Major intra and extra cellular electrolytes

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Electrolytes

Substances whose molecules dissociate into ions when they are placed in water.

CATIONS (+) ANIONS (-)

Medically significant / routinely ordered electrolytes include*:*

<u>Cation</u>: Positively Charged particles.

Sodium (Na +)
Potassium (K+)
Calcium (Ca++)
Magnesium (Mg++)

<u>Anion</u>: Negatively charged particles.

Chloride (Cl-)
Bicarbonate (HCO_3-)
Phosphate (HPO_4 -)

Electrochemical Equivalence

- **Equivalent (*Eq/L*) = moles x valence**
- **Monovalent Ions** (Na^{+}, K^{+}, Cl^{-}):
  - 1 milliequivalent (*mEq/L*) = 1 millimole
- **Divalent Ions** (Ca^{++}, Mg^{++}, and HPO_4^{2-})
  - 1 milliequivalent = 0.5 millimole

Electrolyte Functions

-Volume and osmotic regulation
-Myocardial rhythm and contractility
-Cofactors in enzyme activation
-Regulation of ATPase ion pumps
-Acid-base balance
-Blood coagulation
-Neuromuscular excitability
-Production of ATP from glucose

Sodium

Functions

-Most abundant extracellular cation.
-Regulates body water distribution.
-Aids nerve impulse transmission.
-Aids transfer of calcium into cells.

Regulation of Sodium

- Concentration depends on:
  - intake of water in response to thirst
  - excretion of water due to blood volume or -osmolality changes
- Regulation of sodium
  - Kidneys can conserve or excrete Na^+ depending on ECF and blood volume
    - by aldosterone
      - and the renin-angiotensin system this system will stimulate the adrenal cortex to secrete aldosterone.

Aldosterone

From the (adrenal cortex)

Functions

promote excretion of K

in exchange for

reabsorption of Na

Sodium normal values

Serum – 135-148 mEq/L

Clinical Features: Sodium

Hyponatremia: < 135 mmol/L

- Increased Na+ loss
  - Aldosterone deficiency
    - ***Addison's disease (hypo-adrenalism, result in ↓ aldosterone)***
  - Diabetes mellitus
    - ***In acidosis of diabetes, Na is excreted with ketones***
  - Potassium depletion
    - ***K normally excreted , if none, then Na***
  - Loss of gastric contents

Electrolyte replacement therapy

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- Identify when electrolyte replacement is needed and underlying cause
    - Potassium, Magnesium, Calcium, Phosphorous
- Understand different formulations, route, dosage and adverse effects of replacement
- Identify when goal replacement has been achieved
- Identify when maintenance therapy may be required

Hypokalemia

- Usually secondary to:
  - GI loss (vomiting, diarrhea)
  - Urinary losses (diuretics)

  Also think about : co-existing electrolyte abnormality (hypomagnesemia), hyperaldosteronism, insulin therapy, alkalosis)

- Indications for replacement:
  - Evidence of potassium loss
  - Significant deficit in body potassium
  - Acute therapy in redistributive disorders (periodic paralysis, thyrotoxicosis)

- Symptoms: usually manifest when serum K <3.0
  - Muscle weakness (K <2.5), cramps
  - Respiratory muscle weakness
  - GI symptoms: anorexia, nausea, vomiting
  - Cardiac arrhythmias: atrial tachycardia, junctional tachycardia, AV block, ventricular tachycardia or fibrillation
  - sinus bradycardia, ST segment depression, decreased amplitude of T-wave, increased amplitude of U-wave.
  - If prolonged hypokalemia: functional changes in the kidney and glucose intolerance

Therapy

- Calculate potassium deficit (if normal distribution is present)
  - Acute: 0.27meq/L decrease in serum K+ for every 100meq reduction in total potassium stores
  - Chronic: 1meq/L decrease in serum K+ for every 200-400meq reduction in total potassium stores

Simplified:

$$\frac{\text{Goal K} - \text{Serum K}}{\text{serum Cr}} \times 100 = \text{total meq K required}$$

10meq of KCL will raise the serum K by ~.1meq/L

Formulations

- Potassium Chloride : PREFERRED AGENT
  - Most patients with hypokalemia and alkalosis are also chloride depleted
  - Raises serum potassium at a faster rate
  - Available as liquid, slow release tablet or capsule, and IV
  - **Oral: 40meq tid-qid; IV 10meq/hr- 20meq/hr**
- Potassium Bicarbonate/Citrate/Acetate:
  - can be used in patients with hypokalemia and metabolic acidosis
- Potassium Phosphate:
  - Rarely used (Fanconi syndrome with phosphate wasting)

