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Maintenance parenteral fluids in the critically ill child

Karen Choong,[1] Desmond Bohn[2]

Abstract

Objective: To examine electrolyte-free water requirements that should be considered when administering maintenance fluids in a critically ill child. We examine some of the difficulties in estimating these requirements, and discuss the controversies with respect to the traditional recommendations.

Sources: MEDLINE (1966-2007), Embase (1980-2007), and the Cochrane Library, using the terms: "fluid therapy", "hypotonic", "isotonic solution", and synonyms or related terms.

Summary of the findings: The ideal maintenance solution and fluid regimen remains a topic of heated debate in pediatrics. The traditional recommendations for maintenance fluids are increasingly criticized as they do not consistently apply in acute illness, where energy expenditure and electrolyte requirements deviate significantly from the original estimates. A physiologically based framework for prescribing maintenance fluids is presented, with the objective of maintaining tonicity balance, and infusing the minimum volume of maintenance fluid required to maintain hemodynamics. Indications for isotonic and hypotonic solutions are discussed.

Conclusions: Maintenance fluid prescriptions should be individualized. No single intravenous solution is ideal for every child during all phases of illness, but there is evidence to suggest that the safest empirical choice is an isotonic solution. Hypotonic solutions should only be considered if the goal is to achieve a positive free-water balance. Critically ill children may require a reduction by as much as 40-50% of the currently recommended maintenance volumes. All patients receiving intravenous fluids should be monitored closely with daily weights, fluid balances, biochemical and clinical parameters in order to best guide this therapy.

J Pediatr (Rio J). 2007;83(2 Suppl):S3-10: Fluid therapy, fluid maintenance, blood, electrolytes, isotonic solution.

Introduction

Intravenous (IV) fluid is the commonest medical intervention administered to hospitalized children in developed countries today. The indications for IV fluid are to either expand a contracted extracellular fluid (ECF) space, or as "maintenance" fluids, to replace urine output and insensible losses in a fasting patient. Adverse events related to improper use of maintenance fluids are disturbingly common. What constitutes "proper" or the most appropriate regime for IV maintenance is still furiously debated despite half a century of its practice since Holliday & Segar's original recommendations in 1957.[1] The Holliday & Segar guidelines related maintenance fluid requirements to one of three convenient weight-based categories (≤ 10 kg, 11-20 kg, and > 20 kg). This formula remains the most popular and universally used to date and continues to be the standard recommendation in current pediatric medical texts.[2,3] It is increasingly suggested, however, that while these recommendations may be appropriate for the healthy child, they do not consistently apply in acute illness, where energy expenditure and electrolyte requirements deviate signifi-

1. MB. Division of Pediatric Critical Care and Department of Paediatrics, McMaster University, Hamilton, ON, Canada.
2. MB. Department of Critical Care Medicine, Hospital for Sick Children, Toronto, Canada. Departments of Anaesthesia and Paediatrics, University of Toronto, Toronto, Canada.

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cantly from this formula. This article focuses on the potential electrolyte-free water (EFW) requirements that should be considered when administering maintenance IV fluids in a child in the critical care setting. We will discuss the pitfalls and difficulties in estimating these requirements, particularly in a critically ill child, and some of the controversies with respect to the traditional fluid recommendations. Finally, we will present a physiologically based approach for prescribing maintenance IV fluids. These discussions will not extend to the neonatal population, which have their own unique fluid and electrolyte requirements.

Estimation of EFW requirements

Holliday & Segar's traditional guidelines calculate maintenance fluid volumes to match EFW requirements from estimates of water evaporation (heat dissipation) and caloric expenditure (heat production). The guidelines indexed EFW requirements to metabolic rate, equating 1 mL of water with a fixed consumption of 1 kcal.[1] Using this approach, insensible water loss for a 10-kg child is 50 mL/kg/day. Subtracting endogenous water production from oxidative metabolism of 16 mL/kg/day results in a net insensible water loss of 34 mL/kg/day. Obligatory urinary losses based on the water required to excrete the solute load of cow's milk is 66 mL/kg/day. These calculations result in the convenient estimate for EFW requirements for maintenance therapy of 100 mL/100kcal/day.[1]This estimation of EFW requirements have been criticized for several reasons: a) this model of energy expenditure was based on healthy children, leading to an inaccurate assumption of energy expenditure and hence insensible losses during diseased states, b) there is a restricted ability to excrete EFW due to antidiuretic hormone (ADH) secretion during acute illness and c) the kidney can actually generate EFW under certain conditions. We will discuss these calculations, and how they are important during the consideration of maintenance IV fluid prescription.

