Review article

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Intravenous fluid therapy in intensive care units. Where do we stand?

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ABSTRACT

Intravenous fluid therapy is vital for resuscitation of critically ill patients. However, the procedure is very complex; the standards of operation and monitoring are controversial and the indications of commencement and weaning are fiercely debated. Administration of intravenous fluids is imperative for circulatory stabilization and is potentially lifesaving in shock patients; on the other hand it can be the cause of increased morbidity and mortality if there is a volume overload. Crystalloids and colloids are the two types of fluids which can be used for resuscitation; and each one is associated with its own set of benefits and adverse effects. The population of critically ill patients is significantly heterogeneous, thus the targets, and safety limits cannot be clearly defined which can be applied to all the patients in Intensive Care Unit patients (ICU) alike. The fluids should be considered as any other intravenous drug in ICU with an optimal dose and a therapeutic and toxic window. The amount and the type of Intravenous (IV) fluids used play a crucial role in patient outcome and need to be individualized. The patients who are responsive to fluid resuscitation initially are susceptible to overload later so it is very crucial to know when to stop IV fluids. The monitoring which is generally used in ICU and the static measures of fluid responsiveness are not sufficient to guide the fluid therapy in critically ill patients. Dynamic measures to predict the fluid responsiveness can be helpful to prevent excessive fluid administration.

Key words: Fluid therapy, intensive care, resuscitation, volume overload

INTRODUCTION

Intravenous IV fluid therapy is the most common and usually the first intervention which is done in Intensive Care Unit (ICU). IV fluids are used to restore effective blood volume and to maintain organ perfusion and cellular homeostasis. When used appropriately i.v. fluids can improve outcomes and can be life saving in critically ill patients especially those in shock. An inappropriate use of i.v. fluids on the other hand can be associated with worse outcomes[1]. Improper use may range from inadequate resuscitation leading to tissue hypo-perfusion to fluid overloading which may lead to tissue edema, both of which are associated with complications like organ damage and increased morbidity and even mortality[2]. Therefore the fluid therapy in critically ill patients requires a very skeptical and careful assessment of specific indications and contraindications of the type and dose of fluid to be administered. It has been recommended that the use of fluid therapy should be accorded similar status as drug prescribing[3]. In addition, the population of critically ill patients is significantly heterogeneous, therefore a single approach of fluid therapy cannot be applied to all, instead a goal directed and individualized approach is needed for better outcome.

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The review is an attempt to compile the known facts regarding this very fundamental and essential component of critical care for a better comprehension; and also, to try to find answers to the increasing concerns regarding indications, choice, dosage and monitoring of fluid therapy.

TYPES OF FLUIDS USED IN ICU

Crystalloids and colloids are the two types of fluids which are used for resuscitation of critically ill patients. Cost, patient specifications and regional preferences direct the type of fluid selected[1,4].

CRYSTALLOID SOLUTIONS (TABLE 1)

Crystalloids are solutions which contain inorganic ions like sodium, potassium, chloride, magnesium, calcium as well as small organic substances such as glucose, lactate etc. They are balanced salt solutions, isotonic saline and dextrose containing solutions.

COLLOID SOLUTIONS (TABLE 2)

Colloids consist of homogenous, non crystalline large molecules dispersed throughout a base solution (the dispersion medium) which can be either normal saline or balanced solution like Ringer's lactate. They can be blood derived such as albumin, plasma protein fraction and fresh frozen plasma; or semisynthetic like Hydroxyethyl starch (HES), gelatins, dextran etc.

COLLOID VERSUS CRYSTALLOID

There is an ongoing debate for the choice between colloids and crystalloids and the different impacts of chloride-rich versus balanced solutions for resuscitation in ICU patients. The choice of fluid can affect not only the amount of fluid needed to achieve the goals of fluid therapy but also influences the outcome of patients under resuscitation[4,5]. Crystalloids are the most commonly used initial resuscitation fluids as they are readily available, economic and there are fewer chances of allergic reactions. Use of normal saline is claimed to be associated with hyperchloremic metabolic acidosis in renal insufficiency cases even with low volume doses. Conventionally, balanced salt solutions like plasmalyte and Hartmann's solution are thought to be free of this side effect. (reference) However, in a large cluster randomized trial comparing 0.9% Saline with Plasmalyte (SPLIT) no difference in the incidence of acute kidney injury or mortality was found between the patients receiving saline or plasmalyte[6].

Colloid solutions have the advantage of expanding the volume more effectively and for longer duration by maintaining intravascular oncotic pressure. However, they are associated with their own set of side effects. Besides being expensive they have anaphylactic potentials, can affect coagulation, increase the bleeding risk and can affect renal functions. In Saline versus Albumin Fluid Evaluation Trial (SAFE), a blinded clinical trial comparing 0.9% saline with 4% albumin- no difference was found in the 28 day all cause mortality between the groups[7].

