Management of Electrolyte Disorders Associated with Medications

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Educational Needs

- Recognizing electrolyte disorders associated with commonly used medications.
- Developing a management strategy to correct electrolyte disorders.
- Correction of electrolyte disorders without increasing pill burden.

Learning Objectives

- To identify common medications associated with electrolyte disorders.
- To understand the underlying mechanisms.
- Correction of electrolyte imbalance without increasing pill burden.

Electrolytes

- Sodium
- Potassium
- Calcium
- Magnesium

Approach Outlines

1. Identify the culprit medication on the list.
2. Perform Basic Work Up + Medication Adjustment + Repeat Labs
3. Is the culprit medication still indicated ? (Y/N)
    1. Y -> Is the indicated condition at goal/controlled -> Y/N
        1. Y -> Consider alternative medication which has no or less side effect (or) Choose agent for the other underlying conditions which can counteract.
        2. N -> Choose the second agent which can counteract.
    2. N -> Discontinue
4. Fail -> Replace or Remove Electrolyte

Hyponatremia

- SIADH (Impaired Water Excretion)
  - ↑ ADH Secretion: SSRI,SNRI, TCA, Carbamzepine, Valporate, Lamotrigine, Haloperidol, Olanzapine, Risperidone, Opioids, Cyclophosphamide
  - ↑ Renal sensitivity to ADH: Ibuprofen, Indomethacin, Chlorpropamide
  - ADH analog effect: Desmopressin, Oxytocin
  - Unclear but through ADH: Amiodarone, ACEI/ARB, PPI

- Renal Sodium Loss with ADH activity
  - HCTZ, Chlorthalidone, Indapamide, Trimethoprim, Amiloride, Spironolactone, Eplerenone

Hypernatremia

- ↓ ADH effect (~ NDI): Lithium, Demeclocycline, Amphotericin B, Tolvaptan
- Water Loss (Renal or Extrarenal): Loop Diuretics, Mannitol, Glucocorticoids
- Sodium Gain (only with impaired water intake): Fludrocortisone, Sodium Bicarbonate

Case 1:

A 35-year-old female was seen primary care clinic. She has history of hypertension and devastating trigeminal neuralgia currently controlled by carbamazepine. Her medications include hydrochlorothiazide and carbamazepine. She reports she has been partying over the weekend. She denies vomiting or diarrhea, On exam, she appears euvolemic, with normal blood pressure and no edema or orthostatic changes.

Labs: Sodium 132, S. Osm 260, U. Osm 520, Urine Sodium 58, TSH – Normal.

Her friend reports that the patient has been drinking more water than usual to flush the system out.

Case 1 Cont’

Which of the following best explains this patient’s hyponatremia?

A. Thiazide Use
B. Carbamazepine
C. Psychogenic Polydipsia

Case 1 Cont;

What would be the best course of action in the management of this patient?

1. Prescribe Sodium Chloride Tablet 2 gm PO Q8hr.
2. Change Carbamazepine to Gabapentin.
3. Recommend against drinking too much water and change Hydrochlorothiazide to Furosemide.
4. Repeat BMP in 2 weeks.
5. Fluid Restriction to < 1.5 L per day.

Hyperkalemia

- Reduced Renal Potassium Excretion (Needs intact renal tubules)

↓Distal Na delivery ENaC:

Amiloride, Triamterene, Trimethoprim, Pentamidine, NSAID, Cyclosporin, Tacrolimus

Aldosterone Activity

ACEI/ARB, Spironolactone, Eplerenone, Heparin

↓Renin Release

Propranolol (NSBB), Aliskiren

- Shift from ICF to ECF

Beta-blockers, Digoxin Toxicity, Ammonium Chloride, Drug induced Rhabdomyolysis (Statin, Fibrates, Antipsychotics)

- Excess Potassium Load

Potassium Supplements, Salt Substitutes (contains KCL instead of NaCl) – e.g NoSalt, Morton Salt Substitute, Nu-Salt etc.

