EVALUATING AND MANAGING ELECTROLYTE DISBALANCES IN THE OUTPATIENT SETTING

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NEPHROLOGIST
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DISCLOSURE

- There are no conflicts of interest
TO BE DISCUSSED

Homeostasis
- Potassium
- Water

Evaluation and Management of Electrolyte Disbalances
- Hyperkalemia
- Hypokalemia
- Hyponatremia
- Hypernatremia

Summary
DISORDERS OF POTASSIUM BALANCE: HYPERKALEMIA AND HYPOKALEMIA
POTASSIUM HOMEOSTASIS

Increase Renal K⁺ Excretion

- Aldosterone
- High Na⁺ delivery to distal tubule (diuretics)
- High urine flow (osmotic diuresis)
- High serum K⁺ level
- Delivery bicarbonate to distal tubule

Decrease Renal K⁺ Excretion

- Absence, or very low aldosterone
- Low Na⁺ delivery to the distal tubule
- Low urine flow
- Low serum K⁺ level
- Kidney Injury
MORTALITY IN DYSKALEMIA

HYPERKALEMIA
MY PATIENT HAS HYPERKALEMIA, WHAT SHOULD I DO?

- Changes? Treat EKG and BMP
- Symptoms? Treat H&P and medication review
- Send home Pseudohyperkalemia
- Check other causes
  - Metabolic acidosis
  - Obstruction
  - Hyperosmolarity
  - K+ increasing meds
  - CKD
### Causes of Hyperkalemia

#### Increased Potassium Release from Cells
- Pseudohyperkalemia
- Fist clenching
- Tourniquet use
- Metabolic acidosis
- Insulin deficiency, hyperglycemia, and hyperosmolality
- Increased tissue catabolism
- Drugs
- Hyperkalemic Periodic Paralysis

#### Reduced Urinary Potassium Excretion
- Acute and chronic kidney disease
- Reduced aldosterone secretion or response to aldosterone
- Reduced distal sodium and water delivery
- Drugs
Medications That Cause HK

Biff Palmer A Physiologic-Based Approach to the Evaluation of a Patient with Hyperkalemia 2010 AJKD
**MANAGEMENT OF ACUTE HYPERKALEMIA**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Onset</th>
<th>Duration</th>
<th>MoA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Gluconate 1g/3min</td>
<td>1-2 min</td>
<td>30-60 min</td>
<td>Protect cardiomyocytes</td>
<td>Does not decrease K⁺  May have to repeat</td>
</tr>
<tr>
<td>RegInsulin 10u IV + Dextrose 50% 50ml (if CBG &lt;250mg/dl)</td>
<td>10-30 min</td>
<td>4-6 hrs</td>
<td>Shifts K⁺ into cells</td>
<td>Check CBG q30min for 4 hrs, especially if CKD</td>
</tr>
<tr>
<td>Inhaled Albuterol, 10-20mg</td>
<td>30 min</td>
<td>2-4 hrs</td>
<td>Shifts K⁺ into cells</td>
<td>Usual albuterol dose is 1.25mg or 2.5mg</td>
</tr>
<tr>
<td>Furosemide</td>
<td>&gt;30 min</td>
<td>2-6 hrs</td>
<td>Kaliuresis</td>
<td>2x Cr rule, use with 0.9% NSS</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>Minutes</td>
<td>Permanent</td>
<td>Removal</td>
<td>May be delayed</td>
</tr>
<tr>
<td>Exchangers?</td>
<td>1 hour to days</td>
<td>Permanent?</td>
<td>Remove via GI tract</td>
<td>None approved for acute management</td>
</tr>
</tbody>
</table>
MANAGEMENT OF HYPERKALEMIA IN THE OUTPATIENT SETTING

**Diuretics**
- Loops (Furosemide, bumetadine, torsemide)
  - For patients with CKD, CHF
- Thiazides (Chlorthalidone (preferred), indapamide, hydrochlorothiazide)

**Ion-exchange polymers**
- Sodium Polystyrene Sulfonate (Kayexalate®)?
- Patiromer (Veltassa®)
- Sodium Zirconium Cyclosilicate (Lokelma®)

