


REVIEW

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Narrative review of the role of intravenous fluid in critically sick patients

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Abstract

Background Intravenous fluid administration is regarded as a universal therapy in critical care. It is the mainstay of treatment in patients with dehydration, blood loss, sepsis, electrolyte imbalance, and shock. Crystalloids (for example, normal saline, lactated Ringer's, Hartmann's, Normosol, Isolyte, and PlasmaLyte solutions) and colloids (for example, albumin, or synthetic dextrans, gelatins, and starches) are the two types of commonly used IV fluids.

Main text Resuscitation, replacement, and maintenance are the three main indications for intravenous fluid administration. Despite their widespread use, there is no standard therapeutic dose for IV fluids and clinicians are less familiar with the indications to stop IV fluid administration. Appropriate fluid management to maintain tissue perfusion while avoiding potentially harmful effects of IV fluid administration such as fluid overloading, metabolic acidosis, acute kidney injury, and electrolyte imbalance should be the core principle of treatment.

Conclusion This review will focus on the role of different types of intravenous fluid in critically ill patients, including their side effects and applications in various types of shock.

Keywords IV fluids, Crystalloids, Colloids, Shock

Background

Intravenous fluid (IV) administration is a life-saving therapy commonly used in the hospital setting and it plays a crucial role in the maintenance of cellular homeostasis in critically ill patients [1]. Resuscitation, replacement, and maintenance are the three main indications for intravenous fluid administration. Resuscitation fluids are used to correct an intravascular volume deficit or acute hypovolemia; replacement solutions are prescribed to correct existing or developing deficits that cannot be

compensated by oral intake alone; and maintenance solutions are indicated in hemodynamically stable patients who are unable or not allowed to drink water to meet their daily water and electrolyte requirements. Apart from these three indications, the administration of fluid as a drug diluent or to maintain catheter patency, should also be considered [2]. The type and composition of IV fluids have evolved since their discovery. Dr. Thomas Latta, a pioneer in the field of fluid resuscitation, infused a solution of water, sodium, chloride, and bicarbonate into the veins of critically sick patients via a metal tube during the cholera epidemic of 1831. Latta's original solution, a balanced crystalloid, was composed of 134 mmol/l Na⁺, 188 mmol/L Cl⁻, and 16 mmol/L of HCO₃⁻ [3]. In the mid-nineteenth century, Sydney Ringer and his assistant discovered Lactated Ringer's (LR), a now widely used solution, by combining salt with tap water instead of distilled water to study the cardiac activity of frog hearts [4]. In the late nineteenth century, it was established that the ideal solution for fluid resuscitation needed to be isotonic

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with serum. Subsequently, in 1896, Hamburger used freezing point comparisons of mammalian blood and various saline concentrations to suggest a 0.92% saline concentration as the ideal isotonic IV solution for human fluid resuscitation. This led to the development of the staple 0.9% saline solution, one of the most widely used modern IV fluids [5]. In the following years, intravenous fluid administration became a universal therapy in critical care.

During anesthesia and surgery, intravenous fluid administration is a daily routine to maintain tissue perfusion and electrolyte concentrations or to infuse drugs. I.V. fluids are increasingly being treated as drugs, with dosing guidelines, indications, contraindications, and side effects [6]. Unlike most drugs, there is no standard therapeutic dose for fluids, and while “starting triggers” for fluid resuscitation are well understood, clinicians are less familiar with “stopping triggers” for fluid resuscitation and there have been concerns about the potentially harmful effects of IV fluids due to fluid overloading and electrolyte imbalance [2]. This review will concentrate on the role of different types of intravenous fluid in critically ill patients, including their side effects and applications in various types of shock. The aim of this review is to summarise the different types of IV fluids available, go over the pharmacokinetics of different types of IV fluids, the composition and indication of fluids, and general management of shock, mostly discussing fluid resuscitation.

Main text

Types of IV fluids

The IV fluids can be divided into two categories: crystalloids and colloids, based on the composition. Crystalloids are water-based solutions with electrolytes that can cross freely from the intravascular space into the interstitium, a process referred to as third spacing. Crystalloids should be distinguished from colloids, in which insoluble particles are suspended but not in solution [7]. Crystalloids are used to briefly expand intravascular volume but then quickly permeate vessel walls and re-distribute in the interstitial space. Crystalloids are the most commonly

administered intravenous fluid due to their availability, cost-effectiveness, and comparable outcomes to colloid preparations. Crystalloids form the “first-line” therapy in fluid resuscitation; over 200 million liters are administered each year in the USA [8]. In North America, the most commonly administered intravenous crystalloid is normal saline. [9] More specifically, crystalloid fluids isotonic to human plasma are preferred for fluid resuscitation in the settings of cardiogenic, hypovolemic, and septic shock [10]. Isotonic crystalloid fluids include 0.9% sodium chloride and physiologically balanced solutions such as lactated Ringer’s, Hartmann’s, Normosol, Isolyte, and PlasmaLyte solutions [11] (see Table 1). Balanced crystalloids include sodium, potassium, and chloride, similar to that of extracellular fluid and these solutions also act as buffers by consuming anions to form bicarbonate or gluconate that can be metabolized or excreted, respectively [9].

