Hyponatremia and Other Electrolyte Disorders

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Disclosures

Nothing to Disclose
Hyponatremia

- Most common electrolyte disorder in hospitalized patients
- Chronic hyponatremia is common in the elderly: thiazides, CHF, cancer, SIADH (drugs)
  - Consequences: osteoporosis, gait disturbance, falls

\[ S_{Na} = 130 \text{ mEq/L} \]

\[ S_{Na} = 139 \text{ mEq/L} \]

Renneboog B, AJM 119:e71,2006
Risk of Inpatient Hyponatremia by Age

Berl T.  CJ ASN, in press (10/04/12)
Preoperative Hyponatremia and Mortality
Leung AA, et al. Arch Intern Med (09/10/12)

• **Aim:** to determine association between preop hyponatremia and 30-day mortality

• Reviewed NSQIP database

• Compared those with hyponatremia (< 135 mEq/L) vs. 135-144 mEq/L

• Preop hyponatremia → ↑ risk of 30-day mortality, 5.2% vs. 1.3%, OR 1.44

• Also ↑ CV events, wound infections, PNA, LOS
Preoperative Hyponatremia and Mortality
Leung AA, et al. Arch Intern Med (09/10/12)
Hyponatremia is a **WATER** Disorder
Assessment of Hyponatremia

• Measure serum osmolality
  – **Normal**: isotonic “pseudohyponatremia” (hyperlipidemia, hyperproteinememia)
  – **Low**: true hypotonic hyponatremia

• Assess volume status

• Measure urine sodium and osmolality
## Diagnosis of SIADH

**Ellison DH, Berl T. NEJM 356:2064, 2007**

<table>
<thead>
<tr>
<th>Essential Features</th>
<th>Supplemntal Features</th>
</tr>
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<tbody>
<tr>
<td>• ↓ serum osm &lt; 275 mOsm/kg of water</td>
<td>• Plasma uric acid &lt; 4 mg/dl</td>
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<tr>
<td>• Urinary osm &gt; 100 mg/kg of water while hypotonic</td>
<td>• BUN &lt; 10 mg/dl</td>
</tr>
<tr>
<td>• Clinical euvoelema</td>
<td>• $F_{E_{Na}} &gt; 1%; F_{E_{urea}} &gt; 55%$</td>
</tr>
<tr>
<td>• Urine Na &gt; 40 mEq/L with normal Na intake</td>
<td>• Failure to correct after 0.9% NaCl infusion</td>
</tr>
<tr>
<td>• Normal thyroid, adrenal fnx</td>
<td>• Correction with fluid restriction</td>
</tr>
<tr>
<td>• No recent diuretics</td>
<td>• Abnormal water load test</td>
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<td>• Elevated plasma AVP level</td>
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</table>
Causes

- Hyperproteinemia
- Hyperlipidemia
- Hyperglycemia
- Mannitol therapy
- Hypothyroidism
- Adrenal insufficiency
- Drugs

Water restriction and treatment of underlying disorder.
Hypertonic saline for life threatening hyponatremia
Drug-Related SIADH
Updated from Ellison DH, Berl T. NEJM 356:2064, 2007

• Pain meds: opiates, tramadol, NSAIDs
• Antidepressants: SSRIs, tricyclics
• Proton pump inhibitors
• Chemo: vincristine, cyclophosphamide, cisplatin, ifosfamide, imatinib
• Street drugs: MDMA (ecstasy), nicotine
• Antiepileptics: carbamezepine
• Others: ciprofloxacin, amiodarone, ACEI, clofibrate, antipsychotics, chlorpropamide
**Treatment**

1. Normal (280-295 mOsm/Kg):
   - Pseudohyponatremia
     - Check for: Hyperproteinemia, Hyperlipidemia

2. Plasma osmolality:
   - Low (<280 mOsm/Kg): Hypotonic hyponatremia
   - High (>295 mOsm/kg): Hypertonic hyponatremia
     - Check for: Hyperglycemia, Mannitol therapy

3. ECF status:
   - Euvolemia
     - SIADH (UOsm > 200, UNa > 20):
       - Hypothyroidism
       - Adrenal insufficiency
       - Drugs
         - Water restriction and treatment of underlying disorder.
         - Hypertonic saline for life threatening hyponatremia
Treatment of Symptomatic Hyponatremia

• Hypertonic saline

• **Calculation:**
  – mEq needed = 0.6 x wt (kg) x (desired – actual Na)
  – One liter of 3% NaCl = 513 mEq NaCl
  – ml of 3% NaCl needed = (mEq NaCl needed x 1000)/513

• **Rate of infusion:** adjust to ↑ Na by 1-2.5 mEq/hr

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Hypertonic in SIADH

you give 600 mL of hypertonic saline = 600 mOsm/600 mL

kidney sees 1000 mL of 600 mOsm/L by adding an additional 400 mL of water

all infused + 400 cc free water excreted

Sosm = 250  Uosm = 600  Sosm > 250
Hypertonic and furosemide in SIADH

You give 600 mL of hypertonic saline = 600 mOsm

Kidney sees 300 mL of 300 mOsm/kg + 300 mL of 300 mOsm/kg

→ excreted

→ retained sodium

\[ S_{osm} = 250 \]
\[ U_{osm} = 300 \]

Furosemide

\[ S_{osm} >> 250 \]
Hypertonic vs. Normal Saline?