**Others**
- Bicarbonate
- Fludrocortisone
- Limiting potassium intake?
- Discontinue medications?
<table>
<thead>
<tr>
<th></th>
<th>Veltassa Lokelma</th>
<th>Kayexalate</th>
<th>Advantages</th>
<th>Disadvantages or concerns</th>
<th>FDA Approval</th>
<th>MoA: Exchange</th>
<th>Na⁺ Content</th>
<th>Onset</th>
<th>Dosing</th>
<th>Side Effects</th>
<th>Administration</th>
<th>Cost</th>
<th>Storage</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA Approval</td>
<td>1958</td>
<td>2015</td>
<td>2018</td>
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<tr>
<td>MoA: Exchange</td>
<td>Na⁺ for K⁺</td>
<td>Ca²⁺ for K⁺</td>
<td>Na⁺/H⁺ for K⁺</td>
<td></td>
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<tr>
<td>Na⁺ Content</td>
<td>1,500mg per 15g</td>
<td>N/A</td>
<td>800mg per 10g</td>
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<tr>
<td>Onset</td>
<td>Hours to days</td>
<td>7 hours</td>
<td>1 – 2.2 hours</td>
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<tr>
<td>Dosing</td>
<td>15-60g 1-4x QD</td>
<td>8.4g QD (max TID)</td>
<td>10g TID (for 48 hrs) then 10g QD</td>
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<tr>
<td>Side Effects</td>
<td>GI (nausea, vomiting, constipation)</td>
<td>GI (constipation)</td>
<td>Hypomagnesemia</td>
<td>Hypercalcemia?</td>
<td>GI (diarrhea)</td>
<td>Edema</td>
<td></td>
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<tr>
<td></td>
<td>Severe: GI necrosis, obstruction, perforation</td>
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</tr>
<tr>
<td>Administration</td>
<td>Liquid or Powder</td>
<td>Mix powder with 90ml of water</td>
<td>Mix powder with 45ml of water</td>
<td></td>
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<tr>
<td></td>
<td>Separate other meds by 3 hours</td>
<td>Separate other meds by 3 – 6 hours</td>
<td>Separate other meds by 2 hours</td>
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<tr>
<td>Storage</td>
<td>Room temperature</td>
<td>Refrigerator (2-8 °C)</td>
<td>Room Temperature</td>
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</tr>
<tr>
<td>Advantages</td>
<td>Cost and availability</td>
<td>No sodium</td>
<td>Less GI issues, Onset</td>
<td></td>
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<tr>
<td>Disadvantages or concerns</td>
<td>Lack of randomized trials, Severe GI AEs, High sodium content</td>
<td>Hypomagnesemia, Potential for DDIs, Must be refrigerated</td>
<td>Availability</td>
<td>High sodium content</td>
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<tr>
<td>FDA</td>
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<td>No</td>
<td>No</td>
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</tbody>
</table>
HYPOKALEMIA
MY PATIENT HAS HYPOKALEMIA, WHAT SHOULD I DO?

**History and Physical, medication review**
- GI/skin loss, meds, workplace

**CBC, BMP**
- Leukocytosis, acid-base, magnesium

**Urinary K+**
- >20mmol/24h – meds, RTA, others
- <20mmol/24h – Poor intake, GI loss

**Blood Pressures**
- Elevated – plasma aldosterone, renin activity and cortisol
- Low – Bartter, Gitelman, diuretics
MANAGEMENT OF HYPOKALEMIA

- Weakness or paralysis, decreased GI motility
  - If symptoms or EKG changes, send to ER

- Hypomagnesemia
  - Treat
  - Discontinue offending meds
  - Replenish

- If >2.5mEq/L

>2.5mEq/L

- Oral route preferred
- KCL 40mEq Liquid
- Tablet – risk of pill esophagitis
- Potassium citrate if metabolic acidosis
- Meds that increase serum K+
DISORDERS OF WATER BALANCE: HYPERNATREMIA AND HYPERSONATREMIA
WATER HOMEOSTASIS

Vasopressin (ADH) controls water excretion in collecting system.

Osmoreceptors in hypothalamus control vasopressin secretion in response to changes in tonicity.

