Fluid Resuscitation: Principles of Therapy and "Kidney Safe" Considerations

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Fluid resuscitation in the acutely ill must take into consideration numerous elements, including the intravenous solution itself, the phase of resuscitation, and the strategies toward volume management which are paramount. With the advancement in the understanding and implementation of aggressive fluid resuscitation has also come a greater awareness of the resultant fluid toxicity, especially in those that suffer acute kidney injury, and the realization that there is continued ambiguity with regard to volume mitigation and removal in the resuscitated patient. As such, the discussion regarding intravenous solutions continues to evolve especially as it pertains to their effect on kidney and metabolic function, electrolytes, and ultimately patient outcome. In the section below, we review the foundations of fluid resuscitation in the critically ill patient and the different solutions available in this context, including their composition, physiologic properties, and safety and efficacy including the available data regarding "renal-safe" options.

Key Words: Fluid, Resuscitation, Solution, Volume

INTRODUCTION

Despite its absolute pervasiveness in the management of the acutely ill patient, there remains large practice variations with regard to the selection and administration of IV fluids, not only by geographic location and between medical specialties but even between providers within the same specialty.[1] As such, given that these variations may actually be related more to clinician preference rather than a physiological basis,[2] questions abound not only as to the optimal composition and administration of IV fluids (including fluid dose, timing, and rate) but also as to the relative morbidity attributable to fluid toxicity and whether there are "kidney safe" options. This has led to a greater push in ascribing the same caution toward IV fluid administration as any other medication[2,3] in the hopes of optimizing patient-centered outcomes. However, the challenges of standardizing fluid administration are notably apparent when considering the numerous patient-related clinical variables (including organ failure, infection, nutrition, and electrolyte derangements) in the context of a wide range of clinical settings related to hemodynamic instability in which IV fluid therapy is administered (including sepsis, trauma, and hemorrhage).

FOUNDATIONS OF VOLUME RESUSCITATION

The mainstay of therapy for the modern-day management of sepsis is aggressive IV fluid resuscitation whose efficacy with regard to mortality was first demonstrated in the landmark study by Dr. Emmanuel Rivers.[4] The foundation of this early goal-directed therapy (EGDT) was to maximize preload to augment cardiac output for optimal organ perfusion and included a number of specific interventions geared toward specific hemodynamic and physiological targets (Table 1). This study was the first to emphasize the utility of such measures allowing for a protocolized EGDT in sepsis. The patients were followed for 60 days or until death with the in-hospital mortality significantly lower in the EGDT arm (30.5%) vs the standard therapy (46.5%) as was the amount of overall fluid used in the EGDT arm in the first 6 hours, although by 72 hours, it was approximately the same in both. Since 2001, there have been at least 12 studies that have evaluated variations of the River's study and despite some of their challenges to specific bundled components of the study's protocols, most subsequent studies have considered the administration of 25 to 50 mL/kg (average of 30 mL/kg) of isotonic fluid within the first 6 to 8 hours as defining the EGDT.[5] As such, initiated in 2002, the Surviving Sepsis Campaign was a product of the joint collaboration between the Society of Critical Care Medicine and European Society of Intensive Care Medicine with the inherent goal of reducing mortality due to sepsis (Surviving Sepsis Campaign: http://www.survivingsepsis.org). The collaboration's original treatment algorithm was adopted from Rivers and colleagues[4] and was designed into treatment "bundles." These "bundles" represent core elements of care designed to ensure timely administration of treatments with known benefit to maximize patient outcome while simplifying and reducing the variability in the early management of septic patients. The most recent algorithm (updated April 2015) now provides 3- and 6-hour bundles for the initial resuscitation of patients in septic shock (Fig 1). Recently, in an effort to advance the modern-day understanding of acute fluid resuscitation, the Acute Dialysis Quality Initiative workgroup conceptualized fluid management in the setting of critical illness. Originally formed in 2000 to review emerging evidence and formulate consensus with regard to the management of kidney diseases, the Acute Dialysis Quality Initiative framed their concept of fluid management in the acutely ill population as a dynamic

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Table 1. Original Early Goal-Directed Therapy Interventions and Targets

500 mL IV bolus crystalloid q30 min to achieve CVP 8-12 mm Hg and MAP 65 mm Hg
Vasopressor if BP goal not achieved
PRBCs if $ScvO_2$ <70% with target goal HCT >30%
Dobutamine if $ScvO_2$ remains <70% (until >70% or maximum dose)
Minimum 6 h therapy (EGDT)
Antibiotic therapy at clinician discretion

