sODIUM

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Normal Water Balance

- Approximately 9L of fluid enters GI tract daily
  - 2L by ingestion
  - 7L by secretion
  - 98% of this volume is reabsorbed
  - Fecal fluid loss ~100-200 mL/day

- Insensible water loss
  - 500-650 mL/day
Normal Water Balance

• Serum Na is dependent on total body Na + K and total body water: Serum Na = (TBNa + TBK)/TBW

• The body is able to maintain water balance despite variations in intake/losses by adjusting $U_{\text{osm}}$
  • Kidneys - maximally dilute urine (40-100 mOsm/kg) or maximally concentrated (900-1200 mOsm/kg) to maintain the balance

• Normal plasma osmolality 275-290 mOsm/kg

• ADH and RAAS/ANP

Normal Water balance

• ADH synthesized within neurons of the hypothalamus
  • Distal axons project into posterior pituitary

• Osmoreceptor neurons and stretch-activated cation channels

• Osmolality >285 leads to release of ADH

• ADH acts on renal V2 receptors in the TALH and CD

• RAAS and ANP respond to changes in EAV resulting in retention or excretion of sodium in kidneys
HYPONATREMIA

- Plasma Na <135 mEq/L
- 22% of hospitalized patients
- Water in excess of kidneys’ ability to excrete it (assuming normal kidney function)
  - ADH dependent mechanisms
  - If the urine osm > 100 mOsm/kg you can assume that some ADH is being released
A 82 year old female presents to the Emergency Department for evaluation of a 1-day history of nausea, vomiting, weakness, confusion, and unstable gait. She has fallen several times today.

VS: 130/76, 68 without postural changes, 18, 97.2F
PE: Normal neurologic, cardiac, and pulmonary exam. No ascites or pedal edema.
Labs: Na 120, K 3.6, Cl 83, HCO3 27, Glucose 105, Serum Osm 255, Urine studies: Osm 408, K 32, Na 90

Which of the following is the most appropriate treatment?
A. 0.9% NS IVF
B. 3% saline IVF
C. Furosemide
D. Tolvaptan

Clinical history (critical) and volume status
Serum osmolality
Serum glucose
Serum uric acid
  • >4 mg/dL in hypovolemic
  • <4 mg/dL in euvolemic
Urine Na, K, osmolality
Hypovolemic Hyponatremia

- Extrarenal losses
  - Vomiting, diarrhea, 3rd spacing, burns, pancreatitis, trauma

- Positive orthostatics, dry mucous membranes, diminished skin turgor
  - $U_{na} < 20$

- Increase in ADH
  - Helps to preserve BP
  - Activation of V2 receptors, free water reabsorption

- Treatment
  - Isotonic saline – rapid reduction in ADH $\rightarrow$ brisk water diuresis

Euvolemic Hyponatremia

- SIADH (MC), drugs (i.e.. SSRIs, NSAIDs), hypothyroid, glucocorticoid deficiency, stress/pain
  - $U_{na} > 20$

- Treatment
  - Urine:Plasma electrolyte ($U_K + U_{Na}/P_{Na}$)
    - $> 1$, aggressive fluid restriction (<500 mL/d)
    - $\sim 1$, fluid restriction (500-700 mL/d)
    - $< 1$, fluid restriction (<1000 mL/d)
  - Lasix 20mg PO bid + salt tabs
  - Demeclocycline (avoid)
  - Tolvaptan – V$_2$ receptor antagonist
    - Liberalize fluid restriction
Hypervolemic Hyponatremia

- CHF, Cirrhosis, Nephrotic syndrome
- TBW > TBNa
- Reduced EAV, increased ADH
  - $U_{\text{Na}} < 20$
- Treatment
  - Optimize tx of underlying cause
  - Urine:Plasma electrolyte ($U_{\text{Na}} + U_{\text{K}}/P_{\text{Na}}$)
    - $>1$, aggressive fluid restriction (<500 mL/d)
    - $\sim1$, fluid restriction (500-700 mL/d)
    - $<1$, fluid restriction (<1000 mL/d)
  - Loop diuretics
  - Fluid restriction
  - Tolvaptan