**Response to Changes in Serum Osmolality**

- **Urine osmolality**
- **Thirst**
- **Vasopressin**

- Maximally effective vasopressin levels

**Plasma Osmolality and Dysnatremias**

- **Plasma osmolality**
  - 280–290 mOsm/kg H₂O

- **Decrease**
  - Suppression of thirst
  - Suppression of vasopressin release

- **Increase**
  - Stimulation of thirst
  - Stimulation of vasopressin release

- Disorder involving urine dilution with water intake
  - Dilute urine
  - Hyponatremia

- Disorder involving urine concentration with inadequate water intake
  - Concentrated urine
  - Hypermotremia
MORTALITY IN DYSNATREMIA
HYPERNATREMIA

High salt concentration
MY PATIENT HAS HYPERNATREMIA, NOW WHAT?

**History and physical examination, medication review**
- Spot urine electrolytes and osmolality
- Water deprivation test

**Volume Status Vitals**

**Diagnostic Approach in Hypernatremia**

- **Hypernatremia**
  - Assess volume status
    - **Hypovolemia**
      - Total body water ↓
      - Total body Na⁺ ↓
      - Urinary (Na⁺) >20 mmol/l
        - Renal losses
          - Osmotic or loop diuretic
          - Postobstruction
          - Intrinsic renal disease
        - Extrarenal losses
          - Excess sweating
          - Burns
          - Diarrhea
          - Fistulas
    - Urinary (Na⁺) <20 mmol/l
      - Renal losses
        - Diabetes insipidus
        - Hypodipsia
      - Extrarenal losses
        - Insensible losses: respiratory, dermal
  - Euvolemia (no edema)
    - Total body water ↓
    - No change in total body Na⁺
    - Urinary (Na⁺) variable
  - Hypervolemia
    - Total body water ↑
    - Total body Na⁺ ↑
    - Urinary (Na⁺) >20 mmol/l
      - Sodium gains
        - Primary hyperaldosteronism
        - Cushing’s syndrome
        - Hypertonic dialysis
        - Hypertonic NaHCO₃
        - NaCl tablets
HYPERNATREMIA

1qt ~ 946ml
15ml Soy Sauce ~ 950mg Na+
He drank 59,850mg of sodium!

Survival of Acute Hypernatremia Due to Massive Soy Sauce Ingestion

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Reprint Address: Heather A. Borek, MD, Department of Emergency Medicine, Division of Medical Toxicology, Bernstein Medical Center, 5501 Old York Road, Korman B-6, Philadelphia, PA 19141

Abstract—Background: Intentional massive sodium chloride ingestions are rare occurrences and are often fatal. Objectives: There are a variety of treatment recommendations for hypernatremia, ranging from dialysis to varying rates of correction. We report a case of acute severe hypernatremia corrected with rapid free-water infusions that, to our knowledge, has not been previously reported. Case Report: A 19-year-old man presented to the Emergency Department after ingesting several liters of soy sauce. He had been prescribed lithium carbonate for bipolar disorder. Associated iatrogenic morbidity and mortality (1,2). Other iatrogenic causes of acute hypernatremia include incorrect dilution of oral rehydration solution, as well as hypertonic intravenous fluids, enemas, gastric lavage, and peritoneal lavage (1,3-5). Acute sodium chloride poisoning in adults generally occurs as a suicide attempt in the setting of mental or emotional disorders (2).
DIABETES INSIPIDUS

Central diabetes insipidus
Destruction of neurohypophyseal neurons or mutations in AVP

Primary polydipsia
Excessive fluid intake

Renal resistance to serum AVP

Nephrogenic diabetes insipidus
Decreased response to AVP or mutations in AVPR2 or AQP2

Gestational diabetes insipidus
Excessive activity of placental vasopressinase

↑ AVP degradation

↓ Free water reabsorption
↑ Solute-free water diuresis

Nephrogenic DI:
- CKD
- Hypokalemia
- Hypercalcemia
- Meds
- Pregnancy

Dehydration phase
Desmopressin phase

Urine osmolality (mosm/kg)

Time (hours)

Normal response
Partial central DI
Primary polydipsia
Complete central DI
Partial nephrogenic DI
Complete nephrogenic DI
MANAGEMENT OF HYPERNATREMIA

***Free Water Deficit
Change in serum sodium per L of infusate: (Infusate Sodium) – (Serum Sodium) \( \div (TBW + 1) \)

- Hypovolemia
  - Correction of volume deficit
    - Administer isotonic saline until hypovolemia improves
    - Treatment of the etiology of losses (insulin, relief of obstruction, removal of osmotic diuretics, etc.)