Colloids are water-based mixtures that contain molecules of human plasma derivatives, such as albumin, or synthetic dextrans, gelatins, and starches (Table 2) [12, 13]. These molecules cannot permeate healthy capillary membranes, leading to increased oncotic pressure and intravascular trapping of colloid fluid for more sustained periods of time [13]. Based on recent evidence, the “volume sparing” effect of colloids is less than that of crystalloids in critically sick patients, however, Finfer et al. demonstrated that there is no significant difference in outcomes [14]. The naturally occurring colloid albumin, which was first used to treat trauma casualties [7], is a small protein synthesized by the liver and is involved in maintaining the oncotic pressure in the plasma. Apart from providing plasma colloid oncotic pressure, albumin binds nitric oxide, regulates inflammation, and protects against lipid peroxidation [15]. Albumin may be an appropriate therapy for patients of cirrhosis and those undergoing liver transplantation but its high cost relative to crystalloids makes albumin debatable for use as a ‘first line’ fluid for resuscitation [16]. The limited supply of human albumin solution led to the development of semi-synthetic colloid solutions, which include gelatins, dextrans, and hydroxyethyl starches (HES). The preparation of

Table 1 Composition of crystalloids [12]

	Osmolality (mOsm/L)	Electrolytes Concentrations (mEq/L)				
		Na+	Cl-	K+	Ca2+	Mg2+
Plasma	290	140	103	4	4	2
0.9% saline	308	154	154	0	0	0
Hartmann’s solution	279	131	111	4	2	0
Ringer’s lactate	273	130	109	4	3	0
PlasmaLyte	295	140	98	5	0	3

Table 2 Composition and characteristics of colloids [12]

Types of colloids	Osmolality (mOsm/L)	Oncotic pressure (mmHg)	Duration of expansion (h)	Plasma half-life (h)	[Electrolyte] (mEq/L) Na + Cl-
4% Albumin	300	19–30	< 24	16–24	140 128
Hydroxyethyl starch; 6% Pentastarch; 10%	300–326	23–82	< 12	2–12	154 154

gelatins is done by hydrolysis of bovine collagen, dextrans are biosynthesized from sucrose by bacteria, and HES are obtained from the maize-derived D-glucose polymer amylopectin [17].

Crystalloids vs colloids

Balanced crystalloids are preferred in hypovolemic patients for fluid replacement but colloids are perhaps more effective than crystalloids in intravascular volume expansion. In patients with sepsis, administration of isotonic saline can lead to iatrogenic hyperchloremic acidosis, which can augment the lactic acidosis disease process often seen in sepsis. For this reason, balanced solutions are selected over isotonic solutions for the treatment of septic shock [18]. Despite extensive studies, the effect of albumin solutions on sepsis outcomes remains unclear. HES is the only semisynthetic colloid robustly studied in sepsis and has been found to increase the incidence of AKI and potential mortality. Ongoing research on the endothelial glycocalyx, balanced crystalloids, and early albumin administration hold the potential to further improve sepsis survival [11]. In this review article, we will be discussing the types of IV fluids and their role in critically sick patients.

Type of shock: a primary indications for IV fluids

Critically sick patients may lose intravascular volume secondary to a variety of pathologies, including infections, trauma, or burns, for which urgent fluid repletion is essential to prevent dehydration and end-organ failure [19]. By maintaining hydration, fluid resuscitation restores intravascular volume and improves perfusion and oxygenation of vital organs [20]. The aim of fluid resuscitation is to administer sufficient fluid volume to optimize hemodynamics and maintain both organ perfusion and electrolyte balance, all while avoiding fluid overload. Excess free body water from excess fluid resuscitation can accumulate in lung and subcutaneous tissues, causing pulmonary and extremity edema, respectively [21]. Acute circulatory shock, a common presentation in critical care, is characterized by circulatory failure resulting in underperfusion of tissues. Acute circulatory shock is associated with systemic arterial hypotension with systolic blood pressures below 90 mmHg or mean