Table 1: Commonly used Crystalloid solutions

Crystalloid solution	Components (m Eq in 1,000 ml)	pH	Osmolality (mOsmol/L)
Lactated Ringer's/ Hartmann's solution	Sodium 130, chlorine 109, potassium 4, calcium 3, lactate 28	6 to 7.5	273
Ringer's acetate	Sodium 130, chlorine 112, potassium 5.4, calcium 0.9, magnesium 1, acetate 27	5.1 to 5.9	276
Normal saline	Sodium 154, chlorine 154	4.5 to 7	308
Plasma-Lyte A	Sodium 140, chlorine 98, potassium 5, magnesium 3, acetate 27, gluconate 23	7.4	295
Dextrose 5%,	H2O, dextrose	3.2 to 6.5	252

Table 2: Commonly used Colloid solutions

Colloid solution	Components (per liter)
Albumin 25%	12.5 g/50 ml human albumin
Albumin 5%	50 g/l albumin
Hydroxyethylstarch 130/0.4	Hydroxyethylstarch 130/0.4, 6% in 500 ml normal saline
Hydroxyethylstarch 600/0.75	Hydroxyethylstarch 600/0.75, 6% in 500 ml normal saline
Gelatin 4%	40 g gelatin polysuccinate
Hemaccel	35 g gelatin

In a subgroup analysis of the same trial in patients of traumatic brain injury, the relative risk of death was more in patients who received albumin[8]. On the other hand, in patients with severe sepsis and septic shock, the relative risk of death was less at 28 days in albumin group, suggesting a protective pattern due to the anti-inflammatory properties of albumin[7].

The anti-inflammatory properties of albumin were also investigated in ALBIOS (Albumin Italian Outcome Sepsis) trial. Daily supplementation of 20% albumin to patients with severe sepsis and septic shock was not found to be associated with any significant decrease in mortality, length of stay or degree of organ dysfunction. Though no evidence of harm was found with albumin resuscitation, the cost factor had increased significantly [9].

In the trials where semisynthetic colloids have been compared with crystalloids like CHEST (Crystalloid versus hydroxyethyl starch trial) and CRISTAL (Colloids versus crystalloids for the resuscitation of the critically ill) trial; no difference in the primary outcome of 90-day all-cause mortality between the colloid and crystalloid groups was found. However, an increased risk of pruritus, skin rash, and a greater need for new initiation of Renal Replacement Therapy (RRT) in Hydroxyethyl Starch (HES) group was observed[10,11].

A comparison between the 6% (130/0.42) HES and balanced salt solution Ringer's acetate for resuscitation in septic shock patients showed a significant increase in the composite primary endpoint of death or dialysis dependence at 90 days in patients randomized to receive starch[12].

Thus, currently there is no evidence from randomized controlled trials that resuscitation with colloids, instead of crystalloids, reduces the risk of death in critically ill patients. The use of semi-synthetic colloids for resuscitation purpose is discouraged as they are associated with worse outcomes. The use of albumin is restricted to the patients who have already received a substantial amount of crystalloid.

OPTIMAL INTRAVENOUS FLUID DOSING

The recommended initial dose of IV fluids for septic shock patients had been 30 ml/kg body weight with the goals of Central Venous Pressure (CVP) of 8-12 mm Hg, a mean arterial pressure of > 65mmHg , a urine output of .> 0.5 ml/kg/h, and a mixed venous oxygen saturation of 65%[13]. The role of these targets of resuscitation is disputed and the guiding parameters have been often found to be inaccurate resulting in significant volume overload and its related adverse effects[14,15]. The reason can be the heterogeneity of the critically ill patients, consequent to which the 'single size fits all' formula may not work for all the patients. Both insufficient and excessive fluid resuscitation are associated with worse outcomes. Hence, instead of the goal directed therapy, an individualized fluid therapy which is tailored to the specific indication and the context of patient is likely to be more successful. The resuscitation should be adequate as well as timely, so it's not sufficient to know how much fluid should we give but also when and for how long it should be given.

Stages of Fluid Therapy: Hoste et al.,[16] and Benes et al.,[17] have explored the risks of inappropriate fluid therapy and have emphasized that IV fluid should be considered as a drug therapy with the dose effect relationship and side effects. They also highlighted the usefulness of four stage framework initially proposed by Vincent et al.,[18] for volume resuscitation in critically ill patients. This framework makes use of an individual assessment spread over the time course of illness; and the four stages are- Rescue phase, Optimization phase, Stabilization phase and De-escalation phase (Figure 1).

Rescue Phase: The initial duration of first minutes to hours when the patient is in an immediate life threatening shock state. The main focus is on salvaging the patient by giving an aggressive fluid resuscitation with IV fluid bolus, so as to improve the fluid deficit- with or without the vasopressor support. In this phase the time of action is usually a few minutes.

