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

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Acute Care Committee
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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.1,10 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.1,11 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.13 Other studies have shown an incidence of hyponatremia in hospitalized children as high as 24%.1,10

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.1,8,11,12 Clinical sequelae of acute hyponatremia (a decrease in Na over ≤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 195713 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.10

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.\textsuperscript{[2]}\textsuperscript{[1]}\textsuperscript{[1]}\textsuperscript{[2]}\textsuperscript{[1]}\textsuperscript{[4]} 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.\textsuperscript{[1]}\textsuperscript{[5]} 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\textsuperscript{[1]}\textsuperscript{[6]} 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.\textsuperscript{[2]}\textsuperscript{[1]}\textsuperscript{[7]} At that time, prospective trials comparing the tonicity of IV fluid were limited to small surgical populations and dehydrated children with gastroenteritis.\textsuperscript{[1]}\textsuperscript{[8]}\textsuperscript{[20]} 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.\textsuperscript{[2]}\textsuperscript{[2]}\textsuperscript{[2]}\textsuperscript{[2]}\textsuperscript{[2]}\textsuperscript{[2]}\textsuperscript{[2]} The first study from Spain randomized 122 ICU patients to receive isotonic or hypotonic fluids.\textsuperscript{[2]}\textsuperscript{[2]} 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.\textsuperscript{[2]}\textsuperscript{[2]} 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.\textsuperscript{[2]}\textsuperscript{[2]}

The fourth study, conducted in India, enrolled 167 hospitalized children.\textsuperscript{[2]}\textsuperscript{[4]} 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.\textsuperscript{[2]} showed that isotonic fluids were significantly safer than hypotonic fluids in protecting against acute postoperative hyponatremia. Isotonic fluids did not increase the risk of hyponatremia. In a much smaller study in Montreal, Quebec, of a mixed group of 37 medical and postoperative children, Saba et al.\textsuperscript{[2]}\textsuperscript{[2]} 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\textsuperscript{[2]}\textsuperscript{[2]} 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**

<table>
<thead>
<tr>
<th>Definition</th>
<th>Serum [Na+] mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normonatremia</td>
<td>135–145</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>&lt;135</td>
</tr>
<tr>
<td>Severe acute hyponatremia</td>
<td>&lt;130 within 48 h in child with normal baseline Na</td>
</tr>
<tr>
<td>Hypermantremia</td>
<td>&gt;145</td>
</tr>
</tbody>
</table>

**Recommendations**\textsuperscript{[2]}\textsuperscript{[2]}\textsuperscript{[2]}\textsuperscript{[2]}\textsuperscript{[2]}\textsuperscript{[2]}\textsuperscript{[2]}

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 account-
ed for.
3. Because infants and young children have limited
glycogen stores, dextrose should be part of the IV
maintenance fluid prescription (e.g., 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 wa-
ter 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 hy-
ponatremia, which may include headache, nausea and
vomiting, irritability, decrease in level of conscious-
ness, 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 (e.g., peri- or postoperative; with res-
piratory 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 fre-
quent 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 lact-
ate 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**

<table>
<thead>
<tr>
<th>Commonly used intravenous fluids</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fluid</strong></td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>D5W.0.9% NaCl</td>
</tr>
<tr>
<td>D5W.0.45% NaCl</td>
</tr>
<tr>
<td>D5W.0.2%NaCl</td>
</tr>
<tr>
<td>2/3–1/3</td>
</tr>
<tr>
<td>Ringer’s Lactate</td>
</tr>
</tbody>
</table>
TABLE 3
Intravenous (IV) fluid maintenance recommendations based on plasma Na+ level

<table>
<thead>
<tr>
<th>Children one month – 18 years of age</th>
<th>Recommended IV fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na &lt;138 mmol/L</td>
<td>Isotonic IV solutions</td>
</tr>
<tr>
<td>Na 138 mmol/L –144 mmol/L</td>
<td>Isotonic IV solutions preferred; half-isotonic solutions may be used</td>
</tr>
<tr>
<td>Perioperative period</td>
<td>Isotonic IV solutions</td>
</tr>
</tbody>
</table>

Acknowledgements
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References

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