VIEW POINT

Colloids should be Removed from the Intensive Care Unit Shelf

Amarja A Havaldar

Abstract

Fluid therapy is one of the interventions in a day-to-day practice. It is predominantly used for resuscitating a patient with acute circulatory failure. Fluid therapy aims to improve macrocirculation and thereby oxygen delivery at the tissue level. Various fluids are available for resuscitating patients, classified into crystalloids or colloids. Still, we lack the ideal fluid for resuscitation. Colloids once promised to be the ideal fluid for resuscitation, their effectiveness has been questioned by the recent evidence and also indicated the possible harm associated with its use. Is there any truth in the matter?

Keywords: Colloids, Crystalloids, Endothelium, Glycocalyx, Renal replacement therapy, Starling's equation.

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There is no doubt about the choice of fluid for resuscitation, it is crystalloids, irrespective of the etiology of critical illness, whether it is for septic shock, diabetic ketoacidosis, hypovolemic shock, or trauma.[1]

This makes us reason out "why colloids are out of fashion"?

Theoretical Perspective

Total body water is 60% of the body weight. It is divided into two compartments. Intracellular (40%) and extracellular (20%). The extracellular fluid is further divided into interstitial (15%) and plasma volume (5%). When 1 L bolus of colloid and crystalloid is given, colloid will remain in the intravascular space as against only one third of the crystalloid will remain in the intravascular space.[2]

As colloids remain in intravascular space, the amount of fluid required for resuscitation will be less and can prevent harmful effects due to interstitial edema or cumulative fluid balance. This is based on Starling's equation where filtration is determined by the difference between the hydrostatic and oncotic pressure of capillaries and interstitium. But, this theory will be applicable if the endothelium is intact. If there is damage to the endothelium or endothelial glycocalyx, which is the case in critically ill patients of acute respiratory distress syndrome (ARDS), trauma, shock, and ischemia-reperfusion injury, the colloid is going to enter into the interstitial space.[3–6]

In recent years, there is a revision of Starling's equation. It is not the oncotic pressure of the interstitium but the oncotic pressure of the glycocalyx and the oncotic pressure difference is not the transendothelial but the intraendothelial pressure difference.[4,7] When the glycocalyx is damaged, crystalloids and colloids will behave similarly and there will be a risk of interstitial edema (Fig. 1).[7]

What evidence says:

- The SAFE trial was done in 2004, which compared saline vs 4% albumin and its effect on 28 days mortality. This study had predefined subgroups, and it showed possible harm in patients with traumatic brain injury as suggested by the relative risk of 1.36 (0.99–1.86). In trauma patients with a head injury, after randomization more patients died in the albumin group, and mortality in this group was 24.5% vs 15.1% in the saline group (relative risk 1.62, 95% confidence interval 1.12–2.64, $p = 0.009$). This study did not show any mortality benefit. The daily requirement of crystalloids vs colloids were in the ratio of 1:1.3, 1:1.6, 1:1.3, and 1:1.2 from day 1, day 2, day 3, and day 4, respectively.[8]
- The VISEP study of two by two factorial design, it compared intensive insulin therapy vs conventional insulin therapy and fluid resuscitation with hydroxyethyl starch (HES) 200/0.5 vs Ringer's lactate (RL). There was no difference in 28 or 90 days mortality in the HES vs RL group and the ratio of fluid resuscitation of colloids vs crystalloids was 1:1.32 throughout the study period. In the HES group, more patients developed coagulopathy ($p \leq 0.001$) and renal failure ($p = 0.02$) as suggested by sequential organ failure assessment (SOFA) score parameters. The dose of pentastarch (200/0.5) HES used in the study was 10% higher than the recommended dose of 20 mL/kg/day. During the study, patients who received a higher cumulative dose of HES had a higher requirement of renal replacement, and 90 days mortality was also higher in this group. Thereby, this study showed harmful effects of HES (200/0.5).[9]
- CHEST study comparing 0.9% saline vs HES (130/0.4) solution showed no difference in 90 days mortality. This study again showed patients requiring renal replacement therapy were more in the HES group. During 7 days, HES group patients had an increase in creatinine level. Although patients in the HES

