Brief Review Article

Pediatric Fluid and Electrolyte Therapy

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Managing fluids and electrolytes in children is an important skill for pharmacists, who can play an important role in monitoring therapy. Fluid therapy is divided into maintenance, deficit, and replacement requirements. The Holliday-Segar equation remains the standard method for calculating maintenance fluid requirements. Accounting for deficits when determining the fluid infusion rate is an important factor in treating dehydrated patients; deficit fluid is generally administered over the first 24 hours of hospitalization. Maintenance electrolyte requirements must be taken into account, with particular attention paid to sodium requirements, as recent evidence suggests that sodium needs in hospitalized children are higher than originally thought. Fluid therapy can also have an impact on drug therapy. Hydration status can affect the dose needed to achieve therapeutic concentrations, and dehydrated patients may be at risk for toxicity if standard doses of drugs with high volumes of distribution are used. Monitoring fluid and electrolyte therapy is an important role of the pediatric pharmacist.

KEYWORDS electrolytes, fluid therapy, pediatrics

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INTRODUCTION

Fluid and electrolyte therapy is an essential component of the care of hospitalized children, and a thorough understanding of the changing requirements of growing children is fundamental in appreciating the many important pharmacokinetic changes that occur from birth to adulthood. While there are many factors that contribute to the fluid and electrolyte needs of children, approaching this therapy in a systematic, organized fashion can help pharmacists meet ongoing as well as changing needs of the patient. Organizing fluid therapy into maintenance, deficit, and replacement requirements, and then monitoring the patient for response to therapy makes fluid therapy manageable.

PHYSIOLOGIC DIFFERENCES

Total body water content changes drastically from before birth until one year of age. At 24 weeks gestational age, a baby's total body water content is close to 80% of total body weight.[1] This slowly decreases until the child is around one year of age, when total body water content is about 60% of total body weight.[2] Most adults' total body water is between 50% and 60% of total body weight.[2]

After birth, infants are expected to lose approximately 5%-15% of their body weight, with more being lost in low birth weight infants.[2,3] In fact, if this weight loss does not occur, there is cause for concern for renal dysfunction and sepsis. In addition to total body water differences, the percent of body weight accounted for by intracellular and extracellular water also changes. In adults, who have about 60% of total body weight as water, about 20% of total body weight is extracellular water and 40% is intracellular water.[2] Newborn babies have more extracellular water—45% of total body weight—compared with only 35% of total body weight that is intracellular water.[2] These changes in total body fluid have important implications for drug therapy, particularly for water soluble drugs. Aminoglycosides are a classic example, as the dose varies widely by

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age. Premature babies require large doses, usually 5 mg/kg of gentamicin, in order to achieve adequate peak concentrations (6–10 mg/L) in the blood.[4] The dose required to achieve the same peak decreases with older neonates, as the total body water decreases with age. By the time a patient is out of the neonatal period, the usual dose of gentamicin is 2.5 mg/kg.[5] Drugs generally distribute into the extracellular space, thus the larger extracellular component of fluid in neonates also contributes to the need for larger doses. The interval between doses is longer in premature infants, up to 48 hours, but this is associated with the immaturity of the neonatal kidney, and not total body water.

FLUID THERAPY

Physiologic differences also play a role in fluid therapy. The changes that take place as a child grows have a great effect on fluid requirements, making special attention to fluid therapy essential in pediatric pharmacotherapy. There are three classifications of fluid therapy, maintenance, deficit, and replacement, each of which will be discussed separately. When choosing the type of fluid and volume to be administered, careful consideration should be paid to each component of fluid therapy.

Maintenance Fluids

Maintenance fluids are given to compensate for ongoing losses and are required for all patients.[6] Maintenance fluids are frequently given through an intravenous line, but can also be given orally if the patient is able to tolerate oral therapy. Sensible losses, which include urine output and fecal water, make up the majority of ongoing losses, with additional contributions from insensible losses such as respiration and perspiration.[7]

Requirements for children are higher than those for adults for multiple reasons. First, the higher metabolic rate of children requires a greater caloric expenditure, which translates into higher fluid requirements.[6] Secondly, children, especially infants, have a much higher body surface area to weight ratio, and this translates into relatively more water loss from skin compared with adults. In addition, children, especially infants, have higher respiratory rates,[8] and this equates to higher insensible losses from the respiratory tract (Table 1).