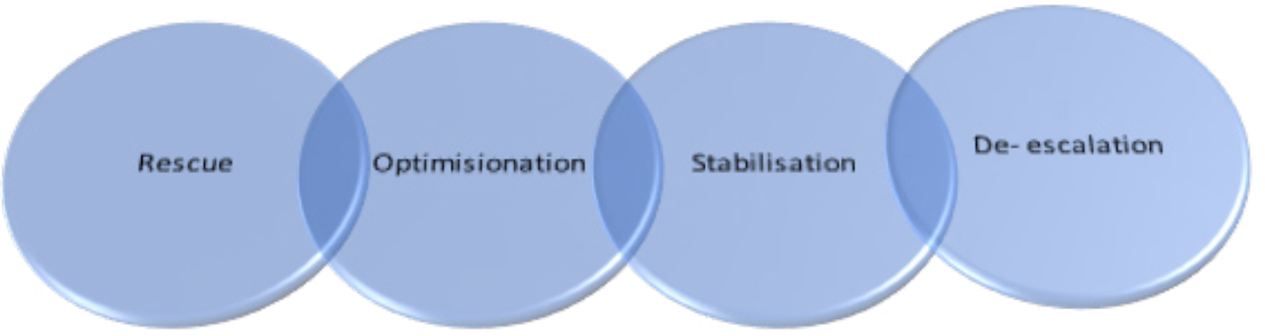

Figure 1. Relationship of different stages of fluid resuscitation.

Optimization Phase: In this phase, the fluid therapy has to be continued but in a lesser aggressive and more judicious way. The aim is to maintain an adequate tissue perfusion by giving a titrated fluid using fluid challenges. Patient is still critical and a supportive therapy of vasopressors and ionotrops may be needed. This stage may last for some hours to 1-2 days.

Stabilization Phase: This phase may last for some days; patient is more stable and is gradually weaned off from the supportive drug therapy. The priority is to prevent the adverse effects of the fluid therapy and the aim is to bring the patient to zero or negative fluid balance by restricting the IV fluids to a minimal maintenance infusion.

De-escalation Phase: This is the last stage, which may last up to several days to weeks. It is of utmost importance in patients where excessive fluid load can be devastating like GIPS (global Increased Permeability Syndrome) please write full name once); Systemic Inflammatory Response Syndrome (SIRS); and multiple organ dysfunction, particularly, ARDS (Acute respiratory distress syndrome) please write full name once) and Acute Kidney Injury (AKI). The goal of "negative fluid balance" is adopted to remove the accumulated fluid which can be either spontaneous or triggered with the use of diuretics.

Most of the patients requiring fluid resuscitation present in the rescue phase. After an initial bolus of fluid, optimization phase will be achieved when the aim should be to maintain tissue perfusion with a more cautious fluid administration. Patients will then proceed to stabilization and de-escalation phase as the clinical condition improves and the priority now should be to prevent the adverse effects of IV fluids.

Monitoring and Fluid Responsiveness: The concept of four stage framework of fluid therapy is dynamic and requires an individual assessment of patient's fluid requirement and timely administration of the required fluid. A minimal monitoring is required when a fluid therapy is initiated which may guide the clinician during initial resuscitation and it includes blood pressure, heart rate, arterial blood gases (lactate) levels, capillary refill or pulse volume, altered mental status and urine output[16]. After the recue phase, during optimization- additional parameters will be needed for further management. The aim of this stage is to maintain an adequate organ perfusion and oxygen delivery, and to prevent organ dysfunction and damage due to both hypo-perfusion and overload. This assessment and reassessment requires monitoring of Central Venous Pressure (CVP), Pulmonary Artery Occlusion Pressures (PAOP), Central Venous Oxygen Saturation ($SCVo_2$), cardiac output and dynamic measures of responsiveness to fluid challenges[16,17].

The CVP and PAOP are the static measures of fluid responsiveness, which assess the right and left ventricular end diastolic volume indirectly. Their utility in assessing the fluid responsiveness may be incorrect in certain situations like poor ventricular compliance due to systemic and pulmonary hypertension, valvular heart disease etc.

Therefore, certain dynamic parameters are needed to assess the fluid responsiveness; which include the stroke volume variation with the respiratory cycle during mechanical ventilation. The pulse pressure variation during mechanical ventilation can be used as a surrogate parameter of stroke volume. Other parameters which can be used to estimate stroke volume variation are- blood flow of the left ventricular outflow tract measured by echocardiography, aortic blood flow assessed by esophageal Doppler, and the amplitude of the plethysmography signal recorded by pulse oximetry. Besides these- the inferior vena cava collapsibility index, end expiratory occlusion test, passive leg raising test and mini fluid challenge can predict the fluid responsiveness and guide us through the fluid therapy after the rescue phase[17,19,20].

The timing of stabilization and de-escalation is overlapping and rather unclear. In some patients de-escalation starts naturally with the start of healing process, in others an active intervention in the form of diuretics is needed to mobilize the fluid which got accumulated in the tissues[21].

CONCLUSION

With the available literature, we can conclude that colloids are in no way better than crystalloids for initial resuscitation of patients with shock; and HES should be avoided as much as possible due to the associated adverse effects IV fluid therapy can be life saving in critically ill patients but like all medical interventions are associated with its own set of complications and hence should be treated with same skepticism as any other drug in ICU. The amount and composition, as well as the timing of fluid administration- can directly impact the outcome of patients. Patients in ICU are significantly heterogenous, so the fluid therapy should be individualized. The newer dynamic indices for the assessment of fluid responsiveness should be used to guide the fluid therapy, rather than the conventionally used blood pressure and CVP centered approach.

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