Fluid and Electrolyte Abnormalities and Disorders

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Learning Objectives

1. Identify the underlying etiology of hypercalcemia and select the appropriate treatment.
2. Identify and treat the underlying etiology of hyponatremia and prescribe appropriate treatment for hyponatremia based on symptoms, degree, and presence of any hypotension.
3. Differentiate the etiology of hypernatremia and prescribe appropriate treatment with caution due to the dangers of rapid correction.
4. Identify the underlying etiology of hyper- and hypokalemia and select appropriate treatment.

Associated Session

- Fluid and Electrolyte Abnormalities and Disorders: Ask the Expert
Audience Engagement System

Step 1
Step 2
Step 3

Agenda
- Utilize evidence-based recommendations and guidelines to diagnose electrolyte imbalances (Na, K, and Ca) in symptomatic and asymptomatic patients.
- Identify patients who are at high risk of developing electrolyte imbalances due to medications
- Treatment goals for Na, Ca, and K disorders

Symptomatic Hyponatremia

- Symptoms include:
  - Polydipsia
  - Muscle cramps
  - Headaches
  - Fatigue
  - Confusion
  - Falls
  - AMS
  - Obtundation
  - Seizures

Morbidity and Mortality

- Patients with hyponatremia have increased rates of morbidity and mortality
- Poor outcomes in patients with myocardial infarction, CKD, pulmonary emboli, and hip fractures
- Associated with increased falls, and cognitive impairment in the elderly

Renneboog B. American Journal of Medicine 2006;119:71; Deitelzweig S. Hospital Practice 2013;41:89-95.

The Down and Dirty

Hyponatremia is a water problem

NOT a sodium problem
Physiology:

Hyponatremia and Volume Status

- Pseudohyponatremia
- Hypovolemic hyponatremia
- Euvolemic hyponatremia
- Hypervolemic hyponatremia

Pseudohyponatremia

- Artificially decreased sodium due to indirect measurement of sodium
  - Hyperproteinemia
  - Hyperlipidemia
  - Mannitol or sorbitol use
  - Recent administration of radiocontrast media

Hyperglycemia

- Most frequent cause of “pseudohyponatremia”
- True sodium concentration is actually low
- Correction Equation:
  \[ \text{Serum Na} = \text{measured Na} + 0.024(\text{serum glucose} - 100) \]

Hypovolemic Hyponatremia

- Decreased total body water and decreased sodium level
  - Renal Loss
    - Diuretics
    - Mineralcorticoid deficiency
    - Renal tubular acidosis
  - Extraenal losses
    - Vomiting
    - Diarrhea
    - Burns
    - Bowel obstructions
    - Third spacing

Diuretics and Hyponatremia

- HCTZ is the most common diuretic to cause hyponatremia
- Loop diuretics rarely are the sole cause
- In a study of 129 patients with hyponatremia and on a diuretic:
  - 73% were on hydrochlorothiazide
  - 7% were on loop diuretics (all patients with CHF)
  - 20% were on a combined HCTZ with another diuretic

Sonneblick, M et al: Diuretic-induced severe hyponatremia. CHEST 2002; 122: 602-608
**Euvolemic Hyponatremia**

- Normal total body water
- Normal total body sodium
- SIADH
- Hypothyroidism
- Beer potomania
- Psychogenic polydipsia
- Secondary adrenal failure
- Drugs and medications

**SIADH**

- Clinically euvolemic
- Hypo-osmolality
- Inappropriately high Uosm (>100 mOsm/L)
- No sodium conservation (urine Na >30 mmol/L)
- No recent diuretic therapy

**Common Causes of SIADH**

- Drugs:
  - SSRI
  - HCTZ
  - Carbamazepine
- CNS:
  - SAH
  - Stroke
- Pulmonary:
  - Pneumonia
  - COPD
  - TB
- Other:
  - HIV
  - Old age