Table 1. Respiratory Rates in Children

Age (months)	Mean Respiratory Rate (breaths per minute)
<2	48
2 to <6	44.1
6 to <12	39.1
12 to <18	34.5
18 to <24	32
24 to <30	30
30 to 36	27.1

Data from Rusconi F, et al.[8]

Additional factors must be taken into consideration when determining insensible fluid losses. Congenital abdominal wall defects such as omphalocele and gastroschisis can lead to higher evaporative losses before surgical correction, and thus careful attention should be paid to fluid balance and electrolytes. There are many mechanisms of determining the maintenance fluid requirements for children. Each of these methods, while providing a reasonable estimate of maintenance fluids, cannot account for the physiologic changes that occur in hospitalized children. For this reason, when calculating maintenance fluids, pharmacists must always keep in mind factors that may affect fluid balance and changed needs. Hospitalized children frequently have elevated fluid requirements due to their illness. Patients suffering from fever, burn injuries,[9] hypermetabolic states, pain, asthma, and increased intestinal losses may all have elevated maintenance fluid requirements. Burn patients in particular are a classic example of patients with increased fluid needs due to higher metabolic rates.[9]

While insensible losses from ventilation may not account for a large amount of ongoing normal losses, conditions that increase respiratory rate (e.g., pain, asthma, and pneumonia) can potentially create a higher maintenance fluid requirement. When considering fluid requirements in hospitalized children, potential increased or decreased needs should always be kept in mind.

The most commonly used technique to calculate maintenance fluids for children is the Holliday-Segar method (Table 2).[6] This equation estimates the amount of kilocalories expended, and equates this with fluid requirements. For every 100 kilocalories used during metabolism, roughly 100 mL of fluid is needed to replace

Table 2. Holliday-Segar Method for Calculating Maintenance Fluid Requirements in Children

	Holliday-Segar Method	Holliday-Segar Estimate
First 10 kg	100 mL/kg/day	4 mL/kg/hr
Second 10 kg	50 mL/kg/day	2 mL/kg/hr
Every kg thereafter	20 mL/kg/day	1 mL/kg/hr

Data from Holliday MA, Segar WE.[6]

losses. Thus, while the Holliday-Segar method actually estimates kilocalories lost, it is estimated that a loss of 1 kilocalorie requires 1 mL in replacement, so the kilocalorie estimate is an efficient target for fluid requirements.

Other methods of estimating maintenance fluid requirements exist, including those using body surface area and basal calorie requirements. Generally these equations involve more calculations, and the basal calorie requirement method requires an indirect calorimeter, which is an expensive piece of equipment. The Holliday-Segar method is usually preferred due to its ease of calculation; however, the other methods are employed in some instances. The Holliday-Segar method may be simplified by estimating the fluid requirements in rate required per hour. This equation, also listed in Table 2, arrives at similar volumes of fluid as the traditional Holliday-Segar equation.

Deficit Fluids

Fluids lost prior to medical care are termed "deficit fluids." Examples of clinical situations where a patient would present with a deficit fluid include gastrointestinal illness with vomiting and diarrhea, traumatic injuries with significant blood loss, and inadequate intake of fluids over a period of time.

Deficit fluids, like maintenance fluids, are most easily handled by approaching the needs of the patient in a systematic manner. Clinical signs of dehydration should be taken into consideration first, as they can provide useful insight into the fluid needs of the patient. One clinical sign of dehydration which can be of use is weight loss. Most young children visit their pediatricians frequently, and a relatively recent pre-illness weight will be on record. Other clinical signs include increased thirst, dry mucous membranes, and decreased urine output (Table 3).[10] Clinical signs usually correlate fairly well with the degree of dehydration, thus making them an important part of the physical exam for a dehydrated patient (Table 4).

