

# Risk of acute hyponatremia in hospitalized children and youth receiving maintenance intravenous fluids

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## Abstract

Hospital-acquired acute hyponatremia is increasingly recognized as a cause of morbidity and mortality in children. It has been attributed primarily to the use of hypotonic intravenous (IV) fluids to maintain fluid and electrolyte requirements. This practice point outlines current understanding of the problem and summarizes recent research dealing with this issue. Detailed recommendations are made for the prescription of IV maintenance fluids in children between one month and 18 years of age. The use of isotonic fluid (D5W.0.9% NaCl) is recommended in most circumstances. Hypotonic IV fluids containing less than 0.45% NaCl should not be used to provide routine IV fluid maintenance requirements.

**Key Words:** Acute hyponatremia; Intravenous fluid prescription; Maintenance intravenous fluids

## The problem

Hyponatremia, defined as a serum sodium (Na)  $<135$  mmol/L, has become increasingly recognized as a cause of morbidity and mortality in hospitalized children.<sup>[1][9]</sup> In recent years there have been many reports of serious morbidity, including severe neurological injury, as well as many deaths among children who developed hospital-acquired hyponatremia while receiving IV fluids.<sup>[1][9]</sup> A case-control study reported that 40 of 432 (9%) of hospitalized children on IV fluids who had a normal baseline serum Na had a subsequent serum Na  $<136$  mmol/L.<sup>[3]</sup> Other studies have shown an incidence of hyponatremia in hospitalized children as high as 24%.<sup>[10]</sup>

Hyponatremia has been attributed primarily to the use of hypotonic maintenance IV fluids. The administration of such fluids provides a source of electrolyte-free water (EFW) to a population of children who are at risk for increased antidiuretic hormone (ADH) secretion.<sup>[3][11][12]</sup> Clinical sequelae of acute hyponatremia (a decrease in Na over  $\leq 48$  h) result from acute cerebral edema, and may include headache, lethargy

and seizures, and potentially even respiratory and cardiac arrest secondary to brain stem herniation. These outcomes are more likely to be seen with severe acute hyponatremia (Na  $<130$  mmol/L). Because of their higher brain/intracranial volume ratio, children are at increased risk for these sequelae compared with adults.

The routine practice of providing hypotonic maintenance IV solutions, usually containing 20 mmol/L to 30 mmol/L of Na, is based on Holliday and Segar's seminal paper published in 1957<sup>[13]</sup> and translates to the use of 0.2% NaCl/dextrose 5%. These recommendations were based on caloric expenditure in healthy children, and electrolyte composition was derived from that of human and cow's milk.

It has been recognized that the great majority of hospitalized children are at risk of nonphysiological antidiuretic hormone (ADH) secretion – due to nausea, stress, pain, pulmonary and central nervous system disorders, surgical interventions, and commonly used medications such as morphine sulfate – which implies that Holliday and Segar's traditional recommendations for administering hypotonic IV fluids are probably inappropriate. The high percentage of EFW in hypotonic IV fluids (78% EFW) compared with normal saline (0% EFW), in combination with an impaired ability to excrete water as a result of ADH secretion, places hospitalized children at increased risk of developing acute hyponatremia.

IV fluid prescription practices for children vary widely among physicians both within and between hospitals. A cross-sectional survey carried out in multiple hospitals in the United Kingdom revealed that 77 of 99 children receiving IV fluids during one day of a specified week were receiving hypotonic solutions. Twenty-one of the 86 children (24%) who had serum electrolytes measured were found to be hyponatremic, and the vast majority of these were receiving hypotonic IV fluids.<sup>[10]</sup>

To avoid the development of acute hyponatremia, it has been recommended that isotonic 0.9% NaCl/dextrose 5% (normal

saline with dextrose) should be the standard maintenance IV solution.<sup>[2][11][12][14]</sup> Normal saline contains 154 mmol/L of Na, which is isotonic with respect to the cell membrane. This suggestion has raised concerns regarding the potential for hypernatremia and salt and water overload.<sup>[15]</sup> However, unless the child has an impaired ability to excrete Na, a renal concentrating defect, significant water loss or prolonged fluid restriction, these risks appear to be largely theoretical. The risk of developing hyperchloremic metabolic acidosis has been recognized in the context of rapid isotonic saline infusion delivered perioperatively<sup>[16]</sup> but has not been reported in the trials of IV saline used for maintenance requirements in children to date.