**Hypervolemic Hyponatremia**

- Increased extracellular volume.
- Heart failure
- Cirrhosis
- Renal injury
- Hypoalbuminemia

**How good are we?**

- Study of 58 patients with hyponatremia without edema.
  - Hypovolemic patients: $U_{Na}$ 18mEq/L
  - Euvolemic patients: $U_{Na}$ 72 mEq/L
- Clinical assessment of volume status was only correct in 48% of patients

**Workup for Hyponatremia**

1. Assess water intake
2. Assess the patient’s volume status
3. Look at the medications
4. Look for causes of ADH release
5. Laboratory evaluation (blood and urine)
Lab work-up of hyponatremia

- Strongly Recommended:
  - Serum Osm:
  - Urine Osm:
  - Urine Sodium:
  - BMP

- Optional/Situation Dependent
  - TSH
  - AM cortisol level
  - Urinary uric acid
  - Urine to serum electrolyte ratio
  - BNP

Urine Osmolality

- Hyponatremia should cause suppression of ADH resulting in a very dilute urine (<100 mOsm/L)
- Urinary Osm (U_osm) can help:
  - Differentiate between normal and impaired water excretion
  - Determine severity of SIADH
- Low U_osm (<100 mOsm/L) - Primary polydipsia or reset osmostat

Urine Sodium

- Used to distinguish between effective volume depletion versus euvolemic states (SIADH)
- SIADH U_Na >40 mEq/L
- Decreased circulatory volume: U_Na <25 mEq/L unless a diuretic is involved.

Treatment Principles

- Acute Treatment: Basics

**Hyponatremia**

**Wet**
- Treat underlying problem
- Fluid restrict

**Dry**
- Give normal saline
- Stop diuretic
- Stop extra-renal losses

**Euvolemic**
- Treat underlying causes

- Unclear volume status?

**Response to 0.9% Saline**

**Wet**
- Little to no change in Na
- Improving in Na symptoms
- Worsening edema/lung sounds

**Dry**
- Improvement in Na

**Euvolemic**
- No change in Na
- Or worsening of sodium
Case One

- 36 year old Male who presents to the Emergency Room with AMS and in active seizure. His medical history is significant for hypertension and depression. He was in the middle of a long distance run when his symptoms occurred.
- **Medications:** Lisinopril 20 mg and sertraline 100mg (started 2 weeks ago)
- **Physical Exam:** BP 124/86, hypovolemic
- **Labs:** Na 119, Cr 0.8, glucose 109

AES POLL QUESTION

What is the appropriate treatment for this patient?
- A. Admit to ward and Give 0.9% NS solution
- B. Admit to ICU and give 0.9% NS solution at 150mL/hr
- C. Admit to ward and give 3% NS at 100mL/hour over 24H
- D. Admit to ICU and give 3% NS at 100mL bolus x 1 dose over 15 min

Treatment of severe hyponatremia:

- Determine acute versus chronic (or unknown duration)
- Goal rate of 4-8 mEq/L in the first 24 hours and Total of 18 mEq/L in 48 hours
- Two options:
  - Infuse 3% saline at 0.5-2 mL/kg/hr until symptoms resolve
  - 100mL bolus of 3% saline over 10 minutes
- Overcorrection is common
- Evidence that concurrent use of desmopressin may limit overcorrection

EXERCISE ASSOCIATED HYponATREMIA (EAh) IN MARATHON RUNNERS

- "Perfect storm" of:
  - Insensible Na loss from excessive sweating
  - Excessive water intake
  - Physiologic ADH release
  - Pathologic ADH: pain, nausea, emotion

Case Two

- 51 yo AD. hyperactive M admitted to the wards for dysuria, weakness, and polyuria. He is afebrile and does not have any neurological symptoms. He only takes fluoxetine for depression. Physical is normal with stable VS (99.9F, 140/90, HR 85, RR 16).
- **Labs**
  - BUN/Cr: 10/1
  - Sodium: 123
  - Potassium: 4
  - Chloride: 91
  - Glucose: 120
  - Plasma Osmas: 260
  - Urine Na: 40
  - Urine Osmas: 600

