Perioperative fluid therapy in children

Ochtendkrans anesthesie 22-01-2016
Dr. Ellen Buts
Dr. Cédric Van Dijck
Dr. Philippe Van Loon
WHY?

- Potential significant morbidity, even mortality when historical recommendations are followed!
  - HypoNa
  - Hyperglycemia
- IV fluids ~ medication
- Importance of our perioperative fluid choices – even with minor procedures + healthy children
- Recent publications challenges the old concepts for maintenance fluid requirements described by Holliday and Segar in 1957
GOAL Perioperative fluid therapy

• Providing:
  - Maintenance fluid requirements
  - Correcting fluid deficit (fever/GI losses/… + fasting)
  - Replace ongoing losses (blood loss/third space)

• Ultimate goal = to maintain a correct fluid and electrolyte balance and, as a consequence, normal cardiovascular stability - to maintain adequate tissue perfusion
EXTRA cellular fluids

- Fluid replacement needs perioperatively:
  - Basal ‘metabolic’ needs
  - Third space
  - Bleeding
  - Fasting deficit

- IV fluids replace extracellular loss and are administered in plasma compartment

- Ideally: high Na, Cl
  low Ca, K, bicarbonate
Physiology
Tonicity [Na]! vs Osmolality

**ISOTONIC**
- NaCl 0.9% in ICF (intracellular fluid)

**HYPOTONIC**
- D5W (5% dextrose in water) in ICF

**ISO-OSMOLAR**
- NaCl 0.9% in ECF (extracellular fluid)

**ISO-OSMOLAR**
- D5W in ECF
<table>
<thead>
<tr>
<th>Fluid</th>
<th>Na⁺ (mEq/L)</th>
<th>Cl⁻ (mEq/L)</th>
<th>K⁺ (mEq/L)</th>
<th>Ca²⁺ (mEq/L)</th>
<th>Mg⁺ (mEq/L)</th>
<th>Buffer (mEq/L)</th>
<th>Osmolarity (mOsm/L)</th>
<th>Tonicity in vivo (after glucose metabolism)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D₅ 0.225% saline</td>
<td>34</td>
<td>34</td>
<td></td>
<td></td>
<td></td>
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<td>D₅ 0.45% saline</td>
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<td></td>
<td></td>
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<td>432</td>
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<tr>
<td>Lactated Ringer’s</td>
<td>130</td>
<td>109</td>
<td>4</td>
<td>3</td>
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<td>Lactate 28</td>
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<tr>
<td>Plasma-Lyte</td>
<td>140</td>
<td>98</td>
<td>5</td>
<td>3</td>
<td></td>
<td>Acetate 27; Gluconate 23</td>
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<tr>
<td>0.9 % saline</td>
<td>154</td>
<td>154</td>
<td></td>
<td></td>
<td></td>
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<td>308</td>
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<tr>
<td>D₅ 0.9 % saline</td>
<td>154</td>
<td>154</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>560</td>
<td>Isotonic</td>
</tr>
</tbody>
</table>

D, Dextrose
PHYSIOLOGY

- Homeostasis of VOLUME
  - [Na]
- Homeostasis of OSMOLALITY
  - free water
Increased renal Na⁺ retention counteracts decreased effective circulating volume.
ADH (Vasopressin)

- Hypothalamus
- Pituitary
- V2 receptors
- Aquaporin
- Free water re-absorption
- Osmoregulation
**ADH upregulation** *(non-osmotic triggers)*

<table>
<thead>
<tr>
<th>Hemodynamic stimuli</th>
<th>Non-hemodynamic stimuli</th>
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</thead>
<tbody>
<tr>
<td>Hypovolemia</td>
<td>Central nervous system disease</td>
</tr>
<tr>
<td>Decreased effective circulatory</td>
<td>Brain tumors</td>
</tr>
<tr>
<td>volume</td>
<td>Meningitis, encephalitis</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Head trauma</td>
</tr>
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<td>Congestive heart failure</td>
<td>Pulmonary disease</td>
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<td>Hypoalbuminemia</td>
<td>Pneumonia</td>
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<td>Hypotension</td>
<td>Bronchiolitis</td>
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<td>Positive pressure ventilation</td>
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<td>Hypoxia</td>
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<td>Oncologic diseases</td>
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<tr>
<td>Postoperative state</td>
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<tr>
<td>Stress</td>
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<td>Nausea/vomiting</td>
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<tr>
<td>Medications</td>
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<td>Narcotics</td>
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<tr>
<td>Vincristine</td>
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</tr>
<tr>
<td>Cyclophosphamide</td>
<td></td>
</tr>
</tbody>
</table>

**Graph:**
- Postoperative ADH
- Baseline ADH

**Table 1** Non-osmotic stimuli for antidiuretic hormone release
Previous Research
THE MAINTENANCE NEED FOR WATER IN PARENTERAL FLUID THERAPY

By Malcolm A. Holliday, M.D., and William E. Segar, M.D.
Department of Pediatrics, Indiana University Medical Center

One of the major objectives of parenteral fluid therapy is provision of water to meet physiologic losses. These per kilogram from a simple formula relating calories per kilogram to age. The following scheme was devised to