Caloric expenditure calculation

EFW needs are based on unreliable criteria, especially if energy expenditure is based on body weight. Investigators have demonstrated that actual energy expenditure can not be predicted reliably from commonly used formulas as this often results in an overestimation.[4] Insensible water loss in acute illness is not constant, and varies with environmental factors such as temperature, air circulation, humidity, cutaneous blood flow and muscle activity. Caloric expenditure and the resultant generation of endogenous water can vary significantly with the level of activity and dietary intake or caloric deprivation and thus considerably differs during diseased states as opposed to health ones.[5,6] Several investigators have observed that the incidence of hypermetabolic states in critically ill children is low compared to adults.[4,7] Actual energy expenditure is much less than previously assumed even in children with sepsis, trauma or surgery for a variety of reasons such as physical immobility, sedation, the use of muscle relaxants, mechanical ventilation, and additional factors such as nonessential or facultative metabolism. Production of endogenous water from tissue catabolism may actually increase during acute illness.[6,8] Water production by metabolism in critically ill patients may balance evaporative water losses via alveoli in a 1:1 proportion. Using indirect calorimetric measurements, energy expenditure in critically ill children may be as low as 50-60 kcal/kg/day.[4,9] Mechanical ventilation decreases the work of breathing as well as evaporative water loss through the respiratory tract and the energy expenditure for thermal regulation. Warmed humidification of respiratory gases through the ventilator circuit can reduce insensible water losses by as much as one third.[10] Hence, traditional estimates for maintenance fluid volumes particularly in critically ill children cannot be quantified from these general guidelines.

Inability to excrete EFW

The most potent stimuli for ADH secretion are an increase in serum osmolality, hypovolemia and hypotension. However, multiple nonosmotic stimuli such as pain, drugs and anesthetic agents, stress, and even nausea and vomiting may also result in increased ADH activity, which has been clearly demonstrated in hospitalized children.[11-13] In such patients, there will be very little if any excretion of EFW, as ADH limits renal water excretion in this setting, even in the presence of a low plasma osmolality.[14] As a result, hyponatremia occurs due to a positive balance of EFW in association with an impaired ability to excrete hypotonic urine. Any exogenous sources of free water, such as the administration of hypotonic IV maintenance fluids, will therefore further exacerbate the fall in plasma sodium (PNa).

Generation of EFW

While ADH acts to prevent the excretion of EFW, the kidney can also generate free water. Steele et al. observed that the expansion of the extracellular fluid (ECF) volume with isotonic or near-isotonic fluids in the perioperative period resulted in hyponatremia due to a generation of EFW during excretion of hypertonic urine, which the authors have termed, a "desalination" phenomenon.[15] The pathophysiology of this process is not fully understood, but it is likely multifactorial and related to the volumes of saline infused to maintain adequate blood pressure after induction of anesthesia, in combination with increased ADH, natriuretic peptide, increased glomerular filtration, and suppression of aldosterone. Postoperatively, when the anesthetic agent wears off, the overexpansion of the ECF volume stimulates urinary excretion of Na^+ and K^+ in hypertonic urine. EFW is not excreted due to the actions of ADH, despite the use of isotonic or near-isotonic solutions. This results in the development of hyponatremia, whose risk and severity are further exacerbated if a hypotonic solution is administered.

In summary, the estimates for EFW needs in maintenance fluids are currently based on unreliable criteria. Additional factors, such as nonosmotic ADH secretion, further limit the ability to excrete EFW. Using the traditional maintenance fluid volume recommendations may therefore result in a gross overestimation of EFW requirements in the critically ill child.