EXERCISE ASSOCIATED HYponATREMIA (EAh) IN MARATHON RUNNERS

Which of the following is the most appropriate management of this patient?
- A. Fluid restriction
- B. Discontinue Fluoxetine
- C. Isotonic saline
- D. A and B
Treatment Euvolemic Hyponatremia

- Correct underlying cause of patient’s hyponatremia
- Fluid restriction without limiting sodium intake
- If fluid restriction does not work consider loop diuretic and oral salt tablets
- Oral Demeclomyclin is third line therapy if other options fail
- Vaptans can be used in SIADH

Case Three

- 59 yo F with h/o SIHD presenting to the ED with SOB, JVD, and peripheral edema. Patient is diagnosed with acute Hfe. Her serum sodium is 123 mEq/L. Her urine potassium is 3.5 mEq. Plasma osmolality is 265 mOsm/kg. Her BNP is 6,000. Her ECHO shows EF 35% with grade one diastolic dysfunction. PE is remarkable for volume overload.

AES POLL QUESTION

How would you treat this patient?
- A. Water restriction
- B. Loop diuretics
- C. Salt tablets
- D. A and B

Treatment Hypervolemic Hyponatremia

- Correct underlying disease
  - Common causes include HF and cirrhosis
- Loop diuretics
  - Not thiazides with exception of metolazam
- Free water restriction
  - Usually < 1L per day
- Consider vaptans if Na <120 despite appropriate therapy

Physiology:

V1/V2 Receptor in the kidneys

1. ADH RELEASE
2. PLASMA OSMOLALITY
3. WATER REABSORPTION
4. PLASMA OSMOLALITY

Vaptans:

- Vasopressin-receptor antagonists (conivaptan and tolvaptan)
- FDA-approved for the treatment of severe hypervolemic and euvolemic hyponatremia
- Risk of overcorrection
- Sodium levels decrease after stopping medication

Case Four

- 31 yo F with h/o neurosarcoidosis and suprasellar mass presenting with sodium level of 125. Patient weened off of prednisone 1 week ago. She is mentating well but is a little slow. PE reveals anasarca and pitting edema in b/l LE. She was placed on lasix 3 days ago.
- Labs
  - Na 125
  - Potassium 4.1
  - Chloride: 87
  - Urine Osms: 600+
  - BUN/Cr: 14/0.7
  - Urine Na: 187 (FENA 0.7%)
  - Serum Osms: 264

AES POLL QUESTION

What is the most likely cause of this patient’s hyponatremia?

- A. SIADH
- B. Lasix
- C. Volume overload
- D. Neurosarcoidosis

Treatment Hypovolemic Hyponatremia

- Treat underlying disease
- Volume repletion with isotonic saline
- Salt tablets
- Ensure to monitor UO

Complications of Overcorrection

- Fatal Herniation
- Osmotic Demyelination Syndrome (ODS)

HYPERNATREMIA

- Sodium concentration > 145mEq/L
- Less common than hyponatremia, but higher morbidity and mortality
- At risk populations: infants, elderly, intubated patients, and patients with altered mental status
- Represents a free water deficit
  - Usually from net water loss
  - Rarely from sodium gain
Cause of Hypernatremia

- Hypovolemic Hypernatremia
  - Body fluid loss, diuretics, GI loss, post-obstruction
- Euvolemic Hypernatremia
  - Central DI, hyperventilation, medications
- Hypervolemic Hyponatremia
  - Cushing syndrome, hemodialysis, hyperaldosteronism

Symptoms:

- Vague and often masked by coexisting disorders
- Infants: hyperapnea, muscle weakness, restlessness, high pitched cry, insomnia, or coma
- Adults: few symptoms until Na >160 mEq/L
  - Irritability, nausea, weakness, abdominal pain, lethargy, intense thirst