- Euvolemia
  - Correction of water deficit
    - Calculate water deficit
    - Administer 0.45% saline, 5% dextrose, or oral water to replace the deficit and ongoing losses
    - In central diabetes insipidus (DI) with severe losses, aqueous vasopressin (Pitressin) 5 U subcutaneously q 6 h
    - Follow serum (Na⁺) carefully to avoid water intoxication

- Hypervolemia
  - Removal of Na⁺
    - Discontinue offending agents
    - Furosemide
    - Hemodialysis as needed for renal failure

- Correction of water deficit
  - Calculate water deficit
  - Administer 0.45% saline, 5% dextrose, or oral water to replace the deficit and ongoing losses

- Long-term therapy
  - Central DI (see Table 8-7)
  - Nephrogenic DI: Remove offending drugs, low Na⁺ diet, thiazide diuretics, amiloride for lithium-induced DI, correction of K⁺ and Ca²⁺
Is the rate of correction of hypernatremia associated with clinical outcomes?

**Methods and Cohort**

- **MIMIC**
  - Data from Medical Information Mart for Intensive Care-III (MIMIC-III)
  - On admission
    - Na >155 mmol/L
    - Hospital-acquired
      - N = 122
      - N = 327

- Rapid correction (>0.5 mmol/L/hr)
- Slow correction (≤0.5 mmol/L/hr)

**Findings**

- **Rapid Correction**
  - 30 day mortality: 25%
  - P=0.80

- **Slow Correction**
  - 30 day mortality: 28%

- **NS**

- 30 day mortality: 44%

- P=0.50

- **NS**

- 30 day mortality: 40%

- 0 cases of cerebral edema, seizures or alteration in consciousness attributable to rapid hypernatremia correction

**Conclusions**

Rapid correction of hypernatremia was not associated with a higher risk for mortality, seizures, alteration of consciousness and/or cerebral edema in critically ill adults with either admission or hospital-acquired hypernatremia.

HYPONATREMIA

Low salt concentration
MY PATIENT HAS HYPONATREMIA, WHAT SHOULD I DO?

Diagnostic Approach in Hyponatremia

- **Hyponatremia**
  - Assess volume status
  - **Hypovolemia**
    - Total body water ↓
    - Total body Na⁺ ↓
    - Measure urinary [Na⁺] ↑
    - Renal losses
      - Diuretic excess
      - Mineralocorticoid deficiency
      - Salt-losing nephropathy
      - Bicarbonaturia with renal tubular acidosis and metabolic alkalosis
      - Ketoacidosis
      - Osmotic diuresis
      - Cerebral salt wasting
      - Hypervolemic
        - <100 mOsm/kg H₂O
        - Measure urine osmolality
  - **Euvolemia (no edema)**
    - Total body water ↑
    - No change in total body Na⁺
    - Measure urinary [Na⁺] 20 mmol/l urinary Na⁺
    - Extrapulmonary losses
      - Vomiting
      - Diarrhea
      - Third spacing of fluids in burns, pancreatitis, trauma
      - Extrarenal losses
      - Glucocorticoid deficiency
      - Hypothyroidism
      - Stress
      - Drugs (see Table 8-2)
      - Syndrome of inappropriate ADH secretion (SIADH)
      - Hypovolemic
        - >100 mOsm/kg H₂O
        - SIADH
  - **Hypervolemia**
    - Total body water ↑↑
    - Total body Na⁺ ↑
    - Acute or chronic kidney injury
    - Nephrotic syndrome
    - Cirrhosis
    - Cardiac failure
    - `<20 mmol/l`
    - Measure urinary [Na⁺]`<20 mmol/l`

Osm = 2 [Na⁺] + Glucose + BUN + Other osmoles
Drugs
- SSRIs
- Carbamazepine
- Ecstasy
- Ifosfamide
- Cyclophosphamide

Basically any pulmonary disease
- Pneumonia
- Cancer
- TB
- Asthma

Basically any CNS disease
- Encephalitis
- Trauma
- GBS
- CVA

Prolonged Exercise

Causes of SIADH
HYponatremia Treatment

**Symptomatic**
- Acute (<48 h)
  - Hypertonic Saline (3%) @ 1-2ml/kg/h or a 100mL bolus for resolution of symptoms
- Chronic (>48 h)
  - High risk for complications (CPM)
  - Hypertonic saline (3%) at 1-2ml/kg/hr but not > 8-10mEq/L/24hrs
  - Can add D5W or DDVAP lock
  - If potassium is replaced, this will also increase plasma sodium