- Relation between: weight – energy expenditure
  energy expenditure – fluid needs
- Easy rule of thumb: 4/2/1 mL/kg/hr

1957
Fig. 1. The upper and lower lines were plotted from data of Talbot. Weights at the 50th percentile level were selected for converting calories at various ages to calories related to weight. The computed line was derived from the following equations:

1. 0-10 kg—100 cal/kg.
2. 10-20 kg—1000 cal + 50 cal/kg for each kg over 10 kg.
3. 20 kg and up—1500 cal + 20 cal/kg for each kg over 20 kg.
Energy Expenditure and Fluid and Electrolyte Requirements in Anesthetized Infants and Children

Sten G. E. Lindahl, M.D., Ph.D.*

In 31 infants and children (body weights ranging from 3.8 to 25 kg), indirect calorimetry was used for the calculation of energy needs (E, kcal/h), fluid volume (FV, ml/h) and electrolyte requirements (sodium, Na+, and potassium, K+, mmol/liter per hour) during halothane anesthesia. The children were spontaneously breathing and undergoing minor lower abdominal or orthopedic surgery. A nonrebreathing anesthesia circuit was used, and gas concentrations were measured by a mass spectrometer. For the evaluation of ventilation during periods of measurements, pneumotachography and in-line capnography were used. Energy expenditure was related to weight and followed the regression equation E = 1.5 × kg + 5.2; r = 0.96. The energy needs were converted to fluid volumes according to the water requirements for heat production, which resulted in the following relationship between FV and weight: FV = 2.4 × kg + 8.6; r = 0.96. The energy expenditure was up to 50% lower than in previous reports. Extrapolations of energy needs from awake values are inappropriate for the anesthetized state, and 3) to address the question of the relationship of energy expenditure to fluid and electrolyte requirements.

Materials and Methods

This study was approved by the Institutional Review Board at the Mayo Clinic, and parental consent for the study was obtained in each case. Thirty-one ASA physical status 1 children between 20 days and 7 yr of age and with body weights ranging from 3.8 to 25 kg were investigated. All patients were fasting for at least 4–5 h before induction of anesthesia. They were scheduled for minor, general, urologic, or orthopedic pediatric surgical procedures, and had body weights within the normal range for a pediatric population.
Fig. 4. Daily caloric expenditure in kilocalories related to weight both at basal metabolic rate (BMR) and at normal activity (from Talbot). Energy needs estimated by Holliday and Segar for hospitalized children are given by continuous line, and those from present study are represented by broken line. (Modified from Holliday MA, Segar WE: The maintenance need for water in parental fluid therapy. Pediatrics 19:823–832, 1957. By permission of Pediatrics.)
Fig. 2. Fluid volume (FV) in milliliters per hour related to weight. Regression equation and coefficient of correlation are given. Regression line is drawn. Standard error of estimate is represented by shaded area.
Lindahl et al.

• Anesthesia
  – 50% lower energy expenditure
  – 150 mL water needed for 100 kcal
  – Corresponds with Holliday & Segar’s formula
  – Exceptions: Disease, metabolic disorders, …
General recommendation: hypotonic fluids

- Electrolyte requirements: 3mEq/100kcal/day Na
  2mEq/100kcal/day K
- Resembles hypotonic fluid composition
The primary basis for the current recommendation of prescribing 3.0 and 2.0 mEq/100 kcal/24 h sodium and potassium, respectively, in maintenance fluids is that this roughly reflects the electrolyte composition of breast and cow milk.\textsuperscript{1,8–10} This electrolyte composition will also result in a urine osmolality of approximately 400 mOsm/kg/H\textsubscript{2}O, which was believed to be ideal, as it is between the range of urinary concentrating capacity.\textsuperscript{11} Although it has been well-established that isotonic saline could be tolerated without any adverse effects, the use of isotonic saline has been avoided to prevent excess urinary water losses in conditions with impaired renal concentrating ability and to prevent the development of postoperative edema.\textsuperscript{9–11} Whereas these recommendations may be
1998

Editorial

Postoperative hyponatraemic encephalopathy following elective surgery in children

Postoperative hyponatraemic encephalopathy in prepubertal children

There are multiple reports of prepubertal children suffering brain damage from postoperative hyponatraemic encephalopathy (6–9). The aetiology of the hyponatraemia usually involves a combination of: a) intravenous hyponatraemic fluids; b) elevated plasma antidiuretic hormone (ADH); c) respiratory insufficiency secondary to hyponatraemic encephalopathy. It has been demonstrated in several

Symptomatic postoperative hyponatraemia carries a mortality of at least 15% (43), particularly in children and respiratory arrest is a frequent occurrence, but once this complication occurs, the morbidity is substantial (6,7). There is no obvious rationale for the administration of hypotonic fluid to a postoperative patient, unless the individual is hypernatraemic (14). If the patient becomes symptomatic, therapy with hypertonic NaCl is indicated (39). The syndrome can be prevented by administration of primarily isotonic fluids to postoperative patients.

