Hypokalemia

Background
1. Definition:
   o Serum potassium < 3.5 mEq/L [3.5 mmol/L]
2. General info
   o Serum deficiency of potassium, the primary intracellular cation, integral for cellular function throughout the body

Pathophysiology
1. Pathology of disease
   o Decreased potassium intake
   o Increased intracellular uptake
   o Gastrointestinal loss
   o Urinary losses
   o Sweat losses
   o Losses via dialysis and plasmapheresis
2. Incidence, prevalence
   o In a series of PICU admissions in India, 14.8% of patients had hypokalemia
   o No other pediatric incidence / prevalence data found in exhaustive literature search
3. Risk factors
   o Underlying renal or GI condition
   o Diuretic use
   o Malnutrition
4. Morbidity / mortality
   o Muscle weakness or paralysis, including respiratory failure
   o Ileus
   o Skeletal muscle paresthesias, tetany, muscle tenderness, atrophy
   o Rhabdomyolysis, including myoglobinuria acute renal failure
   o ECG abnormalities, including U waves and cardiac arrhythmias
   o Renal abnormalities, including impaired renal concentrating ability, increased renal ammonia production, increased bicarbonate reabsorption, and hypokalemic nephropathy
   o Mortality is rare, usually associated with cardiac surgery, arrhythmia, or underlying heart disease requiring digoxin therapy

Diagnostics
1. History
   o HPI
     - Muscle weakness / tenderness / tetany / paresthesias, palpitations, polyuria, oliguria, red or brown colored urine, emesis, abdominal distention, anorexia
   o Medications
     - Diuretics, asthma medications, insulin, psychotropic medications
   o Family and personal Hx
     - Kidney disease, adrenal disease, mucosal GI disease
Social Hx
- Huffing, rapid weight loss dieting, access to inciting medications or chemicals

2. Physical exam
   - General
     - May see cachexia, decreased consciousness
   - Musculoskeletal
     - Weakness, tetany, muscular tenderness, atrophy
   - Cardiac
     - Arrhythmias
   - Respiratory
     - Respiratory failure
   - Gastrointestinal
     - Ileus, distention, emesis

3. Diagnostic testing
   - Laboratory evaluation
   - Serum electrolytes, magnesium, BUN, creatinine
   - Blood gas analysis if suspicion for acid-base disturbance or respiratory failure
   - Urinalysis and urine electrolytes if changes in urination or suspicion of renal cause or sequelae
   - Drug screen if suspicion for sympathomimetic stimulant intoxication (eg amphetamine)
   - Albumin / prealbumin / CRP if concerned about malnutrition

4. Diagnostic imaging
   - Unnecessary unless otherwise indicated

5. Other studies
   - Electrocardiogram to assess for cardiac effects of hypokalemia, or if arrhythmia noted

6. Diagnostic "Criteria"
   - Serum potassium < 3.5 mEq/L [3.5 mmol/L]

**Differential Diagnosis**

1. Key differential diagnoses
   - Gastroenteritis
     - Classically considered the most common cause of hypokalemia in children
   - Malnutrition
   - Renal disease
   - Septicemia
   - Acute diarrhea
   - Heart disease with congestive failure
   - Meningoencephalitis
   - Diuretic use
   - Beta-agonist use
   - Corticosteroid use
2. Extensive differential diagnoses
   
   o Decreased potassium intake
     - Malnutrition
     - Anorexia nervosa
     - Alcoholism
   
   o Increased intracellular uptake
     - Metabolic alkalosis
     - Respiratory alkalosis
     - Increased circulating insulin
       - Insulin therapy / overdose
       - PO or IV carbohydrate load
     - Elevated beta-adrenergic activity
       - Acute illness
       - Theophylline or beta-agonist therapy
     - Hypokalemic periodic paralysis
     - Familial
     - Thyrotoxic
   
   o Increased hematopoiesis, including acute leukemia
   
   o Hypothermia
   
   o Intoxications
     - Barium
     - Chloroquine
     - Risperidone
     - Quetiapine
     - Cesium
   
   o Gastrointestinal loss
     - Vomiting
     - Diarrhea (including laxatives, enemas, homeopathic cathartics)
     - Enteral tube drainage
     - Villous adenoma or VIPoma
   