**Asymptomatic**
- Review for reversible causes
- Fluid restriction
- Tolvaptan
- Increased salt intake (salt tablets)
- Oral Urea
- SGLT 2 inhibitors?
# OUTPATIENT TREATMENT OF EUVOLEMIC HYPONATREMIA

## Treatment of Chronic Asymptomatic Hyponatremia

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mechanism of Action</th>
<th>Dose</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid restriction</td>
<td>Decreases availability of free water</td>
<td>&lt;800ml-1,000ml/day</td>
<td>Effective and inexpensive; not complicated</td>
<td>Noncompliance</td>
</tr>
</tbody>
</table>

**Pharmacologic Inhibition of Vasopressin Action**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mechanism of Action</th>
<th>Dose</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>Inhibits kidney’s response to vasopressin</td>
<td>900-1,200 mg/day</td>
<td>Unrestricted water intake</td>
<td>Polyuria, narrow therapeutic range, toxicities</td>
</tr>
<tr>
<td>Demeclocycline</td>
<td>Inhibits kidney’s response to vasopressin</td>
<td>300-600 mg twice daily</td>
<td>Effective; unrestricted water intake</td>
<td>Neurotoxicity, polyuria, photosensitivity, nephrotoxicity</td>
</tr>
<tr>
<td>Tolvaptan</td>
<td>Antagonizes vasopressin action</td>
<td>15mg-60mg/day</td>
<td>Addresses underlying mechanisms</td>
<td>Limited clinical experience</td>
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<td></td>
<td></td>
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<td></td>
<td>Very expensive</td>
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<td></td>
<td>Limited to 1 month of therapy</td>
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<td></td>
<td></td>
<td></td>
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<td>Liver toxicity</td>
</tr>
</tbody>
</table>

**Increased Solute (Salt) Intake**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mechanism of Action</th>
<th>Dose</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>With furosemide</td>
<td>Increases free water clearance</td>
<td>Titrate to optimal dose; coadminister 2-3 g NaCl</td>
<td>Effective</td>
<td>Ototoxicity, K+ depletion</td>
</tr>
<tr>
<td>With urea</td>
<td>Osmotic diuresis</td>
<td>30-60 g/day</td>
<td>Effective; unrestricted water intake</td>
<td>Polyuria, unpalatable, gastrointestinal symptoms</td>
</tr>
</tbody>
</table>
SGLT2 INHIBITORS

Empagliflozin increases plasma sodium levels in patients with the syndrome of inappropriate antidiuresis (SIAD)

**METHODS**

- Hospitalized patients p-sodium <130 mmol/l due to SIAD
- Inclusion & Randomisation
- Day 0
- Empagliflozin 25mg od for 4 days + standard treatment including fluid restriction <1000mL
- Placebo for 4 days + standard treatment including fluid restriction <1000mL
- Day 4 Primary Endpoint
- 30 day Follow up

**OUTCOME**

- Median (IQR) increase p-sodium in mmol/l:
  - Empagliflozin 10 (5,10)
  - Placebo 7 (3,11)

**CONCLUSION** Empagliflozin in addition to fluid restriction leads to a higher increase in plasma sodium levels compared to placebo in hospitalized patients with SIAD.

doi: 10.1681/ASN.2019090944
Overall, the most important clues that will lead you to a diagnosis are in the history, physical exam and medication review.

Any patient with concerning or severe symptoms or severe electrolyte disbalance, send to an ER.

Hyperkalemia
- Limits use of many beneficial agents, maybe with new binders we can improve outpatient management.

Hypokalemia
- Urine electrolytes will help distinguish between renal and non renal losses.
SUMMARY

- Hypernatremia
  - Most common cause of hypernatremia is loss of hypotonic body fluids with inadequate water replacement because of lack of access or adipsia
  - Oral hydration is preferred method for treatment
- Hyponatremia
  - The most helpful in differential diagnosis is volume status
  - SGLT2 inhibitors may help with chronic SIADH
Thank you!!...
REFERENCES

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