After clinical signs have been observed, the degree (%) of dehydration should be determined.[10] This is calculated by dividing the difference between the pre-illness and illness weights by the pre-illness weight, then multiplying by 100 (Table 5). For example, a 10-kg patient who has lost 1 kg is 10% dehydrated. Every 1 kg of weight lost is equivalent to 1 L of fluid loss. The degree of dehydration calculated should always be compared to the clinical signs, which may be better indicators of hydration status and are also especially useful when a pre-illness weight is unknown.

Once the degree of dehydration is established, the type of dehydration, defined by serum sodium concentrations, needs to be determined. Most dehydrated patients have an isotonic dehydration.[10] A serum sodium concentration of less than 135 mEq/L is considered hypotonic dehydration, while greater than 145 mEq/L is considered hypertonic dehydration.

Patients with mild to moderate dehydration may be rehydrated with oral therapy, even if diarrhea and vomiting continues.[10,11] A volume of 50 mL/kg over 4 hours should be given in small aliquots for mild dehydration.[11] Patients with moderate dehydration should be given 100 mL/kg over 4 hours.[11] The oral rehydration solutions available commercially generally have appropriate amounts of carbohydrates and electrolytes, usually about 140 mmol/L of carbohydrate, 45 mmol/L (mEq/L) of sodium, and 20 mmol/L (mEq/L) of potassium.[10] Liquids such as milk, juice, soda, tea, and sports beverages do not contain appropriate amounts of carbohydrates and electrolytes to meet the needs of dehydrated patients, and should not be used for oral rehydration.[11] However, infants who are fed human milk may continue to breastfeed if they have diarrhea.[10]

Patients with hypotonic or isotonic dehydration are given fluids using the same technique to calculate fluid amount and rate (Table 5). Rehydration is divided into three phases. In phase I, a bolus of fluid is given in order to restore blood volume to ensure adequate perfusion of critical

Table 3. Clinical Signs of Dehydration

Clinical Sign	Mild Dehydration	Moderate Dehydration	Severe Dehydration
Weight loss (%)	3-5	6-9	≥10
Behavior	Normal	Normal to listless	Normal to lethargic or comatose
Thirst	Slight	Moderate	Intense
Mucous membranes	May be normal	Dry	Dry
Anterior fontanelle	Flat	Sunken	Sunken
Eyes	Normal	Sunken	Deeply sunken
Skin turgor	Normal	Decreased	Decreased
Blood pressure	Normal	Normal	Normal to decreased
Heart rate	Normal rate	Increased	Increased
Urine output	Decreased	Markedly decreased	Anuria

Data from Provisional Committee on Quality Improvement, Subcommittee on Acute Gastroenteritis.[10]

organs, such as the brain. Bolus fluids should be isotonic; either normal saline or lactated ringers solution is used at a volume of 20 mL per kg, given over 60 minutes.[11] Repeat boluses are given if necessary to maintain adequate perfusion. Isotonic fluids are used because they provide rapid volume expansion in the plasma and extracellular fluid.[11]

When determining the amount of fluid to be administered in phases II and III, the fluid volume given during phase I should be subtracted from the deficit fluid. Phase II is given over 8 hours.[11] The amount of fluid is equivalent to one third of the daily maintenance plus one half of the remaining deficit. During phase II, 5% dextrose with 0.45% sodium chloride should be used, with 20–30 mEq/L of potassium chloride added only if the patient has voided. Phase III is given over 16 hours. The amount of fluid in phase III is equivalent to two thirds of the daily maintenance plus the remaining deficit. During phase III, 5% dextrose with 0.2% sodium chloride should be used, again with 20–30 mEq/L of potassium chloride added only if the patient has voided. Generally speaking, phases II and III are simply maintenance fluid plus deficit fluid, given over 24 hours, with half of the deficit fluid given in the first 8 hours, and the second half of the deficit fluid given in the last 16 hours (Table 6).

