Intravenous Fluid Management in Critically Ill Adults: A Review

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Topic This article reviews the management of intravenous fluids and the evaluation of volume status in critically ill adults.
Clinical Relevance Intravenous fluid administration is one of the most common interventions in the intensive care unit. Critically ill patients have dynamic fluid requirements, making the management of fluid therapy challenging. New literature suggests that balanced salt solutions may be preferred in some patient populations.
Purpose of Paper The bedside critical care nurse must understand the properties of various intravenous fluids and their corresponding impact on human physiology. The nurse's clinical and laboratory assessments of each patient help define the goals of fluid therapy, which will in turn be used to determine the optimal patient-specific selection and dose of fluid for administration. Nurses serve a vital role in monitoring the safety and efficacy of intravenous fluid therapy. Although this intervention can be lifesaving, inappropriate use of fluids has the potential to yield detrimental effects.
Content Covered This article discusses fluid physiology and the goals of intravenous fluid therapy, compares the types of intravenous fluids (isotonic crystalloids, including 0.9% sodium chloride and balanced salt solutions; hypotonic and hypertonic crystalloids; and colloids) and their adverse effects and impact on hemodynamics, and describes the critical care nurse's essential role in selecting and monitoring intravenous fluid therapy. (*Critical Care Nurse*. 2020;40[6]:e17-e27)

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CE 1.0 hour, CERP A

This article has been designated for CE contact hour(s). The evaluation tests your knowledge of the following objectives:
1. Compare and contrast the various types of intravenous fluids, including their physiochemical properties and effects on hemodynamics.
2. Describe how strategies for selection and dosing of intravenous fluid therapy differ depending on the goals of fluid therapy.
3. Identify potential and actual adverse drug events associated with intravenous fluids.

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Intravenous fluid administration is a near-universal intervention in the intensive care unit (ICU). Use of intravenous fluids is challenging in critically ill patients because of predisposing factors that result in altered fluid distribution and accelerated volume losses. These complexities are perpetuated by the dynamic nature of critical illness, in which fluid requirements can change frequently and rapidly. Critical care nurses must be able to navigate these challenges because uncorrected fluid disturbances are associated with increased morbidity and mortality.[1] Optimal fluid management requires a thorough understanding of fluid homeostasis, composition, and impact on hemodynamics.

The intravenous fluids available for use can be broadly classified as crystalloids or colloids. Indications for fluid therapy include replacement of insensible fluid losses, replacement of volume deficits, and restoration of intravascular volume depletion. The selection of fluid composition, dose, and duration should be tailored to the goal of fluid therapy. For example, intravenous fluid resuscitation to rapidly restore systemic circulation is a fundamental component of treating critically ill patients with sepsis. Although intravenous fluids can be lifesaving, risks associated with treatment also have the potential to influence patient outcomes. Therefore, fluids should be recognized as drugs with individualized prescriptions and vigilant monitoring for each patient. This review article will enhance the critical care nurse's understanding of fluid physiology, composition of intravenous fluids, and intravenous fluid doses, indications, and adverse effects.

The relatively equal osmolarity of isotonic intravenous fluids and human plasma allows for easy passage of fluid between the interstitial and intravascular spaces.

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Fluid Physiology

Safe and effective use of intravenous fluids requires a comprehensive understanding of fluid physiology within the human body and the forces that can affect its distribution. In an average adult, water accounts for 50% of the total lean body weight in women and 60% in men.[2] Total body water is present in the intravascular space (in plasma), the interstitial space, and the intracellular space. Two-thirds of the total body water is intracellular, and the remaining third is extracellular.[3] The distribution of fluid among these compartments and total body water percentages are estimates. These variables can be influenced by several factors, including age, sex, weight, and critical illness.

The semipermeable membrane that separates these compartments allows the free passage of water through the process of osmosis. *Osmosis* refers to the distribution of water from areas of low solute concentration to areas of high solute concentration to maintain equilibrium. The driving force of osmosis is a fluid's tonicity, the solute concentration dissolved within a solution.[4] A solution's tonicity is related to its osmolarity, which is the total concentration of solutes per liter of fluid. The relatively equal osmolarity of isotonic intravenous fluids and human plasma allows for easy passage of fluid between the interstitial and intravascular spaces.

Hypotonic intravenous fluids have a lower solute concentration, which favors the movement of water from the intravascular compartment into the intracellular and interstitial spaces. Hypotonic fluids do not remain in the intravascular compartment to augment circulation. Instead, hypotonic fluids extravasate to hydrate cells and tissues and at times accumulate excessively in the interstitial spaces. Hypertonic intravenous fluids have a supraphysiological solute concentration, which draws fluids from the intracellular and interstitial spaces into the intravascular space to maintain equilibrium.[5] Understanding the relationship between osmosis and tonicity is key to appropriate fluid selection.

