Hyponatremia Guideline

WHY SHOULD WE BOTHER?

R. Zietse, Rotterdam, the Netherlands

Hyponatremia

- Serum Na⁺ < 135 mmol/L
- Most common electrolyte disorder
- Heterogeneous disorder
- Not a disease
Hyponatremia is a disorder of water balance
Regulation of water excretion

Osmoregulation
Hyponatremia remains to be a significant threat
Slow treatment -> Brain edema

- Most often:
  - Children
  - Women
  - Anorexic

Fast treatment -> Osmotic Demyelinisation

- Most often:
  - Children
  - Women
  - Anorexic
  - Hypokalemic
  - Diuretic
Complications hyponatremia

The greatest challenge in the diagnosis and treatment of hyponatremia is the differentiation between acute and chronic hyponatremia, in order to prevent cerebral edema and osmotic demyelination respectively!

Treatment dilemma
Hyponatremia Signs and Symptoms

- Headache
- Nausea and vomiting
- Lethargy
- Psychosis
- Ataxia and gait disturbances
- Non-cardiogenic pulmonary edema
- Seizures
- Coma

Patients with hyponatremia fall four times more frequently!

Mild Chronic Hyponatremia is Associated with Falls, Unsteadiness, and Attention Deficits
Renneboog et al., Am J Med 2006
Hyponatremia induced osteoporosis

Verbalis *et al.*, *J Bone Mineral Res* 2010

Epidemiology
Yes, you can die from acute hyponatremia...

WATER INTOXICATION
REPORT OF A FATAL HUMAN CASE, WITH CLINICAL, PATHOLOGIC AND EXPERIMENTAL STUDIES
FERDINAND C. HELWIG, M.D.
CARL BRYANT SCHUTZ, M.D.
AND
DWIGHT E. CURRY, M.D.
KANSAS CITY, MO.
The Journal of the American Medical Association

...or develop permanent brain damage...

The New England Journal of Medicine
©Copyright, 1986, by the Massachusetts Medical Society
Volume 314 JUNE 12, 1986 Number 24
HYponatremia, Convulsions, Respiratory Arrest, and Permanent Brain Damage After Elective Surgery in Healthy Women
ALLEN I. ARIEFF, M.D.
Acute post-operative hyponatremia

Acute hyponatremia is relatively rare and has a good prognosis when treated promptly

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Therapy</th>
<th>Neurologic Sequela</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3% NaCl 250 mL</td>
<td>Nil</td>
</tr>
<tr>
<td>2</td>
<td>3% NaCl 500 mL</td>
<td>Nil</td>
</tr>
<tr>
<td>3</td>
<td>3% NaCl 500 mL</td>
<td>Nil</td>
</tr>
<tr>
<td>4</td>
<td>3% NaCl 500 mL</td>
<td>Nil</td>
</tr>
<tr>
<td>5</td>
<td>3% NaCl 500 mL</td>
<td>Nil</td>
</tr>
<tr>
<td>6</td>
<td>3% NaCl 500 mL</td>
<td>Nil</td>
</tr>
<tr>
<td>7</td>
<td>3% NaCl 250 mL</td>
<td>Nil</td>
</tr>
<tr>
<td>8</td>
<td>3% NaCl 500 mL</td>
<td>Nil</td>
</tr>
<tr>
<td>9</td>
<td>3% NaCl 500 mL</td>
<td>Nil</td>
</tr>
<tr>
<td>10</td>
<td>3% NaCl 750 mL</td>
<td>Nil</td>
</tr>
<tr>
<td>11</td>
<td>3% NaCl 500 mL</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Hsu et al., J Emerg Med 2005
Osmotic demyelination: devastating, but incidence and mortality relatively low

---

**Table 1. Serum Sodium Concentrations in Eight Patients with Neurologic Sequelae after Correction of Hyponatremia.**

<table>
<thead>
<tr>
<th>PATIENT No.</th>
<th>Age/Sex</th>
<th>CAUSE</th>
<th>Na on Admission</th>
<th>TREATMENT*</th>
<th>MAXIMUM Na Increase</th>
<th>Na at Onset of Sequelae</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54/F</td>
<td>Diabetes?</td>
<td>102</td>
<td>NS</td>
<td>27</td>
<td>136–156 (Days 3–5)</td>
</tr>
<tr>
<td>2</td>
<td>54/F</td>
<td>Diabetic</td>
<td>109</td>
<td>3%</td>
<td>12–17</td>
<td>126–146 (Days 3–10)</td>
</tr>
<tr>
<td>3</td>
<td>60/M</td>
<td>Diabetic</td>
<td>105</td>
<td>NS</td>
<td>27</td>
<td>132 (Day 5)</td>
</tr>
<tr>
<td>4</td>
<td>68/F</td>
<td>Diabetic</td>
<td>103</td>
<td>NS</td>
<td>25</td>
<td>133 (Day 6)</td>
</tr>
<tr>
<td>5</td>
<td>74/F</td>
<td>Diabetic</td>
<td>115</td>
<td>3%</td>
<td>23</td>
<td>138 (Day 2)</td>
</tr>
<tr>
<td>6</td>
<td>75/M</td>
<td>Diabetic</td>
<td>114</td>
<td>3%</td>
<td>18</td>
<td>130 (Day 4)</td>
</tr>
<tr>
<td>7</td>
<td>77/F</td>
<td>Diabetic</td>
<td>108</td>
<td>NS</td>
<td>13</td>
<td>132 (Day 3)</td>
</tr>
<tr>
<td>8</td>
<td>41/M</td>
<td>Dianetia</td>
<td>109</td>
<td>NS</td>
<td>13</td>
<td>152 (Day 3)</td>
</tr>
</tbody>
</table>

---

- Na < 135 mmol/l, n = 14,290
- Patients with hyponatremia had an increased risk of in-hospital mortality (OR 1.47), 1-year mortality (OR 1.38), 5-year mortality (OR 1.25)
- Cardiovascular disease, metastatic cancer, procedures related to the musculoskeletal system
- Resolution of hyponatremia during hospitalization attenuated the increased mortality risk
Community-acquired and hospital-associated hyponatremia have increased mortality rates

Wald et al., Arch Intern Med 2010

"Parabola" relationship between serum sodium and mortality

Chawla et al., Clin J Am Soc Nephrol 2011
Mild hyponatremia in the general population is also associated with decreased survival rates

Hoorn et al.,
J Bone Mineral Res 2011

Disorders in which outcome is worse when hyponatremia is also present

- Heart failure (Gheorghiade et al., 2007, Tribouilloy et al., 2008)
- Liver cirrhosis (Heuman et al., 2004)
- ST-elevation myocardial infarction (Goldberg et al., 2004 and 2006)
- Pneumonia (Nair et al., 2007, Zilberberg et al. 2008)
- Pulmonary embolism (Scherz et al., AJRCCM 2010)
- Pulmonary hypertension (Forfia et al., AJRCCM 2008)
Settings in which outcome is worse when hyponatremia is also present

- **Intensive care** (Funk et al., 2010)
- **General population** (Sajadieh et al., 2009; Hoorn et al., 2011)
- **Hemodialysis** (Waikar et al., 2011)

Hyponatremia and mortality: three scenarios

**Scenario 1**

- Hyponatremia
- Mortality

Hyponatremia and mortality: three scenarios

**Scenario 1**
- Hyponatremia
- Severe underlying disease
- Mortality

**Scenario 2**
- Hyponatremia
- Severe underlying disease
- Mortality

**Scenario 3**
- Severe underlying disease
- Hyponatremia
- Mortality