Electrolyte requirements vs. tonicity balance: the hypotonic-isotonic conundrum

Clinicians continue to argue whether hypotonic or isotonic fluids are the ideal maintenance solutions for hospitalized children (see Appendix at the end of this article).[16,17] Holliday & Segar recommended adding 3.0 and 2.0 mEq/100kcal/24h of sodium and potassium, respectively, based on estimates of dietary requirements, and balancing the sodium intake-to-urinary-excretion ratio in healthy milk-fed infants.[1,5] This rationale is the basis for the widely accepted practice of prescribing hypotonic maintenance solutions (i.e. 0.2% saline in 5% dextrose water) for all sick children. However, inaccurate estimates of maintenance fluid and electrolyte requirements are important determinants of subsequent morbidity. Hyponatremia is the commonest electrolyte disorder amongst hospitalized children,[18] and the association between hypotonic maintenance solutions and the risk of hyponatremia has now been repeatedly identified in several studies.[19-21] The incidence of hospital-acquired hyponatremia has been reported to be as high as 50% in some instances.[22,23] Hypotonic maintenance solutions exacerbate the fall in plasma sodium (PNa) as it provides an exogenous source of EFW during acute illness when ADH secretion limits the renal excretion of EFW. Hoorn et al. demonstrated that the most important factor contributing to hospital-acquired hyponatremia in their case control study was hypotonic fluid administration.[21] Neville et al. demonstrated that infusing a hypotonic solution which is lower in tonicity than that of the urine passed is predictive of a decrease in PNa in children with gastroenteritis.[13] Our recently conducted systematic review of maintenance fluids for hospitalized children revealed that the use of hypotonic fluids remarkably increased the odds of developing hyponatremia by 17 times when compared to isotonic fluids.[19] This risk is particularly evident in the postoperative population. The symptoms of hyponatremia may be non-specific and subtle such as nausea and vomiting,[21] which are typically attributed to other causes until more overt symptoms of cerebral edema and increased intracranial pressure develop. While the morbidity related to hospital-acquired hyponatremia in children receiving hypotonic maintenance solutions is increasingly recognized,[24-28] unacceptably high adverse outcome rates of up to 30% (death or neurological injury) are still reported.[20] What is of concern is that these reports identify previously healthy and not necessarily critically ill patients, who are at highest risk.[29-31] The risk of hyponatremia and adverse neurological sequelae in these patients is seldom recognized or anticipated[12,29,30], and is thus compounded by the administration of hypotonic solutions, and minimal biochemical and fluid monitoring. Several narrative reviews have described the harm associated with the routine use of hypotonic solutions and therefore recommend that their routine use in children be reconsidered or even abandoned.[11,32]

Tonicity balance

It has been demonstrated that it is not simply the sodium intake, but its ratio to free water intake that influences plasma sodium concentrations.[21] PNa is a convenient marker as it reflects the ratio between effective osmoles and total body water. As Na^+ is the principal extracellular cation and therefore the main determinant of ECF volume, it regulates water movement across cell membranes and explains the development of intracellular edema that occurs in the presence of hyponatremia. The expansion of intracellular fluid volume is of major importance in the central nervous system as the brain is confined in a rigid bony cage and has only limited ability to expand. Small increases in intracellular fluid may lead to disproportionately large increases in intracranial pressure, which may be catastrophic in clinical conditions such as in traumatic brain injury or diabetic ketoacidosis. Children are at greater risk of neurological sequelae secondary to hyponatremia because their brains have a larger intracellular fluid volume per total skull volume.[20] These children who develop symptomatic hyponatremia have a substantially higher incidence of permanent brain damage than adults.[33] Advocates for the use of isotonic maintenance solutions therefore emphasize that in acute illness the single most important role of sodium is the maintenance of plasma tonicity and its central role in the distribution of water between intracellular and extracellular compartments.[3,32]

The reluctance to use isotonic solutions in children is primarily attributed to the risks of developing *hypernatremia*.