## New information

Two systematic reviews of the literature comparing hypotonic versus isotonic saline in hospitalized children were published approximately five years ago. Both concluded that there was a paucity of well-designed studies on which to base the prescription of IV fluid for maintenance requirements.<sup>[2][17]</sup> At that time, prospective trials comparing the tonicity of IV fluid were limited to small surgical populations and dehydrated children with gastroenteritis.<sup>[18][20]</sup> In these studies children had lower plasma Na values if treated with hypotonic versus isotonic fluids.

More recently, six randomized controlled trials addressing the issue of tonicity of IV maintenance fluid and hyponatremia in children have been published.<sup>[21][26]</sup> The first study from Spain randomized 122 ICU patients to receive isotonic or hypotonic fluids.<sup>[21]</sup> At 24 hours, 20.6% of patients in the hypotonic group were hyponatremic versus 5.1% in the isotonic group ( $p = 0.02$ ). The second study, performed in Australia, randomized 50 ICU patients to receive isotonic fluids (normal saline) or hypotonic fluids (0.18% NaCl/4% dextrose), at either the traditional maintenance rate or two-thirds of that rate.<sup>[22]</sup> The type of fluid ( $p = 0.006$ ) but not the rate ( $p = 0.12$ ) was significantly associated with the degree of fall in serum Na. The third study included 125 children from three paediatric ICUs in Spain. After adjusting for age, weight and Na at admission, those receiving hypotonic fluids (50 mmol to 70 mmol Na/L) had a decrease in Na of 3.2 mmol/L with a 5.8-fold increased risk of hyponatremia compared with patients receiving isotonic maintenance fluids.<sup>[23]</sup>

The fourth study, conducted in India, enrolled 167 hospitalized children.<sup>[24]</sup> Fourteen percent (8/56) of patients randomized to receive hypotonic IV maintenance fluids (0.18% NaCl/5% dextrose) developed a plasma Na <130 mmol/L versus 1.7% (1/58) in the group randomized to receive isotonic IV fluid (0.9% NaCl in 5% dextrose) [ $p = 0.014$ ]. Eight patients developed hypernatremia (plasma Na >150 mEq/L), none of whom were reported to be clinically symptomatic, and only two of whom had received isotonic fluids.

Two Canadian studies were published in late 2011. In the largest study to date, of 258 children enrolled at the time of surgery in Hamilton, Ontario, Choong et al<sup>[25]</sup> showed that isotonic fluids were significantly safer than hypotonic fluids in protecting against acute postoperative hyponatremia. Isotonic fluids did not increase the risk of hypernatremia. In a much smaller study in Montreal, Quebec, of a mixed group of 37 medical and postoperative children, Saba et al<sup>[26]</sup> did not find a significant rate of change or absolute change in serum Na in the first 12 hours in either of the groups randomized to isotonic or hypotonic (0.45 NaCl) maintenance fluids. These recent studies<sup>[27]</sup> suggest that, compared with hypotonic IV maintenance fluids, isotonic fluids decrease the risk of iatrogenic acute hyponatremia without significant side effects. A study by the Canadian Paediatric Surveillance Program is currently underway (March 2012 to February 2014) to determine the incidence of and explore risk factors for Canadian cases of symptomatic hyponatremia related to IV fluid administration.