ALLEN I. ARIEFF MD
Department of Medicine, University of California School of Medicine,
San Francisco, CA, USA
Acute hypoNa

• Most common electrolyte disturbance in hospitalized adults & children
• Na < 135 mEq/L, symptomatic usually <125 mEq/L
• Early: nausea, confusion, cramps, tachycardia, headache
• Late: lethargy, decerebrate/decorticate posture, seizures, coma and respiratory arrest
• Significant morbidity & mortality!
Hyponatremic encephalopathy

- Slow calibration plasma – BBB – Cell membrane
- Free water moves intracellularly
  → Cerebral edema
- Children: large brain/skull ratio
  → Less accommodation for volume Δ
- Correction: slow!! (0.5 mEq/l/hour)
- Target > 125 mEq/L
  → 2.7% NaCl 2 mL/kg (max 100 mL) over 10’ → 2 mmol ↑
  (repeated up to 6 mL/kg)
Lesson of the week

Acute hyponatraemia in children admitted to hospital: retrospective analysis of factors contributing to its development and resolution

Michael Halberthal, Mitchell L Halperin, Desmond Bohn

Hyponatraemia (plasma sodium concentration less than 136 mmol/l) is acute if the decrease in natraemia occurs within 48 hours. The major dangers from this are brain cell swelling and herniation. Two factors are required for hyponatraemia to develop: a source of electrolyte free water and vasopressin to prevent the excretion of that water. Electrolyte free water is given routinely as maintenance fluids based on formulas developed in studies in healthy children more than 40 years ago. There are many reasons to anticipate that vasopressin will be released in sick patients (box). Patients with an acute illness may arrive in hospital with a low plasma sodium concentration because of previous water intake. Hence, to minimise the potential threat of brainstem herniation it is important to measure the plasma sodium concentration if intravenous solutions are to be given.

We describe symptomatic hyponatraemia developing over 48 hours in children. In each patient, hypotonic solutions were infused using current guide-

Causes of vasopressin release
- Hypernatraemia (most important stimulus, but not in these patients)
- Low "effective" circulating volume (greater than 7% decrease in extracellular fluid volume)
- Nausea, pain, anxiety
- Drugs (some act through inducing nausea)
- Afferent stimuli by way of the vagus nerve—for example, lung lesions
- Disturbances of the central nervous system (meningitis, encephalitis)
- Metabolic and endocrine disorders—for example, hypothyroidism, hypoadrenalism, porphyria
Prevention of Hospital-Acquired Hyponatremia: A Case for Using Isotonic Saline

Michael L. Moritz, MD*, and Juan Carlos Ayus, MD†

WHY ISOTONIC MAINTENANCE PARENTERAL FLUIDS SHOULD BE USED

The administration of isotonic maintenance fluids is the most important prophylactic measure that can be taken to prevent the development of hyponatremia in children who are receiving parenteral fluids. Commonly used intravenous fluids have a significant amount of free water that can contribute to hyponatremia (Table 2); therefore, they should be used with caution in maintenance fluids, to mix intravenous medications or to keep a vein open. Even concentrating capacity. Although it has been well-established that isotonic saline could be tolerated without any adverse effects, the use of isotonic saline has been avoided to prevent excess urinary water losses in conditions with impaired renal concentrating ability and to prevent the development of postoperative edema. Whereas these recommendations may be sodium plus potassium in the aqueous phase of plasma is 154 mEq/L. Although no 1 fluid rate or composition will be appropriate for all children, isotonic saline in 5% dextrose in water seems to be the safest fluid composition in most hospitalized patients. If potassium chloride is to be added to the parenteral fluids, then the sodium concentration can be lowered proportionally to maintain isotonicity. Lactated ringers with 20 mEq/L potassium chloride in 5% dextrose in water would also be an isotonic fluid. Physicians must assess children carefully to
Isotonic Saline Expands Extracellular Fluid and Is Inappropriate for Maintenance Therapy

To the Editor.—

My colleagues and I recently reviewed evidence that rapid and generous expansion of extracellular fluid (ECF) suppresses ADH in acutely ill children with subtle hypovolemia, which is similar to that seen in severe dehydration, burn shock, and septic shock, although much less intense. Once ECF is expanded, IV maintenance therapy can be given safely in the recommended amounts using hypotonic saline. We concluded that the key to preventing hyponatremia is suppressing ADH before undertaking maintenance therapy.

We proposed the more robust response of giving isotonic saline at a rate of 10 mL/kg per hour for 2 to 4 hours. This rapidly and safely expands ECF, suppresses ADH if elevated, and initiates normal urine flow.