Excessive renal solute loading, a greater-than-recommended daily nutritional sodium supply and a urinary tonicity that is less than or approximates half normal saline are the commonest arguments against the use of isotonic fluids in children.[34] However, these concerns have yet to be substantiated in the literature, and hypernatremia has yet to be reported in adults as a result of the routine use of isotonic solutions. On the contrary, the risks of hyponatremia may also extend to patients receiving isotonic or near-isotonic fluids, particularly following surgery. [12,29,31,35,36] This can be explained at least in part by the excretion of relatively hypertonic urine, as described in several studies[13,35-37], and by the "desalination" phenomenon, as described by Steele et al.[15] The use of hypotonic fluids in these settings further exacerbates the severity of hyponatremia, while isotonic fluids may limit this risk. Powell et al. observed that the administration of isotonic maintenance solutions in sick children with elevated ADH resulted in a more rapid return of ADH to normal concentrations, when compared to hypotonic fluids[38] Neville at al. demonstrated in a prospective randomized study of IV fluid solutions in children with gastroenteritis that isotonic saline protected against the development of hyponatremia without causing hypernatremia, when compared to hypotonic fluids.[13] Isotonic solutions were found to be safe, as hyponatremic children retain sodium, while normonatremic children excrete sodium appropriately.

A framework for prescribing intravenous maintenance fluids

Compared to other therapies used in pediatric critical care, salt and water are easy to use and the traditional guidelines appear to be routine. Hence, it is also easy to overlook that this simple daily intervention may have potentially significant morbidity and even mortality. The prescription and administration of IV fluids should be considered an invasive procedure, and therefore should be treated with the same respect and vigilance as any drug prescription. Clinicians should consider the risks and monitor their patients appropriately. Dosages (i.e. type of solution and volume) should be *individualized*. Physiologic and biochemical parameters that are affected by IV fluid therapy, such as electrolytes, glucose, body weight and fluid balances, should be followed closely in response to therapy in a manner similar to therapeutic drug monitoring. Hospitalized patients' insensible losses vary greatly, and so do their activity, body temperature and degree of catabolism. Furthermore, it has been demonstrated that these requirements often change during the course of illness.[4] Similar to drug metabolism and clearance which varies with acute illness, we do not assume that one type of IV solution is ideal for a critically ill patient's entire clinical course. Hence, the "1 size fits all" for maintenance fluid prescription does not have a physiologic rationale. The potential morbidity and mortality related to maintenance IV fluid is unacceptable. Our view is that electrolyte imbalances and thus morbidity are preventable if IV fluid is tailored to the individual, and a physiologically based fluid therapy approach is adopted.

Maintaining tonicity balance: an empirical approach

No single fluid rate or composition is ideal for *all* children, however isotonic solutions *may* be the most physiologic, and therefore the safest empirical choice for maintenance IV fluids in the critical care setting. Isotonic fluids are more likely to preserve intracellular integrity by minimizing changes in PNa and tonicity. Our view is that the choice of a solution in the acute setting should not be for the purpose of satisfying the calculation of the daily sodium or caloric requirements for a healthy child, but should aim to maintain tonicity balance in the acute phase of illness and in the postoperative period when the patients are at highest risk of fluid and electrolyte abnormalities, in particular hyponatremia. Excretion of EFW is limited in these patients, and thus further administration of exogenous EFW in the form of hypotonic solutions increases the risk of acute hyponatremia, and its associated morbidity.[11,13,39] Isotonic IV solutions should be considered (or hypotonic solutions should be avoided/contraindicated) in patients for whom a higher effective osmolality needs to be maintained, or a fall in effective osmolality should be avoided during their critical period of illness – e.g. CNS injury, diabetic ketoacidosis. Isotonic solutions are also indicated in the postoperative period, and in patients with gastroenteritis, especially when accompanied by evidence of increased urinary tonicity. It is important to bear in mind that isotonic solutions do not prevent the risk of hyponatremia, but are more likely to decrease the probability of its occurrence.