• “Well, she is pretty hyponatremic. I don’t really want to move her to the ICU for hypertonic saline, so let’s keep her on the floor and use normal saline.”

• If the urine osm > 300 mOsm/kg, giving normal saline will **WORSEN** hyponatremia
Normal saline in SIADH

You give 2 L NS → 300 mOsm/kg = 600 mOsm

Kidney sees 1L of 600 mOsm/kg
+ 1L of free water

→ excreted
→ retained

Sosm = 250
Uosm = 600 mOsm/L
Fixed

Sosm < 250

😢
What about Conivaptan?

• Non-selective vasopressin V1a/V2 receptor antagonist
• Intravenous, ICU only, 4 days max
• Very effective in raising serum sodium
• Drug interactions are common
• OVERSHOOT can happen easily; monitor serum and urine Na q 2 hours
Asymptomatic Hyponatremia

- Nearly always chronic
- Common causes (esp. in the elderly): thiazides, SSRIs, NSAIDs, PNA, subdural hematoma, cancer/chemotherapy, “tea and toast” diet, idiopathic
- Hospitalization is usually NOT required
- Remove offending culprit(s); fluid restriction
Asymptomatic Hyponatremia

- ALL fluids are mostly water!
- Fluid restriction + NaCl tabs = oral hypertonic saline
  - Example: 1 gm NaCl tablets 3x/daily
- Demeclocycline
- Urea
SALTWATER TRIAL: Tolvaptan
Oral Vaptans: Caveats

• Hospitalization required for initiation; then frequent outpatient monitoring

• Risk of nephrogenic DI if fluids cannot be readily accessed

• Cost is prohibitive to many

• Stop the drug → hyponatremia recurs; not a cure
Common Causes of Hyponatremia in ICU:
- Diarrhea
- Lactulose therapy
- Diuretics
- Insensible loss
- Osmotic diuresis

- Current Body Water (CBW) = 0.6 x Current body weight (in Kg) [Use 0.4-0.5 for females and cachectic patients]
- Desirable Body Water (DBW) = [Current Na+ / 140] x CBW
- Body Water Deficit (BWD) = DBW - CBW

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HYPERKALEMIA

- Too much in
- Too little out
- Redistribution from cells → extracellular fluid
Hyperkalemia: Too Much In

• **Fruits and vegetables:** not all created equal
  – High K: bananas, oranges, lima beans, celery
  – Low K: tangerines, lettuce, green beans, carrots
  – Dietary consult/handouts = essential!
• Ask about OTC K supplements (leg cramps)
• Ask/counsel about salt substitutes
Salt Substitutes – Be Specific!

Ingredients:
Potassium Chloride, Fumaric Acid, Tricalcium Phosphate and Monocalcium Phosphate.

Ingredients:
Onion, Spices (Black Pepper, Chili Pepper, Parsley, Celery Seed, Basil, Bay, Marjoram, Oregano, Savory . . .)
Hyperkalemia: Too Little Out

100 mEq

90 mEq

10 mEq
Renal Potassium Excretion

Tubule Lumen

Low GFR
Low urine volume
Amiloride
Tiamterene
Trimethoprim

Blood

3 Na
2 K

Principal Cell
Renal Potassium Excretion

Tubule Lumen

Na

K

Blood

3 Na

2 K

Principal Cell

Digoxin
Spironolactone
ACEI/ARBs
NSAIDs
CyA, FK506
Heparin
Heparin-induced Hyperkalemia

• Some ↑K in 7% of patients, but usually need other factors for large rise in K
• Mechanism: inhibition of aldosterone production in adrenal zona glomerulosa, mostly via decrease in Ang II receptor number and affinity
• Occurs within a few days of therapy; is reversible; is unrelated to anticoagulant effect or route of administration
• Can occur with low doses [5000 units twice daily] and with low molecular weight heparins
Renal Potassium Excretion

Tubule Lumen

Na

Spironolactone and other aldosterone blockers

K

Blood

3 Na

2 K

Principal Cell
Estimation of Aldo Effect

Transtubular potassium gradient (TTKG)

\[ TTKG = \frac{U_K/P_K}{U_{osm}/P_{osm}} \]

\(< 6 = \text{Hypoaldosteronism} \quad > 10 = \text{Normal} \]

\(6-10 = \text{Indeterminate}\)
Treatment of Hyperkalemia

- Hyperkalemia is a medical emergency
- You can always shove K into the cells FASTER than you can remove it from the body!
  - Kayexalate = too little, too late
- Don’t let a “normal” EKG lull you into a false sense of security
Treatment of Hyperkalemia: Redistribution

- Insulin + glucose = best
- Beta-agonists also work (but very high doses are needed; risk of arrhythmias)
- Bicarbonate is often NOT very effective
Changes in Plasma K in ESRD
Allon M. JASN 6:1134, 1995
Hypokalemia