Malcolm A. Holliday, MD
Emeritus Professor of Pediatrics
University of California
San Francisco, CA 94143
Isotonic Versus Hypotonic Maintenance IV Fluids in Hospitalized Children: A Meta-Analysis

**Authors:** Jingjing Wang, MD, Erdi Xu, MD, and Yanfeng Xiao, MD, PhD

*Department of Pediatrics, Second Affiliated Hospital of Medical School of Xi'an Jiaotong University, Xi'an, Shaanxi, China*

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Hypotonic</th>
<th>Isotonic</th>
<th>Mean Difference IV, Random, 95% CI</th>
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<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
<td>Mean</td>
</tr>
<tr>
<td>brazel 1996</td>
<td>129</td>
<td>3.8</td>
<td>7</td>
</tr>
<tr>
<td>coulthard 2012</td>
<td>136.7</td>
<td>2.7</td>
<td>40</td>
</tr>
<tr>
<td>neville 2010a</td>
<td>136.2</td>
<td>2.1</td>
<td>31</td>
</tr>
<tr>
<td>neville 2010b</td>
<td>136.2</td>
<td>2.1</td>
<td>31</td>
</tr>
<tr>
<td>rey 2011</td>
<td>134.5</td>
<td>2.7</td>
<td>39</td>
</tr>
<tr>
<td>saba 2011</td>
<td>138.1</td>
<td>2.4</td>
<td>20</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>168</td>
<td></td>
<td>167</td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.45; \chi^2 = 9.46, df = 5 (P = 0.09); I^2 = 47\%$

Test for overall effect: $Z = 5.05 (P < 0.00001)$

**Figure 4**
Meta-analysis of data for the outcome of pNa level after hypotonic versus isotonic IV maintenance fluids in hospitalized children.
Overall, isotonic fluids are safer than hypotonic fluids in hospitalized children requiring maintenance IV fluid therapy in terms of pNa levels. However, there is no ideal IV fluid for all children in terms of composition of fluid (0.9% saline/Hartmann’s, etc) and the rate and duration of administration. pNa needs to be monitored when IV fluids are administered. At
Isotonic versus hypotonic solutions for maintenance intravenous fluid administration in children (Review)

McNab S, Ware RS, Neville KA, Choong K, Coulthard MG, Duke T, Davidson A, Dorofeef T

Analysis 1.1. Comparison 1 Isotonic versus hypotonic, Outcome 1 Hyponatraemia.

Review: Isotonic versus hypotonic solutions for maintenance intravenous fluid administration in children

Comparison: 1 Isotonic versus hypotonic

Outcome: 1 Hyponatraemia

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Isotonic n/N</th>
<th>Hypotonic n/N</th>
<th>Risk Ratio M-H,Fixed 95% CI</th>
<th>Weight %</th>
<th>Risk Ratio M-H,Fixed 95% CI</th>
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<tr>
<td>Brazel 1996</td>
<td>1/5</td>
<td>7/7</td>
<td></td>
<td>3.8 %</td>
<td>0.27 [0.07, 1.08]</td>
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<tr>
<td>Choong 2011</td>
<td>26/106</td>
<td>47/112</td>
<td></td>
<td>27.1 %</td>
<td>0.58 [0.39, 0.87]</td>
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<tr>
<td>Coulthard 2012</td>
<td>0/39</td>
<td>7/40</td>
<td></td>
<td>4.4 %</td>
<td>0.07 [0.00, 1.16]</td>
</tr>
<tr>
<td>Cuello 2012</td>
<td>0/20</td>
<td>8/26</td>
<td></td>
<td>4.4 %</td>
<td>0.08 [0.00, 1.24]</td>
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<tr>
<td>Kannan 2010</td>
<td>5/58</td>
<td>18/109</td>
<td></td>
<td>7.4 %</td>
<td>0.52 [0.20, 1.33]</td>
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<tr>
<td>Monta. ana 2008</td>
<td>15/51</td>
<td>20/52</td>
<td></td>
<td>11.7 %</td>
<td>0.76 [0.44, 1.32]</td>
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<tr>
<td>Neville 2010</td>
<td>9/62</td>
<td>23/62</td>
<td></td>
<td>13.6 %</td>
<td>0.39 [0.20, 0.78]</td>
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<tr>
<td>Ray 2011</td>
<td>17/68</td>
<td>39/66</td>
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<td>23.4 %</td>
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<tr>
<td>Saba 2011</td>
<td>0/16</td>
<td>1/21</td>
<td></td>
<td>0.8 %</td>
<td>0.43 [0.02, 9.94]</td>
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<tr>
<td>Yung 2009</td>
<td>3/24</td>
<td>6/26</td>
<td></td>
<td>3.4 %</td>
<td>0.54 [0.15, 1.93]</td>
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<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>449</strong></td>
<td><strong>521</strong></td>
<td></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.48 [0.38, 0.60]</strong></td>
</tr>
</tbody>
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Total events: 76 (Isotonic), 176 (Hypotonic)
Heterogeneity: Chi² = 8.67, df = 9 (P = 0.47); I² = 0.0%
Test for overall effect: Z = 6.34 (P < 0.00001)
Test for subgroup differences: Not applicable
Analysis 1.2. Comparison I Isotonic versus hypotonic, Outcome 2 Hyponatraemia.