The approach to patients with hypertonic dehydration is quite different, due to the hyperosmolar state of their circulating blood. The deficit fluid volume should be added to the maintenance fluid volume needed for 48 hours, and the total should be administered over 48 hours. Administering the deficit fluid faster causes osmotic fluid shifts, which can result in cerebral edema and convulsions.[12] For this reason, serum sodium should be corrected by no more than 10 mEq/L/day.[12] Serum sodium should be checked frequently (every 2 to 4 hours) to ensure that rehydration is not occurring so quickly as to cause an overly rapid decrease in serum sodium. The fluid used should be hypotonic, such as 5% dextrose with 0.2% sodium chloride.[12]

Replacement Fluids

Replacement fluids are defined as those given to meet ongoing losses due to medical treatment. Examples of clinical situations where replacement fluids are needed include patients with chest tubes in place, uncontrolled vomiting, continuing diarrhea, or externalized cerebrospinal fluid shunts. Each of these examples demonstrates a situation where there is an ongoing loss which would not be met by administering only maintenance fluids. Replacement fluids differ from deficit fluids in that they are ongoing, as opposed to a loss of fluid that occurred prior to receiving medical treatment.

MAINTENANCE ELECTROLYTES

Concentrations of electrolytes are determined in large part by renal function,[7] making consideration of the patient's clinical status vitally important when considering electrolyte requirements in children. An anuric patient will recycle sodium and potassium, making supplementation generally unnecessary. Any renal dysfunction requires frequent electrolyte monitoring. Electrolyte replacement in intravenous fluids gener-

Table 4. Degrees of Dehydration

	Mild Dehydration	Moderate Dehydration	Severe Dehydration
Older child	3% (30 mL/kg)	6% (60 mL/kg)	9% (90 mL/kg)
Infant	5% (50 mL/kg)	10% (100 mL/kg)	15% (150 mL/kg)

ally includes sodium, potassium, and chloride. Chloride needs, which are 5 mEq/kg/day,[11] are usually met by administering sodium and potassium as sodium chloride and potassium chloride salts. Requirements for sodium are 3 mEq/kg/day, while the requirements for potassium are 2 mEq/kg/day (Table 7).[6,11]

It is important to consider maintenance electrolyte requirements when choosing a maintenance fluid for a child. For the most part, practitioners can choose from commercially available products to adequately fulfill maintenance needs.

For most children, a 5% dextrose solution with 0.2% sodium chloride provides the estimated needs of sodium when used as a maintenance fluid. However, there has been recent attention in the literature to the potential for causing hyponatremia when using 0.2% sodium chloride.[13,14] The concern arises from the belief that the 3 mEq/kg/day of sodium proposed as maintenance by Holliday and Segar is only enough for healthy children, and that acutely ill children may have higher requirements.[6] Due to this concern, many practitioners use 0.45% sodium chloride in maintenance fluids. Some even argue the need for isotonic fluid.[14]

Recently, two pediatric deaths from hyponatremia have been reported in post-operative situations.[15] In one case, the child received an infusion of 5% dextrose at an incorrect infusion rate after an outpatient tonsillectomy and adenoidectomy. The subsequent symptoms of hyponatremia were mistaken for a dystonic reaction from promethazine, and the child was treated with diphenhydramine. The second case involved a patient who had surgery to repair a coarctation of the aorta. The patient became hyponatremic after receiving ethacrynic acid, and it was unclear whether the patient received the subsequent order for a sodium chloride infusion. On the second post-operative day, the patient was unarousable, and this was confused for a side effect of receiving hydromorphone. Later, seizures were misperceived as fidgeting from pain. In both of these cases, symptoms of hyponatremia were explained as side effects of drugs. The potential for hyponatremia or hypernatremia emphasizes the need for close monitoring of serum sodium in hospitalized children receiving intravenous fluid therapy, particularly in the post-operative period.