• **Etiology:** Too little in, too much out, or redistribution from extracellular fluid → cells

• **Think about:** ↑ Na delivery to distal tubule (IVF, diuretics); beta-agonists; adrenocortical steroids; aminoglycosides; amphotericin, cisplatinum

• **Use the TTKG to help with diagnosis**
  
  < 2 = GI loss  
  > 4 = renal loss, ↑ aldo
Spectrum of Hypercalcemia

Total serum calcium level, mg/dL (mmol/L)

8 (2)  10 (2.5)  12 (3)  14 (3.5)  16 (4)

- Hypercalcemic crisis
- Moderate hypercalcemia
- Mild hypercalcemia
- Normocalcemia

Ionized serum calcium level, mg/dL (mmol/L)

4 (1)  5.6 (1.4)  8 (2)  10 (2.5)  12 (3)

<table>
<thead>
<tr>
<th>Causes of Hypercalcemia</th>
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<tbody>
<tr>
<td><strong>Parathyroid hormone-related</strong></td>
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<tr>
<td>Primary hyperparathyroidism*</td>
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<tr>
<td>Sporadic, familial, associated with multiple endocrine neoplasia I or II</td>
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<tr>
<td>Tertiary hyperparathyroidism</td>
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<tr>
<td>Associated with chronic renal failure or vitamin D deficiency</td>
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<tr>
<td><strong>Vitamin D-related</strong></td>
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<tr>
<td>Vitamin D intoxication</td>
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<tr>
<td>Usually 25-hydroxyvitamin D₃ in over-the-counter supplements</td>
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<tr>
<td>Granulomatous disease sarcoidosis, berylliosis, tuberculosis</td>
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<tr>
<td>Hodgkin's lymphoma</td>
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<tr>
<td><strong>Malignancy</strong></td>
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<tr>
<td>Humoral hypercalcemia of malignancy* (mediated by PTHrP)</td>
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<tr>
<td>Solid tumors, especially lung, head, and neck squamous cancers, renal cell tumors</td>
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<tr>
<td>Local osteolysis* (mediated by cytokines) multiple myeloma, breast cancer</td>
</tr>
<tr>
<td><strong>Medications</strong></td>
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<tr>
<td>Thiazide diuretics (usually mild)*</td>
</tr>
<tr>
<td>Lithium</td>
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<tr>
<td>Milk-alkali syndrome (from calcium antacids)</td>
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<tr>
<td>Vitamin A intoxication (including analogs used to treat acne)</td>
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<tr>
<td><strong>Other endocrine disorders</strong></td>
</tr>
<tr>
<td>Hyperthyroidism</td>
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<tr>
<td>Adrenal insufficiency</td>
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<tr>
<td>Acromegaly</td>
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<tr>
<td>Pheochromocytoma</td>
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<tr>
<td><strong>Genetic disorders</strong></td>
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<tr>
<td>Familial hypocalciuric hypercalcemia: mutated calcium-sensing receptor</td>
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<tr>
<td><strong>Other</strong></td>
</tr>
<tr>
<td>Immobilization, with high bone turnover (e.g., Paget's disease, bedridden child)</td>
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<tr>
<td>Recovery phase of rhabdomyolysis</td>
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</tbody>
</table>

*—The most common causes of hypercalcemia.

**PTHrP** = parathyroid hormone-related peptide.
Metabolic Bone Disease in CKD

• **Treatment of Hyperphosphatemia**
  – Calcium carbonate (TUMS)
  – Calcium acetate
  – Sevelamer
  – Lanthanum

• **Treatment of Hyperparathyroidism**
  – Vitamin D
  – Calcitriol (and others)
  – Cinecalcet
## Mineral Metabolism in CKD

<table>
<thead>
<tr>
<th></th>
<th>Opinion</th>
<th>Meta-Analysis</th>
<th>RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D/calcium/phos/PTH</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Restrict dietary phos</td>
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<td></td>
<td></td>
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<tr>
<td>Oral phos binders</td>
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<td></td>
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<tr>
<td>Vit D or analog supplement</td>
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**Consensus in 2012**
- Calcium and phosphorus are bad
- PTH is bad (unless too low)
- Vit D is good (probably?)
Hypomagnesemia
Moe SM. Prim Care 35:215, 2008

• Occurs in 7-12% of hospitalized patients; up to 20% of ICU patients

• Often associated with other electrolyte abnormalities (hypokalemia, hyponatremia, hypocalcemia, hypophosphatemia)

• Causes: ↓ intake, ↓ GI absorption, ↑ GI or renal losses

• DRUGS
Risks of PPI Therapy

Vakil N. Drugs 72:437, 2012

• PPIs are increasing associated with ↑ risk of:
  – Pneumonia
  – Osteoporosis and bone fractures
  – Infectious diarrhea, C. diff
  – Interaction with clopidogrel → ↑ CV events
  – SIADH
  – Acute interstitial nephritis
  – Hypomagnesemia
References

• Ellison DH, Berl T. The syndrome of inappropriate antidiuresis. NEJM 256:2064, 2007
• Moe SM. Disorders involving calcium, phosphorus, and magnesium. Prim Care 35:215, 2008