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Goals of Fluid Therapy

Fluid management does not use a one-size-fits-all approach. Critically ill patients require individualized fluid types, volumes, infusion rates, and durations tailored to their volume status and fluid therapy goal based on the underlying illness. This individualization is particularly important in critically ill patients because of the acute, unpredictable changes in clinical status and alternative fluid sources that complicate these factors. Fluid losses that can be easily overlooked or difficult to estimate should also be considered. Sensible fluid losses such as losses through urine, stool, wound drainage, or gastric suctioning are measurable. Insensible fluid losses secondary to prolonged fevers, sweating, labored respiration, or mechanical ventilation are not easily measured and are relatively high during critical illness. Given these complexities, an algorithm known as the 5 *R*'s (resuscitation, routine maintenance, replacement, redistribution, and reassessment) has been developed as a useful structured tool for frontline providers to guide safe and effective use of fluids in critically ill patients.[6] The Figure describes an approach to fluid management based on the 5 *R*'s.

Resuscitation

Resuscitation is targeted at restoring intravascular volume in patients with life-threatening hypovolemia and compromised end-organ perfusion. Critically ill patients requiring this intervention are those with excessive fluid or gastrointestinal losses, sepsis, active bleeding, shock, or thermal injury. Resuscitation should be initiated on the basis of objective parameters of hemodynamic instability, including hypotension, tachycardia, decreased urine output, or elevated lactate concentration. Urgent initiation of a large-volume intravenous fluid bolus is required to restore intravascular volume. Rapid intravascular volume expansion increases venous return to the heart to improve cardiac output, circulation, and perfusion to vital end organs.[1] Clinical indicators of successful resuscitation are tailored to the underlying cause but often include mean arterial pressure of 65 mm Hg or greater, urine output of 0.5 mL/kg/h or greater, and in the case of sepsis or septic shock, normalization of lactate level. In addition, patient comorbidities can influence hemodynamic monitoring. For example, patients with heart failure may require invasive monitoring with a right heart catheter to accurately assess whether preload has been optimized. Resuscitation is a lifesaving intervention, so it is paramount for nurses to identify and initiate adequate interventions without delay.

Routine Maintenance

Routine maintenance fluids are required only for euvolemic, hemodynamically stable patients who are otherwise unable to maintain daily fluid intake enterally.[7] Critically ill patients who may require routine intravenous maintenance fluids include those with neurological injuries complicated by dysphagia without enteral feeding tubes, those with impaired gastrointestinal function (eg, obstruction), and those who are receiving nothing by mouth.[6] Maintenance fluids are not indicated to correct ongoing fluid losses or electrolyte disturbances or to provide nutritional support.

Replacement

In contrast to routine maintenance fluids, replacement fluids are administered to hemodynamically stable patients with ongoing volume or electrolyte loss who do not require urgent resuscitation. Causes of volume and electrolyte loss include intermittent vomiting or diarrhea, excessive diuresis, therapeutic hypothermia, and adrenal insufficiency. The purpose of replacement fluids is to provide circulatory support to prevent decompensation requiring resuscitation, to maintain tissue perfusion, and to reestablish electrolyte homeostasis.

Redistribution

The approach to fluid therapy is inherently challenging in the subset of critically ill patients with altered fluid distribution. Redistribution, also known as third spacing, is a consequence of increased capillary permeability that causes fluid to shift extravascularly. Poor retention of fluid in the intravascular compartment results in a complex clinical picture of volume depletion in the presence of edema.[6] Sepsis is a common cause of third spacing secondary to capillary leakage provoked by the systemic inflammatory response.[8] Third spacing also results from low albumin production secondary to liver dysfunction and impaired volume elimination in patients with heart

The 5 *R*'s algorithm provides a useful structured tool for frontline providers to guide safe and effective use of fluids in critically ill patients.