Maintaining tonicity balance: a calculated approach

Changes in natremia are typically analyzed in EFW terms. While an EFW approach predicts the degree of change in PNa, it does not reveal the bases for a change in natremia, nor does it lead to correct therapy. Carlotti et al. have proposed that a more accurate way of determining changes in natremia is by calculating a tonicity balance, where total inputs and outputs, and the mass balance for both Na^+ and K^+ rather than just Na^+ alone, are considered.[40] Calculating actual tonicity balance not only predicts the rise in a patient's PNa, but also provides information about its bases in terms of net balance of Na^+ and EFW. This then provides information to design a specific fluid prescription to correct dysnatremia, while returning ICF and ECF compartment volumes to normal.

While this tonicity balance approach provides a more reliable method for developing fluid therapy, the following information is required – body weight and an estimate of total body water, total inputs and outputs for fluid volume and electrolytes, and the change in PNa.

Isotonic solutions should be avoided in patients with ECF overload, such as cardiac heart failure and liver and renal failure, where increasing effective osmolality exacerbates ECF overload, and therefore sodium restriction should be the goal. Isotonic solutions should also be considered with caution in patients with ongoing EFW losses or deficit.

When should hypotonic solutions be considered?

Hypotonic solutions should be administered if the goal is to create a positive balance for EFW, e.g. on occasions where there is an EFW deficit that may occur with large water or osmotic diureses, or if there is non-renal loss via the gastrointestinal tract or skin. We do not recommend hypotonic solutions if the patient has evidence of increased *intracellular* EFW (i.e. a PNa < 138 mM in the absence of hypoglycemia.) Hypotonic solutions should also be avoided in patients who are at increased risk of a greater drop in PNa with the exogenous administration of EFW, for example in the immediate postoperative period for reasons described earlier, and also in patients with reduced skeletal muscle mass, as 50% of body water is contained in skeletal muscle in normal subjects. As energy expenditure is related to fat-free mass, patients with diminished skeletal muscle mass require less EFW intake to produce a significant drop in PNa – hence increasing these patients' risk of developing hyponatremic encephalopathy. Finally, it is important to account for occult sources of exogenous EFW intake, e.g. ice chips. Hyponatremia *per se* is not necessarily an absolute indication for treatment with isotonic saline. Isotonic saline increases PNa only if it is accompanied by increases in urinary EFW excretion. In patients with syndrome of inappropriate antidiuretic hormone secretion for example, isotonic saline may not increase PNa as it is excreted in hypertonic urine. In this instance, the coadministration of a loop diuretic which blocks the ability to concentrate urine, thereby increasing the excretion of EFW, is warranted.

What is the ideal maintenance fluid volume?

What constitutes an appropriate maintenance fluid volume to be administered to critically ill children remains unclear. The traditional recommendations for EFW requirements will lead to an overestimation, particularly in critically ill, mechanically ventilated patients, and hence there is a rationale for reducing standard maintenance fluid rates by up to 40-50% in some instances, provided the patient is not hypovolemic.[22,32,34,41] This view is increasingly supported in the literature.[11,42] While it is important to prevent hyponatremia, one must not do so at the expense of a large positive fluid balance. The treatment and prevention of hyponatremia are not simply to add more salt, especially if antidiuresis is the patient's primary problem. Isotonic solutions may not be effective in preventing hyponatremia in such instances unless fluid volume is also reduced.[6,43] The minimum volume of isotonic fluid needed to maintain hemodynamics should be infused. Fluid restriction, or rather the reduction of maintenance fluid volumes to a more appropriate estimate of free-water requirements in the critically ill child should be considered. Furthermore, there is substantial evidence within the critical care literature that a conservative fluid strategy should be adopted in patients with acute lung injury, after these patients are out of shock.[44]

Glucose during maintenance fluid therapy

It is generally accepted that children in general require dextrose in their maintenance fluids to avoid the potential risks of hypoglycemia, however hyperglycemia is surprisingly common amongst critically ill children.[45] The importance of tight glycemic control with insulin infusion and its impact on reducing morbidity and mortality in critically ill adults led us to re-examine the hazards of hyperglycemia in the pediatric critical care setting. Hyperglycemia has been shown to be a negative prognostic indicator in children with traumatic brain injury, and is associated with reduced immune function and increased mortality in burn patients.[46] In a retrospective cohort study, early and prolonged hyperglycemia was found to be associated with a 3- and 6-fold increased risk of mortality, respectively, in critically ill children.[45] The incidence of hypoglycemia is not as common as previously thought, in an era where the amount of glucose administration has significantly decreased.[47] It is prudent to avoid dextrose in maintenance fluid infusions in patients who are at highest risk (e.g. traumatic brain injury, and burn patients) with the proviso that glucose monitoring remains vigilant in order to avoid hypoglycemia.