**Assessment of Volume Status**

- **Hypovolemia**
  - Total body water ↓
  - Total body sodium ↓↓
  - $U_{\text{Na}} > 20$
  - Renal losses
  - Diuretic excess
  - Mineralocorticoid deficiency
  - Salt-losing deficiency
  - Bicarbonaturia
  - Ketonuria
  - Osmotic diuresis
  - Cerebral salt wasting

- **Euvolemia (no edema)**
  - Total body water ↑
  - Total body sodium ↔
  - $U_{\text{Na}} < 20$
  - Extrarenal losses
  - Vomiting
  - Diarrhea
  - Third spacing
  - Burns
  - Pancreatitis
  - Trauma

- **Hypervolemia**
  - Total body water ↑↑
  - Total body sodium ↑
  - $U_{\text{Na}} > 20$
  - Glucocorticoid deficiency
  - Hyothyroidism
  - Stress
  - Drugs
  - SIADH
  - Acute renal failure
  - Chronic renal failure
  - Nephrotic syndrome
  - Cirrhosis
  - Heart failure
## Acute Symptomatic Hyponatremia

- Typically develops over <48 hours
  - Thiazides, colonoscopy prep, MDMA

- Cerebral edema
  - GI complaints, lethargy, apathy, agitation, cramps, seizures, and coma

- Treatment
  - 3% saline (513 mEq/L of Na)
    - Usually started at 1-2 mL/kg/h
    - An increase in $S_{Na}$ by 5-6 mEq/L is sufficient to reverse herniation and reduce ICP by 40%

## Chronic Symptomatic Hyponatremia

- Duration unknown or >48hrs

- Treatment
  - 3% saline (513 mEq/L of Na) until symptoms resolve

  - After symptom resolution, rate of correction should not exceed 0.5 mEq/L/h
    - Limit 8 mEq/L correction over 24hrs
    - Limit 18 mEq/L correction over 48hrs

  - Exceed limit, risk of osmotic demyelination syndrome (ODS)
    - D5W
    - dDAVP
HYPERNATREMIA

- Plasma sodium >145 mEq/L and osmolality >295 mOsm/kg
- Mortality rates as high as 40-60%
- Usually combined water and electrolyte deficient
  - Water loss > electrolyte loss
  - GI (osmotic, viral diarrhea) and insensible loss, osmotic diuresis, central/nephrogenic DI, hypercalcemia, hypokalemia
  - Iatrogenic
- Altered mental status, Rhabdomyolysis

CASE

An 80 year old woman presents to the Emergency Department from a nursing home for progressive lethargy. She has had constipation for 3 days and given several doses of lactulose. She subsequently developed persistent diarrhea for 24-48hrs. She has not taken any medications in 48hrs.

VS: 90/42, 117, 16, 97.7F
PE: Lethargic but arousable, dry mucous membranes, minimal skin turgor. Neuro, cardiac, pulmonary, abdominal exam otherwise normal.
Labs: Serum Na 158, K 4.1, Cl 109, HCO3 20, BUN 46, Cr 1.7, Ca 9.6, Glucose 220; Urine studies – spec gravity 1.020, osmolality 850.

Which of the following is the best initial therapy?
A. Desmopressin
B. D5W IVF
C. IV antibiotics
D. 0.9%NS IVF
**Approach**

- Detailed clinical history and exam
- Serum osmolality
- Urine osmolality and electrolytes
  - Urine output <500 mL/d
  - Urine osmolality >800 mOsm/kg
- Calculate free water deficit
  - Men = 0.6 x weight (kg) x \[\left(\frac{SNa}{140}\right) – 1\]
  - Women = 0.5 x weight (kg) x \[\left(\frac{SNa}{140}\right) – 1\]