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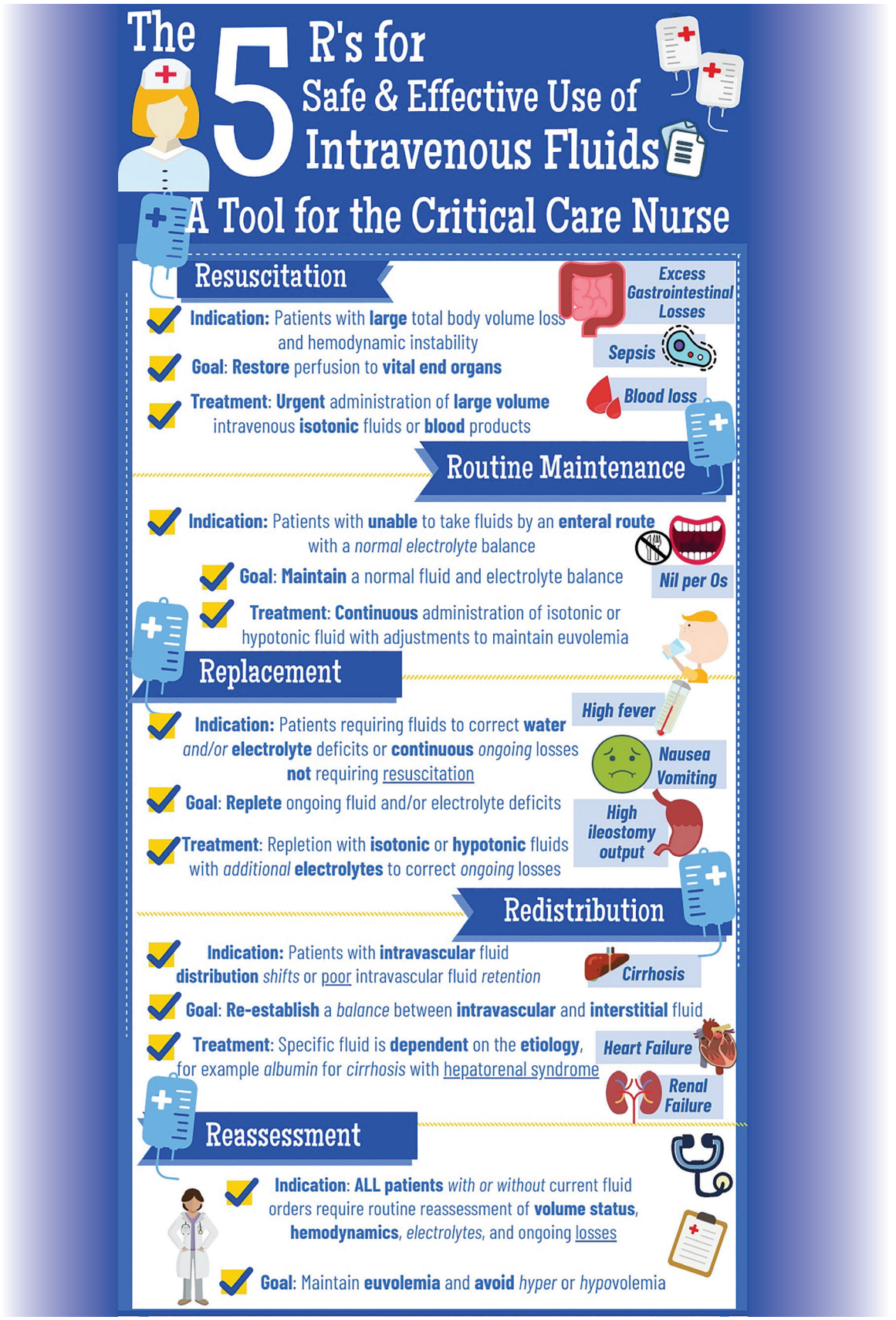

Figure The 5 *R*'s for safe and effective use of intravenous fluids.

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failure or kidney disease. Clinical signs of fluid deficit are unreliable in this population because volume overload may mask underlying intravascular depletion. Volume optimization in these patients requires a delicate balance between replacing intravascular volume and minimizing interstitial fluid accumulation.[4] Strategies to correct fluid imbalance include mobilizing interstitial fluids with the use of colloids; administering small, incremental intravenous fluid boluses for resuscitation; and restricting the total volume and duration of replacement fluids when warranted.[9]

Reassessment

Critical illness is an ongoing, dynamic process in which acquisition of new diseases or acute decompensation of existing conditions can lead to unpredictable sensitivity to fluid administration. Administering intravenous fluids without adapting to these changes can yield detrimental consequences that increase morbidity and mortality. Therefore, it is crucial to vigilantly monitor and routinely assess patients to adjust or discontinue fluids when clinically appropriate. Nurses should integrate clinical and laboratory assessments, including physical examination, vital signs, urine output, electrolytes, renal function, and acid-base status, to identify when changes in fluid therapy are warranted.

