TREATMENT OF ACUTE HYponatremia

Conventional and Novel Therapy

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Hyponatremia is the most common electrolyte disorder seen in hospitalized patients.

<table>
<thead>
<tr>
<th>Electrolyte Disorder</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Hyponatremia</td>
<td>21%</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>12%</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>10%</td>
</tr>
<tr>
<td>Hypernatremia</td>
<td>5%</td>
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</tbody>
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LECTURE GOAL

UNDERSTANDING HYPONATREMIC ENCEPHALOPATHY (HE)

- Risk factors
- Signs and symptoms
- Therapy
Anatomy of Hyponatremia

- Glomerulus – Filtration
- Proximal Tubule – Na Reabsorption
- Loop of Henle – Na K 2 Cl Transport
- Distal Nephron – AVP
AVP RELEASE

Hypothalamus
Supraoptic &
Paraventricular nuclei
axonal flow to
Posterior pituitary (↑ or ↓ release)
AVP RELEASE

Volume Receptors

Baroreceptors and volume receptors
Aortic arch, carotid sinus and atria
Parasympathetic afferent pathway back to Hypothalamus (↑ or ↓ release)
(can override osmolar)
AVP (ADH)

- **V₁a Receptors**
  - Regulate Vascular Tone

- **V₂ Receptors**
  - Regulate H₂O Reabsorption by the Kidney
Intracellular Action of Vasopressin

Antidiuresis Is Regulated Primarily by Plasma AVP Levels

RISK FACTORS FOR HE

- Post-operative state
- Cortisol deficiency
- Nausea, emesis, pain, stress
- Female sex steroids Na/K/ATPase
- Hypoxia-limits adaptation
- CNS disease or surgery
- Children < 16 years

Moritz M. Ped Nephrol 2010; 25: 1225-1238
SYMPTOMS AND SIGNS OF HE

- Headache
- Nausea and vomiting
- Lethargy
- Weakness
- Confusion
- Agitation

- Seizures
- Coma
- Apnea
- Pulmonary edema
- Papilledema
- Cardiac arrhythmias
CHILDREN VS ADULTS

Average serum sodium in children with hyponatremic encephalopathy is 120 mEq/L vs adults is 111 mEq/L.

A child’s brain reaches adult size by 6 years of age but the skull does not reach adult size until 16 years of age.

Therefore, herniation occurs at higher serum sodium levels in children.
ACUTE HYPONATREMIA/TRAUMA (CEREBRAL EDEMA) VS

CHRONIC HYPONATREMIA (BRAIN ADAPTATION, LOSS OF ELECTROLYTES AND OSMOLYTES. MAY LEAD TO CPM SECONDARY TO DEHYDRATION IF OVERCORRECTION OCCURS)
Diagnostic Approach for the Syndrome of Inappropriate Antidiuretic Hormone Release

**Diagnostic Criteria**

Decreased extracellular fluid effective osmolality
(<270 mOsm/kg H$_2$O)

Inappropriate urinary concentration
(>100 mOsm/kg H$_2$O)

Clinical euvolemic

Elevated urinary sodium concentration under conditions of a normal salt and water intake

Absence of adrenal, thyroid, pituitary, or renal insufficiency or diuretic use
Diagnostic Criteria for SIADH

**Supplemental**

- Abnormal H₂O load test
- Plasma AVP level inappropriately high relative to plasma osmolality
- No significant correction of plasma [Na⁺] with volume expansion, but improvement after fluid restriction

SIADH=syndrome of inappropriate antidiuretic hormone secretion
CASE 1

Healthy 3 year old brought to ER with 1 day history N&V. Blood pressure 85/60 mm Hg. Exam-dry. Chemistries normal except increased BUN. Child received 2 boluses of normal saline IV. Child admitted and then treated with “2/3 and 1/3” at 130 mL per hr IV. The child voided about 110 mL urine and received 1.5 liters IV fluid. The child developed lethargy, incontinence and serum sodium now 120 mEq/L. Seizures developed, and mannitol and saline were given prior to demise. What went wrong? Therapy?