**HYPERNATREMIA**

- Treatment
  - Acute (<48hrs) vs chronic (>48hrs)
  - Estimate volume status
  - Identify and fix underlying cause
  - Free water replacement
    - PO or NG
    - IV D5W
### Hypovolemic Hypernatremia

- **Hypotonic fluid loss**
- **Treatment**
  - Restore extracellular fluid with isotonic IVF
    - Relative hypotonicity compared to plasma
  - Once euvoletic, restore water deficit
    - Hypotonic IVF (0.45% saline + D5 or D5W alone)

### Euvolemic Hypernatremia

- **Treatment**
  - Polyuria with positive electrolyte free water clearance
    - Urine:Serum electrolyte \( (U_{Na} + U_{K}/P_{Na}) < 1 \), defect in urinary concentration
  - Central DI vs Nephrogenic DI
    - **Central DI**
      - Hx head trauma, neurosurgery, pituitary mass, evidence of anterior hypopituitarism, sarcoidism, kidney disease, medications (lithium)
      - 0.1-0.2 mg dDAVP
    - **Nephrogenic DI**
      - Lithium-induced - stop lithium or add amiloride if lithium continued
      - Non-drug induced – thiazide diuretic and salt restriction
Hypervolemic Hypernatremia

- Rare
  - ICU setting

- TBNa > TBW

- Treatment
  - D5W + loop diuresis

References


Potassium and Calcium Disorders

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Vignette #1

• You are on call for your practice group and the lab contacts you regarding a critical potassium value of 5.8. You do not know the patient, but know that you clearly need to investigate what is going on.

  – Na 141  K 5.8  Cl 99  Bicar 29  BUN 34  Cr 1.6  Glucose 166
Hyperkalemia

• As you prepare to review the chart, you remind yourself of the causes of hyperkalemia:
  – Spurious
  – Excess intake
  – Medications
    • ACEi, ARB, spironolactone, Bactrim, beta blockers, NSAIDS, digoxin, heparins, calcineurin inhibitors

Hyperkalemia

• Renal disease, acidosis or hypoaldosteronism
  • Chronic Kidney Disease
  • Type 4 RTA
• Weird stuff (Addison’s, hyperkalemic periodic paralysis, tumor lysis, crush injury
Hyperkalemia

- You review the chart and see this is a 62 year old male with a history of long-standing hypertension as well as a relatively new diagnosis of diabetes. Your partner had started him on a low-dose ACE-inhibitor and lasix for some lower extremity swelling.

- You mentally shout AHA!
# Hyperkalemia

- **Treatment of hyperkalemia**
  - Move it into cells
    - Albuterol, Insulin/Glucose, possibly bicarbonate
  - Renal Excretion
    - Increased renal perfusion, possibly lasix
  - GI excretion
    - Sodium Polystyrene Sulfonate

## Hyperkalemia

- Ok, but is 5.8 dangerous? Do I need to call the squad?

- Shortening of QT interval, peaking of T waves
- QRS prolongation, shortening of PR interval, decreased P wave amplitude
- Onset of a wide-complex “sine-wave” ventricular rhythm
- Ultimately asystole

"ECG demonstrating hyperkalemia with absent P waves" by Ecgtocardiology - Own work. Licensed under CC BY-SA 3.0 via Commons - https://commons.wikimedia.org/
Hyperkalemia

- EKG data is based on animal models
- Some correlation with higher potassium levels and EKG changes
- EKG changes are not sensitive or specific
- Our patient would be classified as mild hyperkalemia
  - Very common during initiation of ACE inhibitors


Hyperkalemia

- But this patient should be on an ACE or ARB right?
- New treatment options on the horizon:
  - Patiromer in Patients with Kidney Disease and Hyperkalemia Receiving RAAS Inhibitors
    - FDA approved Valtessa for the treatment of hyperkalemia October 15, 2015
  - Sodium Zirconium Cyclosilicate in Hyperkalemia
    - ZS-9 New drug application submitted for FDA approval July 29, 2015
Vignette #2

• You are seeing patients in an urgent care and triage has drawn labs on your next patient, who is presenting with generalized malaise. You note a K of 2.8.