Work-up of Hypernatremia

- Thorough H&P
- Assess volume status
- Labs: BMP, urine osms, urinary electrolytes, glucose levels
  - Water deprivation test

Treatment:

- Correct the underlying cause
- Correct the water deficit
- Oral or enteral free water should be used whenever possible

Math:

Water Deficit

\[ \text{Volume (L)} = (\text{total body water %}) \times \text{weight (kg)} \times \frac{[(\text{sodium}-140)/140]}{\text{Target sodium is 145 mEq/L}} \]

Correction rate:

- Acute:
  - Can be corrected rapidly
  - 1 mEq/L/hr
- Chronic or unknown:
  - 0.5 mEq/L/hr
  - Total of 8-10 mEq/L over 24 hours

- Target sodium is 145 mEq/L
Potassium Disorders

Case Five

• A 59-year-old female with a medical history of chronic renal insufficiency and heart failure presents to your office with a week of muscle weakness. Her cardiologist recently started her on spironolactone for symptomatic management of her heart failure. Serum potassium is 7.1 mEq per L with the following EKG.

EKG Findings

AES POLL QUESTION
Which of the following medications will decrease total body potassium?

A. Calcium
B. Insulin
C. Albuterol
D. Sodium polystyrene sulfonate

Hyperkalemia

Decreased secretion
• Disorders of low aldosterone
• Disorders of low renin
• Renal failure
• Systemic lupus erythematosus
• Type IV renal tubular acidosis
• Medications (ACEI, ARBS)

Shift from intracellular to extracellular space
• Acidosis
• Destruction of tissue
• Hyperosmolality
• Tumor lysis syndrome

Hyperkalemia Work-up

• Rule out pseudohyperkalemia
• Check medications
• Labs
  – BMP
  – Urine sodium

Treatment Hyperkalemia

• Calcium gluconate 10-20 mL IV over 2-3 minutes
• Regular insulin 10 units IV with 50 mL of D50
• Albuterol 10-20 mg over 10 minutes
• Furosemide 20-40 mg IV
  – Fludrocortisone
• Sodium polystyrene sulfonate (Kayexalate)
• Patiromer
• Dialysis

Hypokalemia

• Serum potassium less than 3.5 mEq/L
• Present in 21% hospitalized patients
  – 2-3% outpatients
• May be asymptomatic
• Weakness, lethargy, ECG changes, arrhythmias

Hypokalemia

Etiology

• Abnormal losses (most common)
  – GI
  – Renal (Diuretics)
• Transcellular shifts
  – Insulin
  – Beta sympathomimetics
  – Alkalosis
• Insufficient intake
  – Rare cause

Hypokalemia Evaluation

• Exclude Pseudohypokalemia
• H&P
  – Check Medications
• Labs
  – BMP
  – Spot Urine Potassium
  – 24H Urine
  – Ratio of urine potassium/urine creatinine
  – Hyperaldosteronism work-up

Treatment hypokalemia

Treatment

• 0.3 mEq/L serum K⁺ = 100 mEq total body K⁺
• Oral 40-100 mmol/day
• IV 20-40 mmol in 1 L NS
  – Infuse 10-20 mEq/hour in peripheral line
• ACE/ARB, beta blocker, “potassium sparing” diuretics
• Concurrently correct hypomagnesemia

Calcium Disorders
Case Six

- A 56-year-old woman with an unremarkable medical history presents to your office for an annual history and physical. Routine laboratory evaluation reveals a serum calcium of 11.0 mg per dL. A review of symptoms is negative.