Summary

The traditional guidelines for prescribing maintenance fluids in children are not based on clinical experimental evidence using patient important outcomes, and do not necessarily provide optimal fluid and electrolyte homeostasis in hospitalized children. While the potential risks associated with IV fluid therapy are recognized, there are no clinical trials that currently demonstrate that one type of maintenance IV fluid is safer than the other. However, we can make recommendations in order to prevent complications. Firstly, the risk factors for hyponatremic encephalopathy should be anticipated and its development avoided. Until there is more evidence to the contrary, we recommend a physiologically based approach when prescribing maintenance IV fluids, which targets tonicity balance and limits changes in ICF or ECF volume. The safest empirical choice is therefore an isotonic solution. Hypotonic solutions should only be considered if the goal is to achieve a positive free-water balance. The minimum volume of maintenance fluid required to maintain hemodynamics should be infused. There are particular considerations unique to the critically ill child that advocate for a reduction by as much as 40-50% of the currently recommended volumes, once the patient is intravascularly replete. No empirical therapy, however, is free of potential adverse effects if therapeutic endpoints are not monitored. All patients receiving IV fluids should be monitored closely with a minimum of daily weights, strict fluid balances, biochemical and clinical parameters of ECF and ICF volume status. Water and solute intake can thus be adjusted accordingly. These parameters are often routinely monitored in the critically ill child. However, it is in children who are less ill and therefore not admitted to critical care areas that these risks are least anticipated, but in whom such vigilance should become routine in order to minimize the iatrogenic complications of this ubiquitous therapy.

Appendix

Definition of tonicity and osmolality

Osmolality is a measure of the number of particles present in a solution. Water moves freely across cell membranes to ensure equal osmolalities in ECF and ICF. Tonicity is the *effective osmolality* and is equal to the sum of the concentrations of the solutes, which have the capacity to exert an osmotic force across the membrane. Sodium is the main cation in the ECF, and hence it is the main determinant of ECF volume ("Effective Osmolality" / "tonicity"). The concentration of salt in a solution determines its tonicity. An isotonic solution will have approximately 154 mEq/L monovalent cations (sodium plus potassium), as the average concentration of sodium plus potassium in the aqueous phase of plasma is 154 mEq/L. An isotonic solution contains 0.9% saline. Lactated Ringer's solution is considered a "near-isotonic" solution. Hypotonic solutions contain between 0.45% and 0.18% of saline. A 5% dextrose (D5W) solution is often used in children to prevent hypoglycemia. After metabolism of the infused glucose, a solution containing only dextrose becomes equivalent to water.

IV solution	Na (mEq/L)	K^+	Cl^-	Osmolality (mOsm/kg/H_2O)	% Electrolyte-free water*
5% dextrose in water	0			252	100
0.2% NaCl in 5% dextrose in water	34		34	321	78
0.45% NaCl in 5% dextrose in water	77		77	406	50
Lactated Ringer's solution	130	4	109	273	16
5% dextrose lactate Ringer's solution	130	4	109	525	16
0.9% NaCl in 5% dextrose in water	154	154		560	0

* Based on a sodium plus potassium concentration in the aqueous phase of plasma of 154mEq/L, assuming that plasma is 93% water with a plasma sodium of 140 mEq/L and a potassium concentration of 4 mEq/L.[48]

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Correspondence:
Karen Choong
Department of Pediatrics
McMaster University
Hamilton, Ontario, Canada
E-mail: choongk@mcmaster.ca