Department of Critical Care Medicine, St. John's Medical College Hospital, Bengaluru, Karnataka, India

Corresponding Author: Amarja A Havaldar, Department of Critical Care Medicine, St. John's Medical College Hospital, Bengaluru, Karnataka, India, Phone: +91 9036082112, e-mail: amarjahavaldar@rediffmail.com

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- $Jv = Lp [Pc – Pi] – \sigma[\pi c – \pi i]$
- $Jv = Lp [Pc – Pi] – \sigma[\pi c – \pi sg]$

- Jv – Filtration coefficient
- Lp – Hydraulic conductivity
- Pc – Capillary hydrostatic pressure
- Pi – Interstitial hydrostatic pressure
- σ – Reflection coefficient
- πc – Capillary oncotic pressure
- πi – Interstitial oncotic pressure
- πsg – Subendothelial glycocalyx oncotic pressure

Fig. 1: Starling's equation, previous and revised

group received lesser fluid and had lower cumulative fluid balance, transfusion of blood products was more in this group (78 ± 250 vs 69 ± 190 mL, $p \leq 0.001$) and use of HES did not result in a significant volume sparing effect. As per the RIFLE criteria, the incidence of risk and injury was more in the saline group, but these patients continued to have rising creatinine suggesting reduced creatinine clearance and worsening kidney injury. Hepatic failure was also higher in the HES group (1.9% vs 1.2%, relative risk 1.56, confidence interval 1.03–2.36, $p = 0.03$).[10]

- 6S trial of HES (130/0.4) was a positive study, which showed mortality benefit with the use of Ringer's acetate. Patients in HES group had higher mortality (51% vs 43%, $p = 0.03$) and more patients required renal replacement therapy (22% vs 16%, $p = 0.04$).[11]
- ALBIOS study of severe sepsis patients compared 20% albumin with crystalloids vs crystalloid alone and did not show any difference in the 28 and 90 days mortality. In this study, albumin was used as a replacement fluid with achieving a serum albumin level of 30 gm/L for 28 days or till the intensive care unit (ICU) discharge. The design of this study in using albumin as a replacement to achieve the target level makes us think that the presence of hypoalbuminemia in critically ill patients is a cause or the effect?[12]
- In resource-limited settings and when the cost of care is paid by the patients, using albumin for replacement or resuscitation does not make an ideal choice of fluid, and also it is not cost-effective.
- Similar results were seen in the pediatric population as suggested by the FEAST trial. This study compared fluid resuscitation with three different strategies (no fluid bolus vs albumin vs crystalloid) and showed higher mortality in albumin and crystalloid groups as compared to no fluid bolus group.[13]
- Based on the above-mentioned evidence, it is clear that HES is harmful and can cause serious adverse events such as renal failure requiring renal replacement therapy.[9–13]

Having said that, crystalloids are also not without adverse effects. The chloride load in the 0.9% saline is much higher and it can cause kidney injury and patients may require renal replacement therapy.[14] So there is a trend in using balanced crystalloids for resuscitation.[15–19] In recent years, various randomised controlled trials (RCT's) compared balanced salt solutions with crystalloids and none of them have shown an improvement in mortality, except for the single-center SMART study.[19]

In last 10 years, there is an improvement in patient care and as a result baseline mortality itself is reduced. Hence, the number of positive trials are very few. In ICU care, fluid therapy is one of the interventions done in the ICU. By doing more RCTs on fluid therapy we are unlikely to find the ideal fluid for resuscitation.

Future research focusing on the structure of glycocalyx and deciding the fluid which can preserve the integrity of the endothelium will be useful. So at this stage, if we can check the composition of crystalloid and select the fluid based on admission diagnosis such as traumatic brain injury (TBI) or patients of acute kidney injury (AKI), monitor the patient during treatment, and use the fluids as a drug, definitely the type of fluid will not be blamed for causing harm.

Orcid

Amarja A Havaldar https://orcid.org/0000-0002-8763-3585

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