AES POLL QUESTION

What is the most common cause of hypercalcemia?
A. Malignancy
B. Primary hyperparathyroidism
C. Vitamin D intoxication
D. Hyperthyroidism

Hypercalcemia

- 1 in 500 patients in a general medicine clinic may have undiagnosed hyperparathyroidism
- 90% of cases are caused by either hyperparathyroidism or malignancy
- Serum calcium > 10.5 mg/dL
  - Ionized calcium > 5.6 mg/dL
- > 14 mg/dL can be life-threatening

Hypercalcemia Work-up

- Parathyroid hormone related peptide (PTHrP)
  - Secreted by solid tumors (lung, head and neck squamous cancers, renal cell tumors)
  - Suppressed PTH
- Bone lysis
  - Multiple myeloma, metastatic breast cancer
- Increased production of calcitriol
  - Hodgkin’s lymphoma

Hypercalcemia

- “Stones”
  - Nephrolithiasis, nephrogenic diabetes insipidus
- “Bones”
  - Bone pain, arthritis, osteoporosis
- “Abdominal Moans”
  - Nausea, vomiting, constipation, abdominal pain
- “Psychic Groans”
  - Decreased concentration, poor memory, confusion, lethargy, muscle weakness

Hypercalcemia

- History and physical
  - Identify symptoms
  - Look for underlying disease
  - Identify possible medications
- Measure intact parathyroid level
  - If suppressed → malignancy workup
  - If normal or high → Hyperparathyroid workup
Hyperparathyroid Work-up

- 24-hour urine calcium
  - If low, familial hypocalciuric hypercalcemia
  - If normal or high, hyperparathyroidism
- 80-85% of hyperparathyroidism is due to solitary adenoma
- Hyperplasia of the parathyroid glands
- Parathyroid carcinoma

Hyperparathyroidism Treatment

- Asymptomatic patients do not need treatment
- Calcium > 14 mg/dL or symptomatic
  - Hydration with normal saline (2-3 L daily for 1-3 days)
  - Furosemide 10-20 mg IV as needed
  - Bisphosphonates
  - Calcitonin
- Surgery in select patients with hyperparathyroidism

Hypocalcemia

- Serum calcium < 2.12 mmol/L
- Parasthesias, muscle cramps, tetany, oral numbness
- Chvostek and Trousseau signs
- Seizures
- ECG changes and arrhythmias

Hypocalcemia causes

- Hypoparathyroidism
- Vitamin D deficiency or resistance
- Hypomagnesemia or hypermagnesemia
- IV bisphosphonates

Hypocalcemia Treatment

- Calcium gluconate IV
  - (serum calcium < 1.9 mmol/L or ionized calcium < 1 mmol/L)
  - 10-mL 10% calcium gluconate diluted in 50-100 mL 5% dextrose over 5-10 minutes
  - Best through central line
  - Monitor ECG during repletion

Practice Recommendations

- Severe symptomatic hyponatremia should be corrected at a rate of 6-12 mEq per liter in the first 24 hours. (SOR C)
- For treatment of severe acute hyponatremia, the regimen that is considered safe and effective is administration of 3% hypertonic saline as a single bolus of 100-150 mL or at an infusion at a rate of 0.5-2 ml/kg/hr. (SOR C)
- Chronic hyponatremia should be corrected at a rate of 0.5 osms per liter per hour, with a maximum change of 8-10 mEq per L in 24 hours. (SOR C)
Practice Recommendations

• Patients with hyperkalemia and ECG changes should be urgently treated with calcium gluconate. (SOR C)

• When giving insulin as an acute/emergency treatment for hyperkalemia, a 25 g bolus of glucose should be administered concomitantly in insulin-naïve patients to prevent hypoglycemia. Concomitant glucose administration is not needed in diabetic patients with serum glucose levels above 250 mg/dL (SOR C)

• The diagnostic evaluation of hypercalcemia should include hyperparathyroidism and malignancy. (SOR C)

Questions

Practice Recommendations

• Patients with hyperparathyroidism should be referred for surgery if they are symptomatic, are age <50 years, or have an estimated glomerular filtration rate <60 ml/min/1.73m², osteoporosis, kidney stones, serum calcium concentration of 1.0 mg/dL or more above the upper limit of normal (11.5 mg/dL), or 24-hour urinary calcium >400 mg/day. (SOR C)

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