Case 2:

- A 68-year-old man with type 2 diabetes mellitus, hypertension, CAD and stage 3 chronic kidney disease (baseline creatinine 1.5 mg/dl) was seen in clinic 2 weeks ago for bilateral leg swelling and duplex ultrasound of the left lower extremity showed DVT for which Eliquis was initiated. His medications include Lisinopril, Eliquis, Metformin, Atorvastatin, Metoprolol and Aspirin.

- Vital Signs are within normal limit, except BP 141/82 mmHg.

- Labs Showed: Serum Sodium 133, Serum Potassium 5.6, Serum Bicarbonate 25, Serum Creatinine 1.45.

- 2 weeks ago: Electrolytes were within normal range.

Case 2 cont’

Which of the following best explains the mechanism of this patient’s hyperkalemia?

A. Lisinopril induced hypoaldosteronism due to chronic RAA blockade.
B. Eliquis induced suppression of aldosterone synthesis.
C. Combined effect of Eliquis and Lisinopril.
D. Beta-blocker induced potassium shift

Case 2 cont’

What would be the best course of action in addition to repeating BMP?

A. Stop Eliquis and Lisinopril and start Lokelma
B. Start Thiazide Diuretic
C. Start Loop Diuretic
D. Start Lokelma
E. Stop Eliquis and Lisinopril and start Patiromer and repeat BMP in 3 days.

Hypokalemia

- Increased Renal Potassium Excretion
  - Loop and Thiazide Diuretics, Amphotericin B
- Increased Mineralocorticoid/ RAAS Activity
  - Steroids, Beta-2 Agonists, Licorice
- Transcellular potassium shift
  - Insulin, Beta-2 Agonists, Theophylline
- GI loss
  - Laxatives, Chloestyramine
- Magnesium Depletion
  - Loop Diuretics, Aminoglycosides, Cisplatin

Case 3:

- A 55-year-old female with type 2 diabetes mellitus, Asthma, Hypertension and Gout was seen in clinic. Her medications include Hydrochlorothiazide, Insulin, Atorvastatin, Allopurinol, colchicine PRN and Low dose Aspirin. Her last gout attack was 3 months ago for which she received corticosteroid injection to her joint. Her Allopurinol was optimized. She has off and on diarrhea from colchicine.

- Vital Signs are within normal limit except BP is 135/75 mmHg.

- Physical Examination showed no signs of leg swelling.

- Labs Showed:

Serum Sodium 144, Serum Potassium 3.2, Serum Bicarbonate 25, Serum Creatinine 1.45, Serum Uric Acid Level 6.3 mg/dl (Normal Range 2.4-6.0 mg/dl), Urine Fractional Excretion of potassium (FeK) is 15% (Normal FeK 4-10%). Her HbA1c was 7.5

Case 3 Cont’

Which of the following best explains the mechanism of this patient’s hypokalemia?

A. Intracellular shift from Insulin Use
B. Extra-renal loss (GI loss) from diarrhea due to Colchicine
C. Renal Potassium Loss from thiazide Use
D. Increased Aldosterone Activity from steroid use

Case 3 Cont’

What would be the best course of action?

A. Change Insulin to Oral Hypoglycemic Agent
B. Change Hydrochlorothiazide to Losartan
C. Add Lisinopril
D. Start KCL 40 mEq PO x 2 doses and continue KCL 20 mEq PO QD while on Hydrochlorothiazide.

Hypomagnesemia

- Renal Wasting:
  - Loop and Thiazide Diuretics, PPI, Aminoglycoside, Cisplatin and derivatives, Tacrolimus, Cyclosporin, Sirolimus, Everolimus, Amphotericin B, Ethanol.
- GI Wasting:
  - PPIs, Laxatives, Phosphate Binders
- Intracellular Shifts:
  - Insulin, Beta-Agonists, Bisphosphonates, Denosumab,
- Other:
  - Pentamidine, Foscarnet, Cetuximab, Panitumumab

Case 4:

A 66-year-old female with PMHx of Dyspepsia, DMII controlled (HbA1c 6.8) by Metformin alone, Obesity, Hypertension, Hyperlipidemia was seen in primary clinic for routine check. Her medications include Hydrochlorothiazide, Atorvastatin, Omeprazole, Lisinopril. She has been feeling well and no acute complaints except that she has occasional dyspepsia. She was prescribed omeprazole 5 years ago and she noticed little to no change in her dyspepsia.