Review: Isotonic versus hypotonic solutions for maintenance intravenous fluid administration in children

Comparison: 1 Isotonic versus hypotonic

Outcome: 2 Hyponatraemia

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Isotonic</th>
<th>Hypotonic</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
<th>Weight</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
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<tr>
<td>Brazel 1996</td>
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<td>0/7</td>
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<td>Not estimable</td>
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<tr>
<td>Choong 2011</td>
<td>3/106</td>
<td>4/112</td>
<td></td>
<td>25.0 %</td>
<td>0.79 [ 0.18, 3.16 ]</td>
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<tr>
<td>Coulthard 2012</td>
<td>0/39</td>
<td>0/40</td>
<td></td>
<td></td>
<td>Not estimable</td>
</tr>
<tr>
<td>Cuello 2012</td>
<td>0/37</td>
<td>0/35</td>
<td></td>
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<td>Not estimable</td>
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<tr>
<td>Kannan 2010</td>
<td>5/58</td>
<td>9/109</td>
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<td>40.2 %</td>
<td>1.04 [ 0.37, 2.97 ]</td>
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<td>Monta. ana 2008</td>
<td>2/51</td>
<td>4/52</td>
<td></td>
<td>25.5 %</td>
<td>0.51 [ 0.10, 2.66 ]</td>
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<tr>
<td>Neville 2010</td>
<td>4/62</td>
<td>0/62</td>
<td></td>
<td>3.2 %</td>
<td>9.00 [ 0.49, 163.70 ]</td>
</tr>
<tr>
<td>Rey 2011</td>
<td>1/63</td>
<td>0/62</td>
<td></td>
<td>3.2 %</td>
<td>2.95 [ 0.12, 71.13 ]</td>
</tr>
<tr>
<td>Saba 2011</td>
<td>1/16</td>
<td>0/21</td>
<td></td>
<td>2.8 %</td>
<td>3.88 [ 0.17, 89.46 ]</td>
</tr>
</tbody>
</table>

Total (95% CI) 437 [500] 100.0 % 1.24 [0.65, 2.38]

Total events: 16 (Isotonic), 17 (Hypotonic)

Heterogeneity: Chi² = 4.16, df = 5 (P = 0.53); I² = 0.0%

Test for overall effect: Z = 0.66 (P = 0.51)

Test for subgroup differences: Not applicable.
### Analysis 1.14. Comparison 1 Isotonic versus hypotonic, Outcome 14 Hyponatraemia (by age).

**Review:** Isotonic versus hypotonic solutions for maintenance intravenous fluid administration in children

**Comparison:** 1 Isotonic versus hypotonic

**Outcome:** 14 Hyponatraemia (by age)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Isotonic n/N</th>
<th>Hypotonic n/N</th>
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<th>Weight</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
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<td>Age &lt; 1 year</td>
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</tr>
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<td>Choong 2011</td>
<td>0/7</td>
<td>1/8</td>
<td></td>
<td>10.2 %</td>
<td>0.38 [ 0.02, 7.96 ]</td>
</tr>
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<td>Coulthard 2012</td>
<td>0/5</td>
<td>1/6</td>
<td></td>
<td>10.1 %</td>
<td>0.39 [ 0.02, 7.88 ]</td>
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<tr>
<td>Cuello 2012</td>
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<td>0/3</td>
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<td></td>
<td>Not estimable</td>
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<td>Kannan 2010</td>
<td>1/13</td>
<td>8/26</td>
<td></td>
<td>38.7 %</td>
<td>0.25 [ 0.03, 1.79 ]</td>
</tr>
<tr>
<td>Neville 2010</td>
<td>0/5</td>
<td>0/1</td>
<td></td>
<td></td>
<td>Not estimable</td>
</tr>
<tr>
<td>Rey 2011</td>
<td>2/8</td>
<td>6/9</td>
<td></td>
<td>41.0 %</td>
<td>0.38 [ 0.10, 1.36 ]</td>
</tr>
<tr>
<td>Saba 2011</td>
<td>0/3</td>
<td>0/2</td>
<td></td>
<td></td>
<td>Not estimable</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>45</strong></td>
<td><strong>55</strong></td>
<td></td>
<td>100.0 %</td>
<td><strong>0.33 [ 0.12, 0.88 ]</strong></td>
</tr>
<tr>
<td>Age 1 to 5 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>105</strong></td>
<td><strong>138</strong></td>
<td></td>
<td>100.0 %</td>
<td><strong>0.33 [ 0.19, 0.57 ]</strong></td>
</tr>
<tr>
<td>Age &gt; 5 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>219</strong></td>
<td><strong>246</strong></td>
<td></td>
<td>100.0 %</td>
<td><strong>0.51 [ 0.38, 0.69 ]</strong></td>
</tr>
</tbody>
</table>

Total events: 3 (Isotonic), 16 (Hypotonic)

Heterogeneity: Chi² = 0.13, df = 3 (P = 0.99); I² =0.0%

Test for overall effect: Z = 2.21 (P = 0.027)

2 Age 1 to 5 years

Total events: 11 (Isotonic), 45 (Hypotonic)

Heterogeneity: Chi² = 7.23, df = 4 (P = 0.12); I² =45%

Test for overall effect: Z = 3.88 (P = 0.0001)

3 Age > 5 years

Total events: 42 (Isotonic), 89 (Hypotonic)

Heterogeneity: Chi² = 4.91, df = 7 (P = 0.67); I² =0.0%

Test for overall effect: Z = 4.37 (P = 0.000012)

Test for subgroup differences: Chi² = 2.30, df = 2 (P = 0.32), I² =13%
Glucose?
Evaluation of current paediatric guidelines for fluid therapy using two different dextrose hydrating solutions

