualized goal-directed therapy (GDT) received less major complications.[3] Colloid GDT did not have the same results within the "fit" (anaerobic threshold >11 ml O2 kg-1min-1) population when compared to the "unfit" (anaerobic threshold 8.9-10.9 ml O2 kg-1min-1) who underwent significant colorectal surgery.[2] Patients who were fit were found to have an extended hospital stay when compared to the controls, while unfit patients had no difference.

Conclusion

Gelatins have not received the same extensive research attention that has been given to albumin and starches.[4] Studies that focus strictly on hemodynamics account for 10% of the patients who were enrolled in the CRYSTAL trial, one of the largest studies to date for comparison on fluid therapy. There has also been an advancement in monitoring hemodynamics without the use of a PAC thus limiting comparison between trials. Large extensive studies on each type of patient have not been completed, so sample sizes for severe septic patients are small. Future research should be focused on patient and condition directed therapies since not every fluid will fit every situation. This will help determine what type of fluid is most useful for which type of patient.

It is hard to justify the cost of using colloid resuscitation without strong evidence of its efficacy when compared to crystalloid fluids. Although, there have been reoccurring themes throughout the literature. There may be a benefit in 90-day mortality with the use of colloid therapy especially albumin in the patient with septic shock or severe sepsis. Providers that are

administering the fluid should be well trained on colloid therapy to avoid side effects such as AKI. In most cases, there is no increased benefit in the use of starches or gelatins when compared to crystalloids therapy and come with an increased profile for adverse complications. Patients should continue to receive crystalloid therapy during salvage therapy unless blood products take priority. Albumin ought to be considered for fluid resuscitation in septic patients as long as there is not an accompanying traumatic brain injury or trauma. Fluid therapy is quite complex and there is no clear consensus. By far, the best recommendation is picking a fluid with the patient's comorbid conditions in mind and proceeding with goal-directed therapy.

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