Types of Intravenous Fluids

Two broad categories of fluids are available for intravenous use: crystalloids and colloids. Consensus on the optimal fluid remains highly debated given the paucity of strong evidence establishing the superiority of one type over another. This lack of consensus leaves fluid composition, effects on hemodynamics, and distinctive adverse effects as the major governing principles guiding fluid selection.

Crystalloid Solutions

Of all available intravenous fluids, crystalloid solutions remain the most widely used in the ICU, with normal saline (0.9% sodium chloride) the most commonly prescribed.[10] Crystalloids are aqueous solutions composed of varied concentrations of molecules such as electrolytes and dextrose that influence the overall osmolality of each solution. In addition, these solutions can be broadly categorized according to their tonicity as isotonic, hypotonic, or hypertonic. The selection of the optimal crystalloid should match its physicochemical properties to the targeted hemodynamic goal.

Isotonic Solutions. Isotonic crystalloids, classified as balanced or unbalanced, are the foundation of volume resuscitation and maintenance therapy in the critically ill. These solutions have a tonicity relatively equal to that of human plasma (about 300 mOsm/L), allowing for free distribution in the body in the same proportions as total body water, of which one-third is distributed intravascularly and interstitially and the other two-thirds intracellularly.[8] The prototypical isotonic crystalloid is normal saline, which contains equal concentrations of sodium and chloride (154 mEq/L of each).[11] The term *normal* is a misnomer because this solution is far from analogous to human plasma. The solution's chloride content far exceeds the physiological concentration (154 mEq/L vs about 100 mEq/L), it is completely devoid of essential electrolytes beyond sodium and chloride, and it lacks an acid-base buffer.[12] Because its sodium content is higher than that of human plasma (154 mEq/L vs about 140 mEq/L), normal saline is slightly hypertonic. These factors have caused normal saline to be subcategorized as an unbalanced solution. Balanced crystalloids, such as lactated Ringer solution, Hartmann solution, and multiple electrolytes injection (Plasma-Lyte A, Baxter), are designed to complement human plasma. Substitution of excess chloride with a buffering agent such as lactate, acetate, or gluconate assists in neutralizing the pH and reducing osmolality, and incorporation of magnesium, potassium, and calcium provides essential electrolytes to create a fluid composition similar to that of human plasma. A detailed outline comparing the composition of the available crystalloid solutions is provided in the Table.

Consensus on the optimal fluid remains highly debated given the paucity of strong evidence establishing the superiority of one type over another.

Isotonic solutions are used as the initial intervention for resuscitation or replacement therapy to restore intravascular volume in states of sepsis, volume depletion, or dehydration.[13] Balanced crystalloids may be preferred when electrolytes and fluid volume must both be maintained (eg, with burns, fistula drainage, gastrointestinal tract losses, trauma, or surgery). Given the frequency of isotonic solution use, critical care nurses should

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Table Components of intravenous solutions[7]

Solution	Osmolarity (mOsm/L)	Electrolytes, mEq/L					Buffer	pH
		Na^+	K^+	Cl^-	Ca^{+2}	Mg^{+2}		
Human plasma	308	140	4.5	100	2.5	1.25	Bicarbonate	7.4
0.9% Sodium chloride	308	154		154				5.0
Lactated Ringer solution	277	130	4.0	109	1.4		Lactate	6.5
Hartmann solution	281	131	5.0	111	2.0		Lactate	5.7
Multiple electrolytes injection (Plasma-Lyte A, Baxter)	294	140	5.0	98		1.5	Gluconate, acetate	7.4
5% Dextrose in 0.45% sodium chloride	406	77		77				5.0
3% Sodium chloride	1026	513		513				5.8

understand the relationships between crystalloid composition and associated outcomes and the available evidence for their use in the ICU.

Universal adverse effects of all isotonic crystalloid solutions are peripheral edema and hemodilution. The rapid, unequal distribution of isotonic crystalloids from the plasma into the interstitium results in poor intravascular retention. Therefore, large volumes and frequent administration are required to restore intravascular volume.[12,14] The excessive volume can contribute to peripheral edema or pulmonary edema, which can compromise respiratory function and increase the duration of mechanical ventilation. Hemodilution causes intravascular dilution of clotting factors, which may complicate bleeding in patients not receiving blood product support.[15]

Increasing evidence suggests that the chloride-rich content of normal saline is associated with deleterious effects on patient outcomes.[16] The occurrence of hyperchloremia with normal saline administration is common, given the frequency of use and large volumes required for resuscitation. Recent evidence has correlated hyperchloremia with increased risk of acute kidney injury (AKI), metabolic acidosis, and ICU-related mortality.[1,17] Hyperchloremic metabolic acidosis is a predictable, dose-dependent, hallmark toxicity associated with normal saline administration.[1] This iatrogenic acid-base disturbance can exacerbate preexisting metabolic disorders in patients with diabetic ketoacidosis or sepsis and can confound interpretation of arterial blood gas results that are used as a markers of clinical improvement. The untoward effects on the kidney result from chloride-induced renal vasoconstriction and decreased diuresis caused by the excessive salt load, resulting in reduced renal perfusion, decreased glomerular filtration, and subsequent fluid overload.[15,18] Increased awareness of these adverse effects has led to increased use of balanced solutions when large fluid volumes are required.