• Prior to seeing the patient you review the possible causes of this finding.

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Hypokalemia

• Movement into cells
  • Albuterol, insulin, alkalosis, increased cell production
  • Weird stuff (hypothermia, barium intoxication, antipsychotics, period paralysis)
• Decreased intake
  • Need only 5meq – 25 meq a day
• GI losses
  • Vomiting (alkalosis, increased aldosterone)
  • Diarrhea (direct K losses)
### Hypokalemia

- Renal losses – remember the distal nephron
  - Diuretics, increased aldosterone activity
  - Polyuria, Type 1 or Type 2 RTA
  - Salt wasting nephropathies
    - (Liddle’s, Barter’s, Giddlemen’s)

### Hypokalemia

- Diagnosis is almost always based on history
- EKG changes may occur
  - Complications are rare
- Check:
  - Urine potassium and acid-base status
  - TSH and cortisol
  - Oral supplementation
    - Consider magnesium
Vignette #3

- An elderly patient is brought into your office by her daughter for confusion. She is a breast cancer survivor who has largely been healthy except for some hypertension. She was in last week complaining of lower back pain.
- There are no signs of infection and exam reveals a confused, dehydrated appearing lady without focal neurologic changes.

- Na 145  K 3.8  Cl 104  CO2 26  BUN 42  Cr 2.1
- Ca  12.7

Hypercalcemia

- “Bones, Stones, Groans, Thrones and Psychiatric Overtones”

- Hyperparathyroid versus malignancy
  - PTH and PTH-rp initially
    - Vitamin D levels
    - TSH, SPEP, UPEP, vit A, CXR
Hypercalcemia

- Albumin is 2.9

- Corrected Ca mg/dl
  - Ca mg/dl measured + 0.8(4.0 – albumin g/dl)
  - 12.7 + 0.8(4 – 2.9) = 13.6 mg/dl

- You recognize this as an emergency and send the patient to the hospital!

Hypercalcemia

- Unfortunately the ED calls you and seems confused about next steps in treatment. You gladly help them and order:

  - IV hydration
    - Isotonic crystalloid boluses
    - Aggressive hydration to keep UOP > 100ml/hr
Hypercalcemia

• Calcitonin - 4 IU/kg to 8 IU/kg q6-12 hours
  • IM or Subcutaneous, intranasal less effective
  • Max effect of 2mg/dl after 4 hours
  • Tachyphylaxis after 48 hours
• Bisphosphonates
  • Zolendronic acid is most potent, 4mg IV over 15-30 minutes

Other therapies:
• Denosumab for refractory hypercalcemia
  • Approved in 2014
• Prednisone if related to lymphoma or ovarian germ cell tumors
• Cinacalcet

Future Directions:
• Infusions of PTH-rp antibodies
### Vignette #4

- You are precepting a medical student who is telling you about a patient. She reports that the patient has a history of Grave’s disease and recently had a partial thyroidectomy. The patient’s main complaint is of peri-oral paresthesias. You ask the student to do additional physical exam maneuvers and check blood work:
  - Corrected calcium is 7.8 mg/dl.
  - You order PTH, creatinine, phosphate, magnesium and vitamin D levels

### Hypocalcemia

- Hypocalcemia with low PTH
  - Surgical or autoimmune destruction
  - Genetic
  - Severe high or low magnesium
- Hypocalcemia with high PTH
  - Sepsis, pancreatitis
  - Vitamin D deficiency or resistance
  - PTH resistance
  - Hyperphosphatemia
Hypocalcemia

• Treatment:
  • Oral supplementation for > 7.5 if mild symptoms
  • Calcium Carbonate 1-4gm in divided doses
  • Calcitriol 0.25-0.50mcg initial
    • Titrate up to a range of 0.5mcg – 2mg for maintenance