Abbreviations: BP, blood pressure; CVP, central venous pressure; EGDT, early goal directed therapy; HCT, hematocrit; MAP, mean arterial pressure; PRBC, packed red blood cells; ScvO2, central venous oxygen saturation.

process which was divided into 4 phases with the goals of fluid administration dependent on the phase of illness (Table 2).[6-8] Within each phase of therapy and dependent on numerous factors, both the requirements of and response to fluid resuscitation can have considerable variation over the course of the illness. Although patients may be perceived as progressing through each phase of resuscitation in a linear fashion, they do not all start at the same point and certainly do not follow a temporal pattern, such as the patient who may present with hypotension but does not require vasoactive support or who may acutely decompensate while mobilizing excessive fluid, therefore requiring repeat resuscitation. This variability presents continued challenges to the design and implementation of standardized protocols regarding fluid management.

CLINICAL SUMMARY

- The evaluation of a fluid's safety and effectiveness must take into account its composition and properties and the clinical features of the population that is receiving it.
- Standardized approaches to fluid resuscitation and maintenance therapy should utilize and integrate multiple objective measures of clinical targets and end points.
- Although there are no solutions to date that show clear superiority, it is recognized that hetastarch should be avoided as a volume expander.
- Although there has been much advancement in the understanding of aggressive fluid resuscitation and resultant fluid toxicity, there is continued ambiguity with regard to accumulated volume removal in the resuscitated patient.

APPROACH TO VOLUME RESUSCITATION

During initial attempts to rapidly reverse the shock state and throughout the patient's clinical course, it is imperative that volume responsiveness be continually evaluated, utilizing, and integrating a number of different physical, biochemical, and/or imaging parameters comprising static and dynamic variables. When used in conjunction with static variables (such as central venous pressure, mean arterial pressure, heart rate, urine output, and pulmonary artery wedge pressure/pulmonary artery occlusion pressure) that are surrogates for preload and routinely used as the customary indicators of volume status, dynamic measures (such as stroke volume variation, pulse pressure variation, end-expiratory occlusion test, and passive leg raise), which represent preload responsiveness, may help avoid over-resuscitation (Fig 2).[7,9,10] Markers, such as $ScvO_2$ or SvO_2 (central venous or mixed venous oxygen saturation) and clearance of arterial lactate, have traditionally been used to evaluate the resolution of tissue underperfusion, thus marking the end point of aggressive fluid resuscitation.[11-13] In Rivers and others,[4] $ScvO_2$ increased with fluid resuscitation which suggested a parallel increase in cardiac output and, therefore, was considered a surrogate for cardiac output. However, the baseline value for $ScvO_2$ in the study was about 50%, which is much lower than a normal value of about 70%,[14] and the $ScvO_2$ and SvO_2 are actually characteristically normal or higher in septic shock patients due to decreased oxygen extraction[15,16] and, therefore, does not necessarily suggest adequate tissue oxygenation. In fact, only Rivers and others[4] found such a low $ScvO_2$ as more recent studies have found much higher $ScvO_2$ values in septic shock patients, either in the emergency department or on admission to the ICU,[17,18] which suggests that other factors such as pre-existing co-morbidities or late arrival to the hospital were responsible. Additionally, measuring $ScvO_2$ is characteristically invasive and requires specific equipment which is not readily available in many facilities globally.[19] However, there is no single absolute physical, biochemical, or imaging measurement that will sufficiently represent the status of a critically ill patient suffering from variable co-morbidities.[3] Therefore, continued assessment and reassessment of volume requirements and responsiveness with any concurrent or occult tissue hypoperfusion utilizing multiple parameters and targets is ideal to avoid toxic accumulation, including those that have developed acute kidney injury (AKI) and, therefore, remain susceptible to progressive and unnecessary accumulation, designated as "fluid creep."[20] A larger degree of fluid overload at the initiation of kidney replacement therapy is associated with a higher mortality[21] and lower likelihood of kidney recovery[22] and quantitative fluid toxicity will lead to a longer intubation period and hospital stay.[23] To date, however, there is no applicable data to direct what degree of fluid mitigation or removal is optimal as the patient progresses toward the de-escalation phase.

SOLUTION COMPOSITION

Modern-day medicine has availed itself of numerous types of fluid compositions in each class of solution available for delivery in multiple clinical scenarios (Table 3).[24-28] IV fluid distribution within the body fluid compartments can vary considerably depending on the acute illness that the patient is suffering, and therefore, any resuscitative fluid can contribute to the formation of interstitial edema especially in septic or inflammatory conditions.[3] Crystalloid solutions are sterile aqueous solutions comprising mineral salts or other