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years of age. This study suggests that the use of a 5% dextrose hydrating solution in 0.3 N saline is more likely to result in hyperglycaemia and hyponatraemia than a 2.5% dextrose in a 0.4 N saline, particularly in children younger than 4 years of age.
Perioperative Blood Glucose Concentrations in Pediatric Outpatients

Leila G. Welborn, M.D.,* Willis A. McGill, M.D.,† Raafat S. Hannallah, M.D.,‡ Catherine L. Nisselson, M.D.,§ Urs E. Ruttimann, Ph.D.,‖ Jocelyn M. Hicks, Ph.D.**

Fig. 1. Perioperative changes in blood glucose concentrations (glucose-oxidase method) when LR and D₅LR are infused during surgery.
Intraoperative fluid management in children — a comparison of three fluid regimens

Magdalena Mierzewska-Schmidt

Table 1. Characteristics of the study groups (means ± SD or n)

<table>
<thead>
<tr>
<th>Group</th>
<th>G5W</th>
<th>GNaCl</th>
<th>RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>33</td>
<td>27 (initially 28)</td>
<td>30</td>
</tr>
<tr>
<td>Age (years)</td>
<td>6.17 ± 2.07</td>
<td>6.51 ± 2.46</td>
<td>6.06 ± 2.05</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>22.7 ± 6.82</td>
<td>25.8 ± 9.45</td>
<td>23.1 ± 8.28</td>
</tr>
<tr>
<td>Gender F/M</td>
<td>14/19</td>
<td>11/16</td>
<td>6/24</td>
</tr>
<tr>
<td>Exclusions</td>
<td>0</td>
<td>1 (bleeding)</td>
<td>0</td>
</tr>
</tbody>
</table>

Gender: F — female, M — male

Table 2. Comparison of glucose concentrations before and after surgery. Data given as median (range)

<table>
<thead>
<tr>
<th>Group</th>
<th>G5W</th>
<th>GNaCl</th>
<th>RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative glucose (mg dL⁻¹)</td>
<td>92.2 (72.0–121.0)</td>
<td>88.1 (67.0–107.6)</td>
<td>88.4 (46.8–111.7)</td>
</tr>
<tr>
<td>Postoperative glucose (mg dL⁻¹)</td>
<td>259.0 (175.0–652.0)</td>
<td>192.0 (123.0–345.0)</td>
<td>93.3 (49.2–124.0)</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
<td>0.044</td>
</tr>
</tbody>
</table>

Figure 1. Glucose concentrations after surgery — intergroup comparisons. Significant intergroup differences observed (P < 0.0001); description in the text
The Effects of Dextrose Infusion and Head Position on Neurologic Outcome after Complete Cerebral Ischemia in Primates: Examination of a Model


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**Graphs**

- **Graph 1:**
  - Title: Histopathology Score
  - X-axis: Monkey Rank
  - Y-axis: % Neurologic Function
  - Legend: Lactated Ringer's, Dextrose
  - Symbols: S = Supine, P = Prone, L = Lateral

- **Graph 2:**
  - Title: Histopathology Score
  - X-axis: Monkey Rank
  - Y-axis: Histogram of Histopathology Scores
  - Legend: Lactated Ringer's, Dextrose
  - Symbols: S = Supine, P = Prone, L = Lateral
Lactated Ringer with 1% dextrose: an appropriate solution for peri-operative fluid therapy in children

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Department of Paediatric Anaesthesia, Hôpital Saint Vincent de Paul, Paris, France

to the normal ranges at T2 and T3 in the RL group. Sodium values remained unchanged post-operatively in both RL and RLD1 groups, while a significant decrease was observed in the RLD2.5 group ($P < 0.001$). Total protein decreased in the three groups post-operatively ($P < 0.001$) towards normal values. These data suggest that RLD1 is appropriate for peri-operative fluid therapy in children. Its administration at the infusion rate used in this study, resulted in moderate post-operative hyperglycaemia while avoiding the risk of peri-operative hypoglycaemia, maintaining a constant extracellular fluid composition and correcting pre-operative fluid deficit.
Clinical guidelines for intraoperative fluid therapy

Intraoperative administration of glucose-free isotonic hydrating solutions should be the routine practice for most procedures in children over 4–5 years of age. In infants and young children, 5% dextrose solutions should be avoided, but 1% or 2% dextrose in lactated Ringer is appropriate (19,20,24). Glucose infusion at a rate of 120–300 mg·kg⁻¹·h⁻¹ is sufficient to maintain an acceptable blood glucose level and to prevent lipid mobilization in infants and children (34,35). Polyionique B66 contains 0.9% dextrose that is adequate to maintain normal blood glucose values in infants and young children during surgery. (Table 4) This 'golden compromise solution' (36) has been used in France for more than 15 years and marketing authorization was granted in 2001 by the French authorities.