**TABLE 1**  
**Definitions**

Definition	Serum [Na+] mmol/L
Normonatremia	135–145
Hyponatremia	<135
Severe acute hyponatremia	<130 within 48 h in child with normal baseline Na
Hypernatremia	>145

## Recommendations <sup>[28]-[30]</sup>

The following recommendations apply to the prescription of IV maintenance fluids in children one month corrected age to 18 years of age, excluding patients with renal or cardiac disease, diabetic ketoacidosis, severe burns or other underlying conditions that significantly affect electrolyte regulation.

### General principles

1. Any child in hospital who requires IV fluids should be considered at risk for developing hyponatremia due to increased risk of ADH secretion. At particular risk are:
  - children undergoing surgery
  - children with acute neurological or respiratory infections (eg, meningitis, encephalitis, pneumonia and bronchiolitis).
2. Oral fluids are generally very low in Na content (hypotonic). Where the total fluid intake (TFI) is a combi-

nation of oral and IV fluids, both need to be accounted for.

3. Because infants and young children have limited glycogen stores, dextrose should be part of the IV maintenance fluid prescription (eg, D5W.0.9%NaCl or D5W.0.45%NaCl) if no other source of glucose is provided.
4. The approach to prescribing IV fluids should be as cautious as that for medications, with close attention paid to indications, monitoring, the type of fluid and the volume/rate of administration.

### Monitoring

1. Baseline serum electrolytes (Na, K, glucose, urea, creatinine) should be measured when starting IV fluid therapy in hospitalized children.
2. Children receiving maintenance IV fluids should have their serum electrolytes checked regularly, with patients who may be at high risk of impaired renal water excretion checked daily if not more frequently.
3. All children receiving IV maintenance fluids should have their intake/output carefully monitored, as well as a daily weight measurement.
4. Clinicians should be aware of the symptoms of hyponatremia, which may include headache, nausea and vomiting, irritability, decrease in level of consciousness, seizures and apnea.

### Prescription of IV fluids for maintenance requirements

1. In children whose serum sodium is normal at baseline but who are considered to be at particularly high risk of ADH secretion (eg, peri- or postoperative; with respiratory or neurological infections) the use of isotonic saline (D5W.0.9% NaCl) is recommended.
2. For other hospitalized children whose serum sodium is normal, the options are D5W.0.9% NaCl or D5W.0.45% NaCl. The first option is preferred, especially when the serum Na is in the low normal range (135 mmol/L to 137 mmol/L inclusive).
3. Hypotonic IV fluids containing <0.45% NaCl should not be used to provide routine fluid maintenance and should not be generally available on paediatric wards.
4. When serum electrolyte results are not yet available, it is recommended that D5W.0.9% NaCl be initiated as the maintenance IV fluid.
5. If the serum sodium is 145 mmol/L to 154 mmol/L, then D5W.0.45% NaCl should be initiated and frequent monitoring of the serum sodium performed.
6. Ringer's Lactate is commonly used in the operating room but the absence of dextrose and presence of lactate make it generally inappropriate for maintenance IV therapy, especially in young children.

Note that these recommendations are not intended for use in infants and youth outside the one month to 18 year age group.

**TABLE 2**  
Commonly used intravenous fluids

Fluid	Na mmol/L	K mmol/L	Cl mmol/L	Lactate mmol/L	Dextrose gram/L	Tonicity versus plasma
D5W.0.9% NaCl	154	0	154	0	50	Isotonic
D5W.0.45% NaCl	77	0	77	0	50	Half-isotonic (hypotonic)
D5W.0.2% NaCl	33	0	33	0	50	Hypotonic
2/3-1/3	45	0	45	0	33	Hypotonic
Ringer's Lactate	130	4	110	28	0	Isotonic

**TABLE 3**  
**Intravenous (IV) fluid maintenance recommendations based on plasma Na<sup>+</sup> level**

Children one month –18 years of age	Recommended IV fluid
Na <138 mmol/L	Isotonic IV solutions
Na 138 mmol/L –144 mmol/L	Isotonic IV solutions preferred; half-isotonic solutions may be used
Perioperative period	Isotonic IV solutions

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