Ongoing Losses

- In general, use oral therapy
- KCL with normal or elevated serum bicarb
- Potassium citrate/acetate/bicarbonate in presence of acidosis (diarrhea)
- no need for continued supplementation with chronic renal potassium wasting (potassium sparing diuretic is more effective):
  - Chronic diuretic therapy
  - Primary aldosteronism

Adverse Effects

- Hyperkalemia
- Potassium is osmotically active- can increase tonicity of IV fluids
- Oral therapy- pills are large, can be difficult to swallow
- Peripheral IV therapy:
  - Pain
  - Phlebitis

Make sure to recheck serum potassium 2-4 hours later to assess response to therapy

Goal of Therapy

- Prevent life threatening complications

- Urgency of replacement depends on severity, rate of decline and co-morbid conditions
  - Elderly
  - underlying heart disease
  - on digoxin or anti-arrhythmic drugs

Example

- 72 year old female admitted for weakness and dehydration due to acute gastroenteritis. She is having up to 6 BM/day. Her serum K on admission is 2.5 meq and serum Cr is 2.0. ECG reveals u-waves.

1. How much potassium do you order?

$$\frac{4-2.5}{2} \times 100 = 75\text{meq}$$

2. What formulation do you choose?

KCL; if bicarb is low then consider potassium bicarb or acetate

3. What route should the potassium be administered?

40meq (initial) oral and 40meq IV; (re-assess 2-4 hours l later and give more orally if needed and tolerating po)

3. Serum potassium remains low, what else could be contributing?

Low magnesium, ongoing diarrhea

Hypomagnesemia

- Average daily intake: 360mg
- Presence of low magnesium (nearly 12% of hospitalized patients) suspected in following cases:
  - Chronic diarrhea
  - Hypocalcemia
  - Refractory hypokalemia
  - Ventricular arrhythmias
- Symptoms/Signs :
  - Tetany (seizures in children/neonates)
  - Hypokalemia
  - Hypoparathyroidism→ hypocalcemia (<1.2mg/dL)
  - Vitamin D deficiency (due to low calcitriol)
  - ECG changes: widened QRS, peaked T-waves,→ dimunition, PR interval prolongation,
  - Ventricular arrhythmias (especially during ischemia or bypass)

Therapy

- IV if symptomatic (magnesium sulfate)
  - 1.5-1.9mg/dL→ 2g magnesium sulfate IV
  - 1.2-1.4mg/dL→4g
  - .8-1.1mg/dL→ 6g
  - <.8mg/dL→ 8g
  - **Low K/Ca w/ tetany/arrhythmia: 50meq (~6g) of IV Mg given slowly over 8-24 hrs**
- Oral if asymptomatic: each tablet contains 60-84mg, give 2-4 tabs/day in mild cases, 6-8 tabs for severe depletion

  -Slow Mag (magnesium chloride)

  -Mag-Tab SR (magnesium lactate)

  -**Magnesium Oxide**
- Avoid replacement in patients with reduced GFR
- Treat underlying disease (diuretics, alcohol, uncontrolled diabetes)

Therapy

- Goal of therapy:
  - maintain plasma magnesium concentration over 1.0mg/dL acutely in symptomatic patients
  - In cardiac patients, maintain Mg >1.7 (usually goal 2.0mg/dL) to avoid arrhythmias
  - Serum levels are poor reflection of actual body stores (mostly intracellular) so aim for high-normal serum level
- Adverse effects:
  - Abrupt elevation of plasma Mg can remove the stimulus for Mg retention and lead to increased excretion
  - Diarrhea
  - Drug interactions
  - Magnesium intoxication

Hypocalcemia

- Clinical Manifestations:
  - Acute: serum Ca <7.5mg/dL
    - Neurologic: tetany (from paresthesias to seizures and bronchospasm)
    - Cardiac: prolonged QT, hypotension, heart failure, arrhythmia
    - Papilledema
    - Psychiatric manifestations
  - Chronic:
    - EPS, dementia, cataracts, dry skin
- Etiology:
  - Vitamin D
  - PTH
  - Hypomagnesemia
  - Drugs

Therapy

- Correct for albumin
  - Ca lower by 0.8mg/dL for every 1g/dL reduction in serum albumin
  - or check ionized calcium
- Level can be altered by acid/base disturbance
- Symptomatic or acute serum Ca <7.5mg/dL:
  - **IV Calcium gluconate 1-2g(amp) over 10-20min (**temporary rise for 2-3 hrs, must be followed by slower infusion 50mL/hr if Ca remains low)
- Asymptomatic and serum Ca >7.5mg/dL or chronic:
  - **Oral therapy: calcium carbonate or citrate 1-2g/day (500mg bid-qid)**
- Add Vitamin D in following cases:
  - Hypoparathyroidism: **Vitamin D (Calcitriol .25-.5mcg bid)**
  - Vitamin D deficiency: 50,000IU/week for 6-8 weeks then 800-1000IU daily
    - Erogcalciferol (D3)
    - Cholecalciferol (D2)

