

The Evolving Art of Fluid Resuscitation

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The maintenance of fluid and electrolyte homeostasis is an important treatment objective during the management of critically ill patients; the association of the administration of resuscitation fluids with attaining hemodynamic stability for patients has led to recommendations for its timely administration for injured, bleeding, burned, hypovolemic and septic patients [1, 2]. During the last centuries resuscitation principles were based on a classical compartmental model eloquently described by Ernst Starling which placed great importance on preserving the plasma oncotic and hydrostatic pressures as a means of restoring intravascular volume. Some of the assumptions of this model are being questioned by recent research findings because studies have found it difficult to demonstrate significant differences of plasma oncotic pressure (COP) among septic and non-septic patients [3, 4]. Additionally, measures of COP has not been robustly associated with clinical outcomes of critically ill patients and randomized trials of the infusion of HES or plasma substitutes to restore intravascular volume have not consistently demonstrated clinical benefit for disease states including hypoalbuminemia [5, 6] acute respiratory distress syndrome [7] and pulmonary edema [8]. Research exploring novel concepts of fluid physiology culminated in the identification of an endothelial glycocalyx layer (EGL) on the luminal aspect of the vascular endothelium [9]. This layer is now recognized as a major determinant of membrane permeability and it can be disrupted by mediators that are known to be present during sepsis, trauma, diabetes and surgery [10-12]. The combined Starling-Endothelial glycocalyx model appears to better account for the clinical responses to fluid resuscitation.

Many individual fluids are available for medical treatment, however, these fluids can be divided in to two broad categories namely: colloids and crystalloids. Numerous studies have compared both fluid types with little evidence in support of superiority of one over the other with regard to mortality or safety [13, 14]. Proponents of colloid fluids reckon that they are more effective for intravascular fluid repletion, have properties that are more similar to host fluids, and have beneficial effects on glycocalyx function, while crystalloid proponents argue that they are less expensive, and more widely available and have less toxicity.

Albumin has long been considered the prototypical colloid solution, interestingly clinical studies have yielded mixed results. The Saline versus Albumin Fluid Evaluation (SAFE) study was

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a randomized control trial that compared 4% albumin with saline with mortality as the primary outcome that failed to detect significant clinical benefits [15]. The Fluid Expansion as Supportive Therapy (FEAST study) compared fluid boluses of 5% albumin to 0.9% Saline and found no difference of mortality among febrile pediatric patients in Sub-Saharan Africa [16]. Because albumin is expensive to produce and more difficult to distribute especially in resource limited settings, semi-synthetic colloids are being investigated as a substitute, the most common of which is Hydroxyethyl Starch (HES). High concentration HES solutions (10%) have a propensity to accumulate in tissues such as the kidney and the skin and can cause acute renal failure and pruritus respectively. Lower concentrations (6%) are less toxic and have been more commonly used in clinical practice. Clinical studies have compared HES to a crystalloid solution with some showing increased mortality and greater incidence of acute renal failure in the HES groups [17, 18]. In a recent prospective analysis of the Crystalloid versus Hydroxyethyl Starch Trial (CHEST) [18], the authors failed to detect mortality benefit for HES compared to crystalloids at 6 and 24 months and the probability of HES being cost effective was reported to be very low [19]. Based on this evidence, the use of currently available semisynthetic colloids for critically ill patients is not thought to be associated with survival benefits, and there are persistent concerns about toxicities.

Isotonic saline (0.9% saline) is the most commonly used crystalloid worldwide with over 200 million liters administered annually to

critically ill patients in the United States alone [20]. Crystalloid administration is also associated with toxicities. Isotonic saline administration is known to cause a hyperchloremic metabolic acidosis and has been associated with renal failure when administered in large volumes, hence balanced solutions such as Ringer's Lactate are an alternative for those with preserved renal function because the hyperchloremic metabolic acidosis is mitigated by the conversion of the L enantiomer of lactate to bicarbonate equivalents. It is important to note that these solutions are hypotonic and contain anions such as D lactate and acetate which can accumulate when renal function is compromised and cause toxicities.

In conclusion, there is little controversy regarding the importance of the timely administration of resuscitation fluid. Despite the importance of fluid resuscitation, clinical science

has not yet identified a solution that will yield superior results in all circumstances and at affordable cost. Studies that have modified our conception of the goals of resuscitation to consider preservation or enhancement of the barrier functions of the endothelial glycocalyx must also be evaluated in the context of their costs and toxicities. The selection of the best resuscitation fluid continues to require clinical judgement that includes careful consideration of the properties of the fluids including their toxicities, availability and costs. The recipe for optimal outcomes includes a clinician with experience and training who is able to integrate properties of the resuscitation fluid with patient characteristics including the type of illness or injury, the amount and rate of volume loss, electrolyte levels, and renal function. Judgement, clinical skill, experience, and alacrity matter during resuscitation.

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