Koczmarz C. CJHP 2009; 62: 512-515
CASE 2

A 7 year old girl with cloacal exstrophy presented with 2 large bladder stones in association with cutaneous fistulae after a prior gastric-ileal augment, bladder-neck reconstruction. During the 35 minute procedure to remove the stones, a total of 2 liters of sterile water was used for bladder irrigation for stone fragment removal. Postoperatively, she was extubated but became lethargic and irritable prior to respiratory arrest. Serum sodium 120 mEq/L. CT showed massive cerebral edema. What went wrong? Therapy?

SEVERE CEREBRAL EDEMA

Figure 1: Postoperative CT of a 7-year-old girl intubated after a witnessed respiratory arrest in the recovery room consistent with severe cerebral edema and absent ventricles.
SODIUM AND WATER SAMPLE CALCULATION

\[ 18 \text{ L} \times 140 \text{ mEq/L} = 133 \text{ mEq/L} \]

19 L
13 year old boy admitted with depressed level of consciousness secondary to severe hyponatremia of 116 mEq/L. At age 3 months nasofrontal encephalocele repaired with subsequent DI, hypothyroidism and AI. Treated with corticosteroids, thyroid and DDAVP. Following admission, serum sodium increased during 48 hours to 176 mEq/L. Neurologic status worsened and MRI demonstrated changes consistent with extrapontine myelinolysis. What went wrong? Therapy?

Ranger A. Ped Neurosurg. 2010; 46:318-323
AVOIDANCE OF AND MANAGEMENT OF DYSNATREMIA

- Frequent monitoring and measurement of serum sodium levels in at risk patients
- Infusion of 3% saline for hyponatremic encephalopathy
THREE PERCENT SALINE AND TRANSPORT (n=101)

Mean age 5.9 y
Mean weight 27.6 kg
MVA (n) 23
Hyponatremia (n) 6
Mean dose 5.3 mL/kg (1.2-24)
Sodium change 135 -> 143 mEq/L
range (115-152) -> (127-183)
Access Peripheral line (central, osseous)

Luu JL. Ped Emerg Care. 2011; 27: 113-117
OUTLINE FOR USE OF 3% SALINE IN HE

- 2 mL/kg of 3% NaCl over 10 minutes. Maximum 100 cc
- Repeat bolus 1-2 times as needed until symptoms improve. Goal 5-6 mEq/L increase
- Recheck SNa following second bolus or Q 2 H
- HE is unlikely if no improvement
- Stop therapy if either symptom free or SNa increases > 10 mEq/L

Moritz M. Ped Nephrol 2010; 25: 1225-1238
Avoidance of Overcorrection of Hyponatremia

Goal: 4 - 6 mEq/L

Remedy: 5% D/W at 6 ml/kg over 1 - 2 Hr

DDAVP 2 µg q 6 - 8 Hrs

Adrogué-Madias Formula

Change in serum sodium concentration

with 1L of infusate = \[
\frac{\text{Infusate sodium concentration} - \text{Patient Serum Na concentration}}{\text{Total body water} + 1}
\]

Ratio of actual rise in sodium to the expected rise

Frequency

The safety and effectiveness of vaptans in pediatric patients have not been studied.
SERUM SODIUM RESPONDERS

B. Metzger, M. DeVita, M. Michelis. *Int Urol Nephrol* 2008;40:725-730
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B. Metzger, M. DeVita, M. Michelis. *Int Urol Nephrol* 2008;40:725-730

Day 0  Day 1

Urine Osm
mOsm/kg

100  200  300  400  500  600
CHF VS SIADH

TOLVAPTAN IN A SIX YEAR OLD

Ten kg male with CHF treated with furosemide, thiazide and spironolactone gained weight and serum sodium decreased to 118 mEq/L. Treated with tolvaptan 2-3-4-5 mg per day over 30 days. Serum sodium increased to 133 mEq/L and Uosm decreased to 216 mOsm/kg. Body weight decreased by 1.5 kg.

HYPONATREMIA THERAPY

SUMMARY:

- Boluses or infusions of 3% saline are the most effective therapies for acute or severe hyponatremic encephalopathy.

- Chronic hyponatremia with limited symptoms and mild/moderate decreases in serum sodium can be managed by traditional and/or newer therapeutic approaches.
THANK YOU