Although in theory balanced solutions are similar to physiological fluids, their electrolyte composition and buffers to restore acid-base balance are not devoid of adverse effects. For example, the buffer sodium lactate contained in lactated Ringer solution is predominantly metabolized by the liver into bicarbonate. Patients with advanced liver disease have impaired lactate metabolism resulting in excessive accumulation of sodium lactate, which can falsely elevate serum lactate levels.[14,19] Exogenous lactate is also converted to glucose via gluconeogenesis, resulting in hyperglycemia. Additionally, because of its relative hypotonicity, large-volume administration of lactated Ringer solution may cause transient cerebral edema and increased intracranial pressure. Lactated Ringer solution should be used with caution in patients who have brain injuries or are at risk of increased intracranial pressure.[20] The acetate buffer in Plasma-Lyte A is rapidly metabolized through extrahepatic pathways, making it an attractive option for patients with advanced liver disease.[20] Acetate is, however, not without risk. It may suppress myocardial contractility and cause profound hypotension, specifically in patients undergoing renal replacement therapy.[14]

The different ancillary cations added to balanced crystalloid solutions also affect fluid selection. Lactated Ringer solution and Hartmann solution contain calcium, which can chelate the anticoagulant citrate present in dialysis catheters and in blood products administered through the same intravenous catheter, leading to a risk of clot formation.[19] Normal saline is the preferred fluid to be coadministered with citrate-containing solutions.[21]

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Ceftriaxone, a frequently used cephalosporin antibiotic, is incompatible for administration through a Y connector with lactated Ringer solution or Hartmann solution because of possible insoluble calcium precipitation.[22]

The potassium content in balanced crystalloids, although minimal, has led to the practice of avoiding these solutions in patients with hyperkalemia. This misconception has been refuted by clinical trial data demonstrating that the risk of hyperkalemia in high-risk populations (kidney transplant recipients and patients with AKI) is no different for balanced crystalloid solutions than for normal saline.[20] In fact, metabolic acidosis secondary to normal saline administration resulted in a higher frequency of hyperkalemia because of the extracellular shifting of potassium.[1] Nurses must understand the adverse effects of each crystalloid solution and how adverse effects translate into patient-centered outcomes in critically ill patients.

The optimal crystalloid fluid selection in critically ill patients remains an area of major controversy. The first randomized controlled trial comparing balanced and unbalanced crystalloid solutions in critically ill patients was the 0.9% Saline vs Plasma-Lyte 148 for Intensive Care Fluid Therapy trial.[23] This study evaluated 2278 patients admitted to the ICU and failed to demonstrate a difference in development of AKI (relative risk, 1.04; 95% CI, 0.80-1.36; $P = .77$), need for renal replacement therapy (relative risk, 0.96; 95% CI, 0.62-1.50; $P = .91$), or mortality (relative risk, 0.88; 95% CI, 0.67-1.17; $P = .40$) at 90 days between patients receiving Plasma-Lyte 148 and those receiving normal saline. However, most patients in the study cohort were surgical patients without sepsis, categorized as low risk for AKI and mortality. Furthermore, the conservative approach to fluid administration (median volume of 1 L) may have substantially undermined the true treatment effect in critically ill patients.

Another pilot study, Isotonic Solution Administration Logistical Testing, compared normal saline and balanced crystalloids in 1 medical ICU. The results indicated no difference between normal saline and balanced crystalloids in occurrence of overall major adverse kidney events within 30 days after enrollment (MAKE30), the composite outcome of in-hospital mortality, new renal replacement therapy, or final inpatient serum creatinine level 200% or greater of baseline (24.7% vs 24.6%, respectively; $P = .98$). However, among the subgroup of patients who received a larger volume of intravenous fluid, those who received normal saline were more likely to experience an adverse renal outcome as defined by the composite outcome.[24]