Vital signs are stable; blood pressure is controlled. BMI 30. Her weight has been slowly improving since recent initiation of Metformin 500 mg PO BID.

Labs:

Serum Magnesium 1.4 (Normal 1.7-2.4) which was 1.5 (1 years ago), Serum Calcium 8.3, Serum potassium 3.8, Serum Sodium 138, Serum creatinine 0.9. Fractional Excretion of Mg (FeMg) = 1% (Normal 2-4%)

Case 4 Cont’

Which of the following best explains this patient’s electrolyte disturbance?

A. Metformin-associated magnesium loss through gut absorption and urinary excretion
B. Chronic Proton Pump Inhibitor Use causing GI magnesium Loss
C. Renal Magnesium Wasting from Hydrochlorothiazide
D. She is a picky eater.

Case 4 Cont’

What would be the best course of action for management of this patient?

A. Stop PPI and start Tums as needed.
B. Change Metformin to Ozempic.
C. Prescribe Magnesium Lactate.
D. Prescribe Magnesium Oxide.

Hypercalcemia

- Bone Resorption
  - Vitamin A, Teriparatide, PTH analogs
- Increased Intestinal Absorption
  - Vitamin D, Calcitriol, Calcium Supplements
- Decreased Renal Excretion
  - Thiazides, Lithium
- Hemoconcentration/Volume Effect
  - Loop Diuretics
- Rare/Indirect
  - Milk Alkali, Tamoxifen

Case 5:

- A 72-year-old man with PMhx of osteoporosis (stable without fractures and not on medications, and being monitored with DEXA), hypertension, Bipolar disorder, and chronic kidney disease stage 3 taking Vitamin D OTC, chlorthalidone, and Lithium seen in clinic for routine examination. He reports having dyspepsia lately and started taking Tums

- Physical Examination showed BP 148/84 mmHg, HR 90, Dry Mucus Membrane.

- Labs:

Serum Calcium 11, Serum Creatinine 1.6, Serum Phos 5.0, iPTH suppressed, Vitamin D 25 OH 50 (Normal 20-50), Urinary Calcium – Elevated

Case 5 Cont’

Which of the following is the most likely cause of this patient’s hypercalcemia?

A. Vitamin D toxicity
B. Thiazide-Induced Hypercalcemia
C. Milk-Alkali Syndrome
D. Lithium-Induced Hypercalcemia
E. Primary Hyperparathyroidism

Case 5 Cont’

What would be the best course of action for the management of this patient?

A. Discontinue Vitamin D and Tums.
B. Change Tums to PPI.
C. Change Chlorthalidone to Furosemide
D. Start Bisphosphonate.

Hypocalcemia

- Decreased Intestinal Absorption
  - PPIs, Phenytoin, Carbamazepine, Cholestyramine, Orlistat
- Increased Renal Calcium Excretion
  - Loop Diuretics, Cisplatin, Aminoglycosides
- Suppression of Parathyroid Hormone
  - Bisphosphonate, Denosumab, Cinacalcet, Calcitonin
- Chelation or Binding of Calcium
  - Citrate, EDTA, Phosphate replacement (Chelation)
- Secondary to Hypomagnesemia
  - PPI, Loop Diuretics, Cisplatin, Aminoglycosides

Electrolytes

- Sodium (It is always a water disorder, not the salt)
- Potassium (Needs immediate attention)
- Calcium (Usually from Vitamin D)
- Magnesium (Look for PPI & Metformin)

Nutshell

- Careful medication reconciliation and removal (if no longer indicated) or replacement of culprit medication is the key.
- Use electrolyte side effects of other indicated medications for underlying medical condition as a leverage.
- Electrolyte replacement or removal by binder should be considered last.
- Achieving the goal while limiting the amount of medications patient needing to take.

Thank
You