arterial pressures (MAPs) below 70 mmHg. Clinically, acute circulatory shock presents with signs of tissue hypoperfusion including cold, clammy skin, decreased urine output (less than 0.5 ml/kg/h), and altered mental status. Underperfusion of tissues, due to acute circulatory shock, leads to affected tissues' utilization of alternative metabolic pathways resulting in hyperlactatemia with levels over 1.5 mmol/L [22]. There are four, commonly referred to categories of acute circulatory shock: hypovolemic shock, cardiogenic shock, obstructive shock, and distributive shock. Hypovolemic shock is characterized by a pathologic decrease in intravascular volume and can be further classified as either hemorrhagic or non-hemorrhagic hypovolemic shock. Hemorrhagic hypovolemic shock is associated with a loss of intravascular volume due to extravasation of blood caused by conditions such as gastrointestinal bleeding, aneurysmal rupture, or other trauma to vasculature. Non-hemorrhagic hypovolemic shock involves loss of intravascular volume through non-hemorrhagic pathways such as diarrhea, vomiting, excessive diuresis, or third-spacing due to ascites or edema. Intravascular volume loss associated with hypovolemic shock leads to decreased central venous pressure (CVP), which lowers the pulmonary capillary wedge pressure (PCWP), causing decreased blood return to the heart, ultimately leading to both decreased left atrial pressure and cardiac output [23]. Distributive shock is characterized by peripheral vasodilation of arterioles and veins that leads to a pathologic accumulation of intravascular volume in the peripheral vasculature. Fluid trapped in the periphery is unable to be properly circulated by the heart and lungs, leading to shock. Distributive shock can be further classified as anaphylactic shock, endocrine shock, septic shock, systemic inflammatory response syndrome (SIRS), and neurogenic shock. Anaphylactic distributive shock is caused by an Ig-E-mediated hypersensitivity reaction that occurs within seconds to minutes of exposure to an antigen to which the host has been sensitized. Endocrine shock is caused by endocrine-related pathologies such as hypotensive Addisonian crisis due to Addison's disease or myxedema due to hypothyroidism. Septic shock is associated with a host response to infection that leads to hypotension and ultimately tissue hypoperfusion. SIRS is defined by a massive inflammatory response

to both infectious and non-infectious pathologies that leads to vasodilation and distributive shock. Common causes of SIRS distributive shock include infectious, pancreatitis, burns, and more. Neurogenic distributive shock is defined by damage to the central nervous system resulting in autonomic nervous system derangements that lead to decreased vascular tone and hypotension. Cardiogenic distributive shock is defined by intracardiac-related failures of the heart to properly circulate blood and perfuse tissues. In other words, cardiogenic shock is caused by intrinsic failure of the heart as a pump. Common etiologies of cardiogenic shock include arrhythmias, cardiomyopathies, and cardiac valve dysfunction. Lastly, obstructive distributive shock is defined as distributive shock secondary to extracardiac causes of decreased left ventricular output. Common causes of obstructive distributive shock include tension pneumothorax, severe pulmonary hypertension, massive pulmonary embolism, and more. [23]

Selecting the proper IV fluid

Changes in body weight, serum sodium concentration (as a measure of water balance), blood pressure, acid-base status, kidney function, and the presence of diabetes are the parameters that influence the choice of IV fluid therapy [7]. Crystalloid fluids with high chloride contents have been found to decrease blood flow to the kidneys, leading to potential acute kidney injury (AKI). Delivery of chloride to the macula densa cells of the kidney also causes mesangial contraction and reduces glomerular filtration. A meta-analysis comparing studies of crystalloids with high and low chloride concentrations found that those with higher chloride concentrations were associated with increased incidence of AKI, but not mortality [24]. The varying effects of balanced crystalloids and saline appear amongst severely ill patients, patients who have received high volumes of fluid, and patients with septic shock. Colloids are generally less preferred because they have been associated with AKI and increased mortality [7].

When selecting balanced crystalloids or saline for a patient, it is important to consider their comorbidities, acute conditions, hemodynamic status, laboratory values, and organ function. Until data, such as patient laboratory values, and contraindicating balanced crystalloids becomes available, balanced crystalloids should be administered first-line for fluid resuscitation.