A subsequent randomized controlled trial compared the use of balanced and unbalanced solutions in high-risk critically ill patients. The Isotonic Solutions and Major Adverse Renal Events Trial compared normal saline with lactated Ringer solution or Plasma-Lyte in 15 802 ICU patients. Inclusion of patients in medical, surgical, and neurological ICUs helped diversify the applicability of the data.[25] Patients received a median of 2.5 L of crystalloid solution. The trial demonstrated a reduction in MAKE30 occurrence with the use of balanced crystalloids compared with normal saline (14.3% vs 15.4%; $P < .04$; odds ratio, 0.90 [95% CI, 0.82-0.99]). Patients with sepsis or septic shock derived the greatest benefit from balanced crystalloids (number needed to treat, 20 patients to prevent 1 from experiencing MAKE30). Although the absolute difference in mortality was only about 1%, these findings have substantial clinical relevance owing to the vast number of critically ill patients who receive intravenous fluids in real-world practice. On the basis of this evidence, clinicians should strongly consider the use of balanced crystalloids in critically ill patients, especially those who have AKI, are receiving renal replacement therapy, or require large volumes of fluid (eg, patients with sepsis).

Patients with traumatic brain injury were seldom randomized to receive balanced crystalloids because of the theoretical risk of potentiating elevations in intracranial pressure. Clinicians prescribed normal saline for many patients with traumatic brain injury in these trials, so balanced crystalloids cannot be recommended for patients with traumatic brain injury until further studies are conducted. Two recent meta-analyses also found no differences between balanced crystalloids and normal saline relative to in-hospital and ICU mortality, AKI development, and new requirement for renal replacement therapy in critically ill patients.[26,27] However, these meta-analyses are limited by the quality of the included studies, some of which reported small sample sizes, receipt of other fluid types before study enrollment, different designs, and brief (24- to 72-hour) durations of fluid administration.[26,27] Further clinical trials need to be conducted to be able to conclusively state that no differences exist between the solutions. Therefore, despite outcomes reported by these meta-analyses, using

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balanced crystalloid solutions in the patient populations studied is reasonable to reduce the risks of new or worsening AKI and new requirement for renal replacement therapy.

Hypotonic Solutions. Hypotonic solutions include dextrose 5% in water, 0.45% sodium chloride, and the combination of dextrose 5% in water and 0.45% sodium chloride. Although glucose contributes to the osmolarity of a solution, it does not contribute to the tonicity of a solution, because glucose can cross cell membranes, unlike sodium and chloride ions.

Hypotonic solutions provide free water to restore intracellular fluid deficits. Common indications for hypotonic solution administration are states of excessive free-water loss, such as diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome, and correction of hypernatremia.[5,28] Upon administration, hypotonic solutions distribute into the interstitial or intracellular spaces with little intravascular retention. Therefore, hypotonic solutions are not used for resuscitation or to correct hypovolemia because they will not restore intravascular volume. Additionally, redistribution into the central nervous system can lead to increased intracranial pressure and cerebral edema. Large-volume or prolonged duration of hypotonic fluid administration has been associated with hospital-acquired hyponatremia, with more than 100 reports of iatrogenic death or permanent neurological impairment related to hyponatremic encephalopathy.[7] Avoidance of hypotonic fluids has become standard in patients with traumatic brain injuries or other central nervous system disorders.[28] The risk of peripheral edema is also of concern, especially in patients predisposed to redistribution. A prevailing practice is to administer hypotonic fluids as routine maintenance, often as a combination of dextrose 5% in water and 0.45% sodium chloride. This dextrose content is insufficient for complete nutritional support but may provide adequate calories to prevent hypoglycemia, depending on the rate of infusion.

Hypertonic Solutions. Hypertonic solutions, such as 3% sodium chloride, have substantially higher osmolarity and sodium and chloride content than human plasma. These fluids are called plasma expanders because the strong osmotic force draws extravascular fluid into the intravascular space. Smaller volumes are required to restore intravascular volume as compared with isotonic solutions, minimizing the risk of volume-related adverse effects.[2] Common indications for hypertonic saline administration include severe symptomatic hyponatremia and elevated intracranial pressure. Hypertonic solutions carry a risk of volume overload, and vigilant monitoring is required for critically ill patients with predisposing conditions such as cardiac or renal disease.[9] In contrast to hypotonic fluids, hypertonic saline can potentiate cellular dehydration and should be avoided in patients with diabetic ketoacidosis or dehydration. Rapid correction of hyponatremia (more than 10-12 mEq/L/d) with hypertonic saline may result in an irreversible neurological condition called *central pontine myelinolysis*. Diligent monitoring of sodium level and osmolality is necessary to prevent abrupt increases. Hypertonic saline should be administered through a dedicated central catheter to reduce the risk of phlebitis because of the high osmolarity.[28] Because of the potential risks associated with hypertonic saline, it should be administered only in high-acuity areas with increased nursing surveillance.[28]