Therapy

- Goals of therapy:
  - Treat and prevent manifestations of hypocalcemia
  - In hypoparathyroidism: to raise serum Ca to low-normal range (8.0-8.5mg/dL)

- Adverse Effects:
  - Rapid infusion- bradycardia, hypotension
  - Extravasation- tissue necrosis
  - Hypercalcemia
  - Hypercalciuria
  - Constipation
  - Hypophosphatemia
  - Milk-alkali syndrome

Example

35 y/o male with hypoparathyroidism , presents with serum Ca of 6.2, albumin of 3.8, ionized Ca .77. Has some mild muscle cramps, otherwise asymptomatic.

1. How do you initially treat his hypocalcemia?
   - IV Calcium Gluconate 1g IV over 10-20min
2. Repeat serum Ca is 6.6, how do you proceed with treatment?
   -start Calcium gluconate 1mg/mL in D5W 50mL/hr infusion
2. After initial treatment, what maintenance regimen should you initiate?
   -Calcitriol (.5mcg bid, titrated up in this patient)
   -Calcium carbonate (1950mg po tid in this patient)

Hypophosphatemia

- Due to:
  - Restribution
  - Decreased intestinal absorption (small bowel)
  - Increased urinary excretion

- Common situations:
  - Chronic alcoholism
  - IV hyperalimentation w/o phosphate supplementation
  - Refeeding syndrome
  - "Hungry Bone" syndrome
  - Respiratory alkalosis (hyperventilation)
  - Chronic ingestion of antacids (containing aluminum or Mg)
  - Hyperparathyroidism (primary or secondary)
  - Vitamin D deficiency
  - Fanconi syndrome (associated with multiple myeloma in adults)

Hypophosphatemia

- Signs/Symptoms: <2.0mg/dL, severe usually when serum PO4 <1.0mg/dL

Acute:

- Metabolic encephalopathy- irritability, paresthesias→ confusion, seizure, coma
- Respiratory failure due to weakened diaphragm
- Reduction in cardiac output leading to heart failure
- Proximal myopathy, dysphagia, ileus
- Elevated CPK, rhabdomyolysis
- Coagulopathy with thrombocytopenia

Chronic:

- Hypercalciuria
- Increased bone resorption: Osteomalacia, Ricketts

Treatment

- Usually aimed at treating the underlying cause (resolution of diarrhea, Vit D therapy, d/c antacid, etc.)

- If tx is needed, oral therapy is preferred
  - Asymptomatic, serum PO4 <2.0mg/dL or symptomatic with serum PO4 1.0-1.9mg/dL
  - Available as tablet and powder/packets (sodium phosphate, potassium phosphate) 250-500mg tid-qid (w/ meals) over 24 hours
  - ~~Decrease dose by one-half in patients with reduced GFR~~
  - Increase dose in severely obese patients
  - Recheck after 12 hours to determine if additional/continued supplementation is required

Treatment

- IV therapy if symptomatic and serum PO4 <1.0mg/dL
  - sodium phosphate is preferred
  - Weight based
    - PO4 >1.3mg/dL: .08-.24mmol/kg over 6 hours
    - PO4 <1.3mg/dL: .25mmol-.05/kg over 8-12 hours
    - Increased dosage for critically ill patients in ICU
    - Frequent monitoring- recheck levels every 6 hours
    - Switch to oral when patient able or serum PO4 >1.5mg/dL

- Goal of therapy: increase serum PO4 to 2.0mg/dL
- Side effects of therapy:

  -Oral: Diarrhea, nausea, hyperkalemia (K-phos)

  -IV: Hyperphosphatemia→ hypocalcemia, AKI, arrhythmia

- Maintenance therapy is not usually required

	Preferred Route	Preferred Formulation	Dosage	Response
Potassium	**Oral**	Potassium Chloride	10meq tabs	.1 increase serum K for 10meq given
Magnesium	**Oral** IV- arrhythmia	Magnesium Oxide Magnesium Sulfate	2-4 tabs/day (420mg; 20meq/tab) 2g IVP or slow infusion	.5 increase for 2g (50meq) IV
Calcium	**IV- acute** Oral- maintenance	Calcium Gluconate Calcium Carbonate	1-2amp (rapid) 1mg/mL in D5W, 50mL/hr Infusion 1-2g/day	.5mg/dL increase serum Ca for 1g given
Phosphate	**Oral**	Sodium Phosphate (neutra-phos)	1-2 packet tid-qid 1packet=250mg or 8mmol (weight based)	1.2mg/dL increase serum PO4