<table>
<thead>
<tr>
<th>Composition</th>
<th>Polyionique B66</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>120</td>
</tr>
<tr>
<td>Potassium</td>
<td>4</td>
</tr>
<tr>
<td>Calcium</td>
<td>2.2</td>
</tr>
<tr>
<td>Chloride</td>
<td>108</td>
</tr>
<tr>
<td>Lactate</td>
<td>20</td>
</tr>
<tr>
<td>Dextrose</td>
<td>50.5</td>
</tr>
<tr>
<td>Indications</td>
<td>Maintenance fluid therapy during surgery in infants and young children</td>
</tr>
</tbody>
</table>
Lessons from past research

- Fluid needs correspond to metabolic needs ~ weight
- Risk population for hypoNa
- Significant morbidity & mortality
- Isotonic IV fluids
- Dextrose 1%
Guidelines – general recommendations

- Plasma electrolyte profile at least daily
- Plasma osmolality, urine osmolality, urinary [Na] in case of hypoNa
- BP, HR, weight, fluid balance daily
- Frequent reassessment fluid type + rate ~ medication
NPSA (2007)

- Patient Safety Alert (UK)
- Development of fluid-induced hypoNa in the previously well child undergoing elective surgery or with mild illness may not be well recognised:
  - 2000-2007: 4 child deaths (and one near miss) < neurological injury from hospital-acquired hypoNa reported in the UK
  - International literature cites > 50 cases of serious injury or child death from the same cause associated with the administration of hypotonic infusions
- **Stop general use of NaCl 0.18% + Glc 4%**
- Produce and disseminate clinical guidelines for the fluid management of paediatric patients. These should give clear recommendations for fluid selection and clinical and laboratory monitoring
APA CONSENSUS GUIDELINE ON PERIOPERATIVE FLUIDS IN CHILDREN (2007)

• 1. Children can safely be allowed clear fluids 2 hours before surgery without increasing the risk of aspiration.
• 2. Food should normally be withheld for 6 hours prior to surgery in children aged 6 months or older.
• 3. In children under 6 months of age it is probably safe to allow a breast milk feed up to 4 hours before surgery.
• 4. Dehydration without signs of hypovolaemia should be corrected slowly.
• 5. Hypovolaemia should be corrected rapidly to maintain cardiac output and organ perfusion.
• 6. In the child, a fall in blood pressure is a late sign of hypovolaemia.
• 7. Maintenance fluid requirements should be calculated using the formula of Holliday and Segar:
   
   Body weight - Daily fluid requirement
   0-10kg: 4ml/kg/hr
   10-20kg: 40ml/hr + 2ml/kg/hr above 10kg
   >20kg: 60ml/hr + 1ml/kg/hr above 20kg

• 8. A fluid management plan for any child should address 3 key issues:
   i. any fluid deficit which is present
   ii. maintenance fluid requirements
   iii. any losses due to surgery e.g. blood loss, 3rd space losses

• 9. During surgery all of these requirements should be managed by giving ISOTONIC fluid in all children >1 month.
• 10. The majority of children > 1 month will maintain a normal blood sugar if given NON-DEXTROSE containing fluid during surgery.
• 11. Children at risk of hypoglycaemia if non-dextrose containing fluid is given are those on parenteral nutrition or a dextrose containing solution prior to theatre, children of low body weight (<P3) or having surgery of more than 3 hours duration and children having extensive regional anaesthesia. These children at risk should be given dextrose containing solutions or have their blood glucose monitored during surgery.
• 12. Blood loss during surgery should be replaced initially with crystalloid or colloid, and then with blood once the haematocrit has fallen to 25%. Children with cyanotic congenital heart disease and neonates may need a higher haematocrit to maintain oxygenation.
• 13. Fluid therapy should be monitored by daily electrolyte estimation, use of a fluid input/output chart and daily weighing if feasible.
• 14. Acute dilutional hyponatraemia is a medical emergency and should be managed in PICU.
European Consensus Statement (2011)

• Intraoperative use of isotonic solutions with 1-2.5% Glc in children is considered well established use in Europe and other countries.
• Unfortunately, a European marketing authorisation of such a solution is currently missing!!
• Consequence paediatric anaesthetists tend to use suboptimal IV fluid strategies that may lead to serious morbidity and even mortality because of iatrogenic hypoNa, hyperglycaemia or medical errors…

• Intraoperateieve vloeistoffen
  – Osmolarity close to the physiologic range (→ tonicity)
  – Glc 1-2.5% instead of Glc 5% (to avoid hypoglycaemia, lipolysis or hyperglycaemia)
  – Balanced: includes metabolic anions (i.e. acetate, lactate or malate) as bicarbonate precursors (to prevent hyperchloraemic acidosis)
BAPA (2012)

- Perop (intraop + postop) fluid management → **isotonic balanced + ↓Glc (1-2.5%)**
- (~ European): not commercially available
- **Large margin of safety** – accidental hyperhydration…
- ~ Plasmalyte + RL (without Glc)
  (+ Glc 1%: 10 mL Glc 50% in 500 mL)
- Replacement fluids → ~ composition losses (frequently NaCl 0.9%)
- Hypovolemia: bolus isotonic fluids
• 1 month – 16 years
• (+ Glc 5%: + 50 mL Glc 50% in 500 mL)

• Minor surgery/Day surgery
  – ‘Superhydration’
  – ↓ PONV adults/children
NICE guidelines (12/2015)