Colloid Solutions

Colloid solutions contain large insoluble molecules (eg, proteins or starches) that are relatively impermeable to cell membranes. These molecules restore fluid balance by establishing a high oncotic pressure gradient that draws fluid from the interstitium into the intravascular space. These solutions are often referred to as plasma expanders, similar to hypertonic crystalloids. Intravascular persistence gives colloids a durable duration of fluid expansion of 12 to 24 hours, as compared with 1 to 4 hours for crystalloids.[29] By extracting excess fluid from interstitial spaces, colloids are considered volume sparing. Traditionally, administration of 1 L of colloid solution was thought to provide a similar volume expansion as 3 to 4 L of crystalloid solution, but new studies in patients with critical illness demonstrate that the true ratio is closer to 1 L of colloid solution to 1.4 L of crystalloid solution.[3]

Albumin is a large endogenous protein that is synthesized exclusively by the liver and serves to maintain a high oncotic pressure within the intravascular space. Commercially available albumin is harvested from pooled human plasma and is available in a 5% or 25% solution. The 5% solution is classified as iso-oncotic. This solution is used for hypovolemic states and effectively increases intravascular fluid volume by 100%. The 25% solution is hyperoncotic, increasing plasma volume by approximately

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400%. This solution is selected for critically ill patients with third spacing requiring fluid mobilization from the interstitium.[1] The 25% albumin solution may cause circulatory compromise in the presence of total body water deficits because mobilization relies on adequate stores of interstitial fluid.

Albumin is the most commonly used colloid in the ICU, but its role in clinical practice has been a longstanding controversy. Hypoalbuminemia can be a consequence of critical illness secondary to malnutrition, advanced liver disease, sepsis, inflammation, or trauma.[29] Although low concentrations of circulating endogenous albumin are associated with longer ICU stays and increased mortality, replacement with exogenous albumin has not been consistently correlated with improved clinical outcomes.[29,30]

The Saline Versus Albumin Fluid Evaluation trial compared 4% albumin with normal saline for ICU resuscitation. For the primary outcome of 28-day all-cause mortality, no differences were observed between the 2 groups (relative risk, 0.99; 95% CI, 0.91-1.09; $P = .87$). These findings were not consistent in all populations. A heightened relative risk of death was observed in the subgroup of patients with traumatic brain injury who received albumin, as compared with those who received normal saline (relative risk, 1.62; 95% CI, 1.12-2.34; $P = .009$).[31] This difference was driven by altered blood-brain barrier permeability allowing leakage of albumin into the cerebral space, causing detrimental elevations in ICP.[32] In contrast, a trend toward reduced mortality was observed in patients treated for severe sepsis who received albumin (relative risk, 0.87; 95% CI, 0.74-1.02).[31] Although promising, this effect has not been consistently reproduced in other clinical trials and meta-analyses.

Because the available evidence demonstrates no alarming safety concerns and overall outcomes are similar to those of crystalloids, the sepsis guidelines recommend considering albumin if crystalloids fail to restore intravascular volume.[33] Given the comparable efficacy of albumin and crystalloids and the higher cost of albumin, it is prudent to reserve the use of albumin for scenarios in which albumin has demonstrated survival benefits aside from sepsis. Indications with the most robust evidence include spontaneous bacterial peritonitis, large-volume paracentesis, hepatorenal syndrome, and therapeutic plasmapheresis.[29,34] Albumin should not be used for the sole purpose of normalizing plasma albumin levels in malnourished or critically ill patients.[34] With respect to safety, albumin is a plasma-derived product and carries the potential risk of transmitting blood-borne infections. Anaphylactic reactions are a rare, potentially life-threatening adverse effect. Nurses should be vigilant about checking patients' allergy histories and should monitor patients closely for bronchospasm, increased oxygen or ventilator requirements, and new or worsening tachycardia or hypotension during albumin infusions.

Hetastarch and dextran are carbohydrate-based semisynthetic colloids that provide an unpredictable duration of volume expansion and are associated with significant adverse effects, including AKI, hepatotoxicity, coagulopathies, and bone marrow failure.[2,35] Several clinical trials have suggested harm with the use of hetastarch and dextran in critically ill patients with sepsis.[36] Furthermore, a recent meta-analysis confirmed an increased risk of AKI requiring renal replacement therapy and mortality associated with hetastarch.[37] To reflect the increased risk of mortality and AKI requiring renal replacement therapy, the Food and Drug Administration mandated a black box warning for hetastarch and placed a contraindication for its use in critically ill patients, including individuals with sepsis.[38] Consequently, use of these products in clinical practice is limited.