Management of shock

Fluid replacement is fundamental in the management of critically ill patients who present with signs of shock, with hypovolemic and septic shock being the most common presentations [25]. Hemorrhagic shock is one

of the most common shock presentations in patients suffering from hypovolemic shock. In addition to interventions that reduce the ongoing bleeding, adequate resuscitation is also required in order to increase the blood pressure and maintain the cardiac output. Isotonic crystalloids were some of the first fluids used in the management of hemorrhagic shock. However, the administration of large boluses of crystalloid fluids led to the disruption of many biochemical processes, causing defects in pancreatic insulin secretion [26], dilutional coagulopathy, and acute respiratory distress syndrome (ARDS), to name a few [27]. Thus in order to safely resuscitate a patient suffering from hemorrhagic shock, damage control resuscitation is carried out, which consists of four main components: Minimized isotonic crystalloids, Transfusion of a balanced ratio of blood products, Permissive hypotension, and Goal-directed correction of coagulopathy [28]. In patients with severe trauma, transfusion of plasma, platelets, and red blood cells in a 1:1:1 ratio is associated with a slight decrease in mortality [29]. Therefore, maintaining the minimum blood pressure required for the perfusion of vital organs while carefully administering blood products is the method of treatment for patients with hemorrhagic shock.

Septic shock is associated with damaged endothelium leading to increased permeability of the vessels as well as a decreased vascular tone, and thus intravascular volume expansion is the first line of therapy [30]. However, large amounts of crystalloid administration can further lead to deleterious effects if the patient becomes non-fluid-responsive, and cause adverse effects like edema, deterioration of right ventricular function, hemodilution, etc. [31]. In order to overcome this barrier and to ensure safe resuscitation, a more individualized approach is carried out and an administration of around 10 ml/kg crystalloids is done within the first hour, after which the patient's response to the preload is checked by measuring the stroke volume and pulse pressure variation, among other parameters. Another fluid bolus is only considered in patients who are fluid-responsive and have not developed ARDS [32]. Along With this, prompt administration of narrow-coverage antibiotics should be done in order to eliminate the source of infection. If a patient is suffering from life-threatening hypotension, early initiation of norepinephrine should be carried out in order to increase vascular tone. [10] This increase in cardiac preload leads to an increase in the cardiac output of patients [33]. Thus, efficient calculation of the risk vs benefit in patients suffering from septic shock is the best approach for this treatment, as it minimizes the adverse reactions caused due to excessive intravascular fluid expansion.

Patients suffering from anaphylactic shock have an increased level of histamines in the blood, causing vasodilation as well as increased permeability of vessels. In addition to ensuring adequate oxygenation and administration of intramuscular epinephrine [34], a bolus of 10–20 ml/kg of colloid is given rapidly in order to replace the plasma losses that have occurred. This has been seen to replace the circulatory losses effectively, and further treatment is most likely not required [35].

It can be challenging to administer fluid resuscitation to patients in cardiogenic shock because excessive fluids can cause cardiac overload. Volume status and adequacy of resuscitation can be definitely assessed by right heart catheterization in patients suffering from right heart failure. If hypovolemia is present, conservative boluses (250–500 ml) of crystalloids are administered in order to achieve stabilization for cardiac catheterization. Constant hemodynamic monitoring is required in order to achieve adequate tissue perfusion and stable vital signs [36]. Along with crystalloid infusion, vasopressors like norepinephrine (NE) and inotropes like dobutamine are used adjunctively to manage patients with cardiogenic shock [37]. Patients who have suffered large fluid losses due to conditions like diarrhea, vomiting, or excessive diuresis, presenting with symptoms of non-hemorrhagic hypovolemic shock, are managed by administering balanced crystalloids. In patients whose chloride losses are high due to conditions like hyperemesis, 0.9% NaCl is used [38].

Conclusion

Intravenous fluids are one of the most abundantly used therapies in a hospital setting. Their use is of utmost importance in critically ill patients, especially those suffering from shock. A variety of crystalloid solutions are used to treat different types of shock, depending on the pathology involved. The major types of fluids administered to patients are crystalloid and colloid fluids, among which colloids are more effective at expanding intracellular volume since they cannot permeate the capillary membranes and redistribute fluid. Crystalloid fluids are more cost-effective, however, and are used more commonly and albumin-containing colloids are primarily administered to liver cirrhosis patients. While crystalloid fluids are the first line of treatments for shock, they come with a multitude of adverse effects and have been found to decrease blood flow to the kidneys which might result in acute kidney injury. Thus, it is imperative to take into consideration the patient's comorbidities, hemodynamic status, and electrolytes among other factors before administering crystalloid solutions for intravascular volume repletion. There is also limited research on the effect of albumin solutions in patients with sepsis, and its potential effect on mortality, and balanced crystalloids remain the first line of fluids in patients with septic shock.

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Authors' contributions

MS, AK, and PS collected data and wrote the first draft. FNU-A, SKG, and VG assisted in data collection and editing of the second draft. MP did proofreading. RJ helped with the concept, design, and final approval. All authors read and approved the final manuscript.

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