ELECTROLYTE ABNORMALITIES

Severe Hyponatremia

Patients with a serum sodium of less than 125 mEq/L are at high risk for serious central nervous system symptoms; lethargy followed by seizures is common.[16] Due to the emergent nature of this condition, boluses with hypertonic saline, usually 3% sodium chloride, are warranted. The volume of 3% sodium chloride is determined by the sodium deficit, which is calculated using the following equation[17]:

(desired serum sodium concentration – current serum sodium concentration) × 0.6 × (weight in kg)

Multiplying the sodium deficit by 2 gives the volume of 3% sodium chloride needed. This is generally given over a few hours, with serum sodium checks done throughout in order to avoid hypernatremia. Serum sodium should not be corrected faster than 12 mEq/L within 24 hours

Hyperkalemia

Hyperkalemia is usually defined as a serum potassium of greater than 6 mEq/L, as this is where changes in the electrocardiogram are usually seen.[18] Before deciding to treat hyperkalemia, it is important to discover how the blood was acquired. If the blood came from a heel stick, as is frequently done in infants, cell lysis due to the trauma of the needle can cause intracellular potassium to enter the serum locally, leading to falsely elevated serum potassium.

Hyperkalemia can be treated with a variety of medications. There are multiple mechanisms for decreasing serum potassium, and medications are chosen based upon their mechanism and the level of urgency of the clinical situation. In

Table 5. Method for Calculating Rehydration Fluid in Isotonic or Hypotonic Dehydration

Rehydration Phase	Fluid Volume	Example 10-kg Child with 1-kg weight loss (deficit = 1000 mL)
Phase I Emergency Phase	20 mL/kg May repeat if necessary	200 mL (remaining deficit = 800 mL)
Phase II First 8 hours	1/2 remaining deficit + 1/3 daily maintenance	400 mL + 333 mL = 733 mL = 92 mL/hr
Phase III Next 16 hours	1/2 remaining deficit + 2/3 daily maintenance	400 mL + 666 mL = 1066 mL = 67 mL/hr

emergencies, agents which cause a rapid influx of potassium intracellularly are useful as they provide an acute decrease in serum levels. These medications include insulin and beta adrenergic agonists such as albuterol.[19] Sodium bicarbonate is sometimes used to treat hyperkalemia, but its mechanism in lowering serum potassium levels is unknown and generally not immediate.[19] Other medications help by increasing elimination of potassium from the body. Sodium polystyrene sulfonate is an exchange resin which exchanges sodium for potassium in the gut;[19] its use is generally for less emergent situations. Diuretics such as furosemide can also be used to increase potassium excretion into the urine, however, diuretics should be used cautiously, as the resultant volume depletion can cause decreased potassium excretion.[19] Calcium is used in symptomatic patients for cardioprotective effects, as it antagonizes the membrane effects of potassium.[19] Frequently, long-term treatments are needed to control the cause of the hyperkalemia.

MONITORING FLUID AND ELECTROLYTE THERAPY

Determining an initial fluid rate for children based upon their needs is essential. However, once therapy is begun, appropriate monitoring is necessary due to the frequently changing needs of a hospitalized patient. The first parameter for monitoring is oral intake (Table 6). Generally speaking, the oral route for providing fluid therapy is preferred as soon as it is clinically indicated, as any intravenous administration brings with it the risk of infection. Patients who are not allowed anything by mouth for a short time, such as for an uncomplicated surgery, and for whom only maintenance fluids are required, may have their fluids decreased and eventually stopped once they tolerate oral hydration.

When monitoring patients who are being treated with maintenance and deficit fluids for dehydration, the most important monitoring parameters are those which defined the dehydration in the first place, such as skin turgor, urine output, and thirst (see Table 4 for a complete list). Monitoring patients' weights can be especially important, particularly in infants, as younger patients tend to present with more significant weight loss when dehydrated. Urine specific gravity can also be used to assess hydration status.