- **Fluid resuscitation**
  - **Children:**
    - Glucose-free crystalloids that contain 131-154 mmol/L sodium
    - Bolus of 20 mL/kg (< 10 min).
    - *Cave:* pre-existing conditions (such as cardiac/renal disease) - may require smaller fluid volumes
  - **Term neonates:**
    - Glucose-free crystalloids that contain 131-154 mmol/L sodium
    - Bolus of 10-20 mL/kg (< 10 min)

- **Maintenance**
  - **Isotonic crystalloids** that contain 131-154 mmol/L sodium are appropriate for initial maintenance requirements

- **Replacement and redistribution**
  - *Adjust the maintenance needs:*
  - Existing fluid and/or electrolyte deficits or excesses
  - Ongoing losses
  - Abnormal distribution (such as tissue edema in sepsis)
  - Consider isotonic crystalloids that contain 131-154 mmol/L sodium for redistribution
  - Use 0.9% NaCl containing K to replace ongoing losses
  - Base any subsequent fluid prescriptions on plasma electrolyte [ ] and blood glucose [ ]
NICE (2)

- IV fluids are potentially dangerous → should be used only when indicated and with close observation.
- Children > adults at risk of permanent neurological complications and death due to hypoNa from inappropriate use of IV fluids.
Measure plasma electrolyte concentrations and blood glucose when starting intravenous fluids (except before most elective surgical procedures) and at least every 24 hours thereafter.

Term neonate:
- Calculate routine maintenance intravenous fluid rates using the following as a guide:
  - From birth to day 1: 50-60 mL/kg/day
  - Day 2: 70-80 mL/kg/day
  - Day 3: 80-100 mL/kg/day
  - Day 4 and 5-28: 120-150 mL/kg/day

  Is neonate in a critical postnatal adaptation phase? For example:
  - Respiratory distress syndrome
  - Meconium aspiration
  - Hypoxic ischaemic encephalopathy

  No
  - Initially use isotonic crystalloids that contain 131-154 mmol/L sodium and 5-10% glucose
  - Give no or minimal sodium until postnatal diuresis with weight loss occurs

  Yes
  - Initially use isotonic crystalloids that contain 131-154 mmol/L sodium

Child or young person:
- Using body weight to calculate intravenous fluid needs?
  - No
    - When using body surface area to calculate needs, estimate insensible losses of 300-400 mL/m²/24 hours plus urinary output
  - Yes
    - Calculate routine maintenance intravenous fluid rates for children and young people using Holliday-Segar formula:
      - 100 mL/kg/day for first 10 kg of weight
      - 50 mL/kg/day for second 10 kg of weight
      - 20 mL/kg/day for weight over 20 kg

      Be aware that over a 24 hour period, males rarely need more than 2500 mL and females rarely need more than 2000 mL.

- Risk of water retention associated with non-osmotic antidiuretic hormone secretion?
  - No
  - Consider either:
    - Restricting fluids to 50-80% of routine maintenance needs
    - Or
    - Reducing fluids, calculated on basis of insensible losses of 300-400 mL/m²/24 hours plus urinary output
  - Yes

Base any subsequent intravenous fluid prescriptions on plasma electrolyte concentrations and blood glucose measurements.
Fig 1 Algorithm for assessment and monitoring
• R/ HypoNa

**ASYMPTOMATIC**

Fluid status?

- In case of hypotonic infusion → switch to isotonic
- (Risk of ) hypervolemia (ADH↑) - ↓ Routine maintenance rate to 50-80%

OR

- ↓ Maintenance rate to sum: (insensible losses 300-400 mL/m²/24h + urinary losses)

**SYMPTOMATIC**

! FLUID RESTRICTION ALONE IS NOT ENOUGH!

Fluid status?

Immediate expert advice (PICU)

1) **Bolus** of 2 mL/kg (maximum 100 mL) of 2.7% NaCl over 10-15´
2) Further bolus of 2 mL/kg (maximum 100 mL) of 2.7% NaCl over the next 10-15´ if symptoms still present
3) If symptoms are still present - check the plasma [Na] and consider a third bolus of 2 mL/kg (maximum 100 mL) of 2.7% NaCl over 10-15´

Measure the plasma [Na] at least hourly

As symptoms resolve, ↓ frequency of measurements ~ of the response to treatment.

After symptoms have resolved, ensure that plasma [Na] does not increase by > 12 mmol/L in 24 hr
To remember:

- Risk population for hypoNa
- Isotonic fluids prevent hypoNa
- Hypoglycemia is infrequent
- Hyperglycemia should be avoided
- Isotonic, balanced fluids + Glc 1% (exceptions)
- Monitoring of plasma levels!
Future perspectives

A novel isotonic-balanced electrolyte solution with 1% glucose for perioperative fluid management in children - an animal experimental preauthorization study

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*Klinik für Anästhesiologie und Intensivmedizin, Medizinische Hochschule Hannover, Hannover, Deutschland, †Klinik für Neurochirurgie, Medizinische Hochschule Hannover, Hannover, Deutschland and ‡Klinik für Rinder, Tierärztliche Hochschule Hannover, Hannover, Deutschland

Section Editor: Dr Andrew Davidson
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