Monitoring Fluid Therapy

Fluid therapy is a well-established lifesaving intervention, but aggressive administration without adequate monitoring and reassessment can negate the beneficial effects of this treatment. The development of fluid overload has been directly associated with increased mortality in critically ill patients. Furthermore, fluid overload can cause heart failure; pulmonary edema resulting in impaired gas exchange; bowel dysfunction; and peripheral edema resulting in delayed wound healing, wound infections, and pressure ulcers.[39] Therefore, the importance of nurses in monitoring and assessing fluid status to prevent these complications cannot be underestimated. To detect hypervolemia, nurses should assess for signs and symptoms of fluid overload such as bounding pulse, pulmonary crackles, shortness of breath, peripheral edema, jugular venous distention, and extra heart sounds (S3).[39]

Because of the risks of intravenous fluid therapy and because approximately 50% of patients respond to this

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therapy, predictors of fluid responsiveness can be used to help determine if an individual patient is likely to respond to intravenous fluid therapy. Static measures of fluid responsiveness such as right ventricular end-diastolic volume, left ventricular end-diastolic volume, central venous pressure, and pulmonary artery occlusion pressure are no longer routinely recommended to guide or assess response to intravenous fluid therapy.[40] Dynamic measures such as stroke volume variation, pulse pressure variation, and inferior vena cava collapsibility are better able to predict fluid responsiveness.[40]

Effectiveness of intravenous fluid therapy is frequently defined as an increase in blood pressure or cardiac output, and the degree and rapidity of the desired increase is patient specific. Additionally, increases in urine output to greater than 0.5 mL/kg/h or decreases in lactate level may indicate that a patient is responding appropriately to intravenous fluid therapy. Dynamic measures of fluid responsiveness, including echocardiography to measure cardiac output, stroke volume variation measurement, and others, may be more appropriate measures of response to intravenous fluids.[41]

The development of fluid overload has been directly associated with increased mortality in critically ill patients.

It is also important to recognize additional factors that contribute to fluid overload, such as intermittent administration of intravenous medications and continuous infusions of vasopressors, antihypertensives, sedatives, analgesics, and total parenteral nutrition products, which can account for a significant portion of administered fluid. Having greater than 10% fluid overload (calculated by subtracting total fluid output in liters from total fluid intake in liters, dividing by admission body weight in kilograms, and multiplying by 100) is associated with a higher mortality rate.[3,42] Monitoring for underresuscitation and underreplacement is another essential role of the critical care nurse. To detect hypovolemia, nurses assess for lower-than-anticipated blood pressure (either systolic or mean arterial pressure), tachycardia in a patient with hypotension (which may be a compensatory response to hypotension), decreased urine output, and increased capillary refill time.[42] Conversely, patients with diabetes insipidus, hyperglycemic emergencies, or iatrogenic diuretic overuse may have excessive urine output leading to hypovolemia. Other adverse effects of fluid therapy that require monitoring are electrolyte disorders, acid-base disorders, and AKI. Laboratory values that pertain to volume status and adverse effects associated with fluid therapy are sodium, creatinine, and lactate, which should be monitored at least once daily in patients whose condition is unstable. Other electrolytes, such as potassium, chloride, and magnesium, should also be checked before fluid therapy and at intermittent intervals because they play an important role in appropriate fluid selection and ensure that safe electrolyte balance is maintained.[3] Patients present at different stages of fluid needs and may develop acute illness processes that affect their fluid status and needs in a dynamic manner. For this reason, constant reevaluation of patients and their fluid therapy by the bedside critical care nurse is essential.[43]

Conclusion

Critical care nurses serve an essential role in the management of intravenous fluid therapy in critically ill patients. The lack of uniform consensus on the ideal intravenous fluid underscores the importance of having a comprehensive understanding of the fluid types, fluid physiology, and evidence to support and refute their use in specific populations. It is paramount to recognize that intravenous fluid therapy in critically ill individuals requires a patient-specific approach with frequent reassessment to ensure that the desired outcomes are achieved while minimizing toxicity. CCN

Financial Disclosures
None reported.

See also

To learn more about fluid management in the critical care setting, read "Clinical Presentation and Treatment of Amniotic Fluid Embolism" by McBride in *AACN Advanced Critical Care,* 2018;29(3):336-342. Available at **www.aacnacconline.org**.

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