Table 6. Monitoring Parameters for Parenteral Fluid Therapy

Oral intake
Weight changes
Urine volume and specific gravity
Physical signs and symptoms of dehydration (see Table 4)
Serum electrolytes

Another monitoring parameter which the pharmacist can impact is the amount of fluid used in the patient's medications. For example, if a parenteral antibiotic is being mixed in 100 mL and given four times per day, this could provide a significant amount of fluid to the patient. Ensuring that the patient is not getting an excessive amount of fluids in medications can help prevent overhydration. The fluid in which the medication is being mixed should also be taken into account. A medication mixed in a large volume of 5% dextrose could put the patient at risk for hyponatremia due to the administration of too much dextrose, which amounts to free water. Monitoring serum electrolytes is necessary if the patient has electrolyte abnormalities, but when examining hydration, the

Table 7. Determining Maintenance Fluids, Step By Step

	Description of Steps	Example: Determine the appropriate fluid and delivery rate for maintenance fluids and electrolytes for a 28-kg child.	
		Calculations	**Answer for each step**
Step 1	*Determine daily maintenance fluid requirement* Using the Holliday-Segar method, determine the patient's fluid requirements (volume in liters) for 24 hours.	a. 100 mL/kg x 1st 10 kg = 1000 mL b. 50 mL/kg x 2nd 10 kg = 500 mL c. 20 mL/kg x each additional kg (8) =160 mL	1660 mL = 1.66 L
Step 2	*Deliver appropriate dose of electrolytes* Choose a commercially available fluid and determine how much sodium and potassium will be delivered considering the volume that will be administered.	*Sodium requirements:* 3 mEq/kg x 28 kg = 84 mEq sodium a. D5 ¼NS x 1.66 L = 38.5 mEq sodium/L x 1.66 L = 63.9 mEq sodium b. D5 ½NS x 1.66 L = 77 mEq sodium/L x 1.66 L = 128 mEq sodium c. D5 NS x 1.66 L = 154 mEq sodium/L x 1.66 L = 255.6 mEq sodium	D5 ¼NS provides the most appropriate amount of sodium for this patient.
		Potassium requirements: 2 mEq/kg x 28 kg = 56 mEq potassium a. 10 mEq/L x 1.66 L = 16.6 mEq potassium b. 20 mEq/L x 1.66 L = 33.2 mEq potassium c. 30 mEq/L x 1.66 L = 49.8 mEq potassium d. 40 mEq/L x 1.66 L = 66.4 mEq potassium	Generally, when beginning fluid therapy, more conservative potassium amounts, in this case 20 mEq/L, are used due to the risk of accumulation, particularly in hospitalized children.
Step 3	*Choose a fluid* Pick a commercially available fluid that delivers the desired amount of electrolytes.		Answer D5 ¼NS with 20 mEq KCl per liter at 69 mL/hr
Step 4	*Monitoring* Monitor patient fluid status and electrolytes and adjust the rate and fluid type accordingly.		

most important indices to watch are the clinical parameters mentioned earlier.

FLUIDS IN CHILDREN: EFFECTS ON DRUG DISTRIBUTION

Understanding appropriate fluid and electrolyte therapy for children is essential for every pharmacist practicing in pediatrics, but these concepts have additional implications in drug therapy. Pharmacists are in a unique position to make a positive impact by applying physiological fluid differences and basic pharmacokinetics to pediatric pharmacotherapy.

As mentioned previously, the large percentage of total body water in neonates has a great impact on therapy with water-soluble drugs, such as aminoglycosides. The increased volume of distribution necessitates a large dose. However, if the infant presents in a dehydrated state, and therefore has a smaller volume of distribution, giving a standard dose for the patient's age may result in a toxic serum concentration. The opposite problem may happen after a patient has been given multiple fluid boluses. In this situation, the volume of distribution may temporarily be increased, and thus a standard dose may lead to subtherapeutic serum concentrations. Hydration status can have an important impact on drug therapy, and should be considered when using medications with large volumes of distribution.

CONCLUSION

Organizing fluid needs into maintenance, deficit, and replacement therapy can provide a systematic, understandable approach to determining fluid therapy. By paying close attention to the fluid needs of pediatric patients and monitoring response to fluid therapy, the pediatric pharmacist can have a positive influence on the health of the child. Pharmacists should always pay particular attention to the hydration status of patients, as the volume of distribution for water soluble drugs can be drastically affected by a change in volume status. Applying the principles of pharmacokinetics to a working knowledge of fluid and electrolytes in children can help pharmacists individualize medication therapy to the specific needs of the patient.

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