   o Urinary losses
     - Increased aldosterone effect
       - Primary mineralocorticoid excess, pheochromocytoma, Conn's syndrome
     - Increased distal nephron flow
       - Diuretics (acetazolamide, thiazides, loop diuretics)
       - Nonreabsorbable anions
         - Renal Tubular Acidosis type 1 and type 2
         - Diabetic ketoacidosis
         - Toluene abuse (glue-sniffing / huffing)
         - High-dose penicillin therapy
       - Hypomagnesemia
       - Polyuria of any cause
     - Increased potassium secretion
       - Amphotericin B therapy
   
   o Salt-wasting nephropathies
     - Bartter's or Gitelman's syndrome
     - Tubulointerstitial diseases (eg interstitial nephritis)
• Hypercalcemia
• Acute leukemia (esp monocytic, myelomonocytic)

 o Sweat losses
  ▪ Exercise in hot climate
  ▪ Cystic fibrosis
 o Losses via dialysis and plasmapheresis

Therapeutics

1. Acute treatment
   o Potassium >3 mEq/L and asymptomatic:
     ▪ Potassium chloride 2 mEq/kg/day PO divided BID to QID (Grade 2B)
       ▪ More aggressive if heart disease
     ▪ Use potassium bicarbonate or citrate if metabolic acidosis present (Grade 2B)
     ▪ May use crystalline form (salt substitute from grocery store), which contains 50-65 mEq per teaspoon
     ▪ If unable to take PO, treat as severe symptoms below
   o Potassium 2.5-3 mEq/L or Mild to Moderate Symptoms:
     ▪ Potassium chloride 4 mEq/kg/day PO divided BID to QID until serum potassium concentration >3 mEq/L and symptoms resolve (Grade 2B)
     ▪ If unable to take PO, treat as severe symptoms
   o Potassium <2.5 mEq/L or Severe Symptoms
     ▪ Potassium chloride IV in saline solution, esp if receiving insulin or bicarbonate therapy (Grade 1B)
       ▪ 0.5-1 mEq/kg (maximum 30-40 mEq per dose) every 3-4 hrs as needed, to infuse at 0.3-0.5 mEq/kg/hr (max 1 mEq/kg/hr)
         ▪ Infusion rate >0.5 mEq/kg/hr may be necessary in critical hypokalemia, and warrants continuous ECG monitoring
           ▪ Absolute maximal IV rate in an adolescent or adult is 20 mEq/hr
         ▪ Maximal IV concentration is 200 mEq/L
           ▪ Concentrations >60 mEq/L are painful and should only be infused into a central vein via infusion pump
     ▪ Try not to use dextrose solutions, as stimulation of insulin secretion will shift potassium into cells from the intravascular space
     ▪ Check serum potassium concentration between IV doses to avoid over correction
   o Identify and treat any predisposing conditions

2. Further management (24 hrs)
   o Match any subsequent replacement to ongoing losses
     ▪ For chronic replacement, consider PO potassium chloride, potassium-based salt substitutes sprinkled on food, or potassium-sparing diuretic (Grade 2B)
Combination of potassium supplement and potassium-sparing diuretic requires close monitoring of serum potassium level
  - At least every 4 months in any patient with chronic therapy
  - More frequently if concurrent chronic kidney disease, ACEI therapy or ARB therapy, or recent change in potassium or diuretic dosing
    - Follow-up ECG if abnormalities were initially present
    - Identify and treat any predisposing conditions

3. Long-term care
   - Depends upon precipitating cause and predisposing conditions, medications

Follow-Up
1. Return to office
   - Time frame for return visit
     - Depends upon etiology and stability of potassium level after intervention
     - Follow potassium level at least every 4 months in patients on potassium supplementation and/or potassium-sparing diuretic therapy
   - Recommendations for earlier follow-up:
     - Unstable potassium levels, recent change in medication(s) that affect potassium

2. Refer to specialist
   - After correction of hypokalemia, consultation with specialist may be necessary to manage predisposing conditions
     - Consider nephrology if unclear etiology or renal etiology
     - Consider endocrinology if contributing endocrine etiology
     - Consider GI if underlying GI cause

3. Admit to hospital
   - Recommendations / urgency
     - No evidence regarding criteria for inpatient admission
   - Consider admission if
     - Potassium <2.5 mEq/L, or
     - Pt is symptomatic of hypokalemia

Prognosis
1. Excellent with control of potassium level and control / resolution of predisposing conditions
2. Complications of treatment include hyperkalemia, cardiac dysrhythmia, and gastric erosions or strictures (from PO tablets)

Prevention
1. Follow potassium level at least every 4 months (more frequently after medicine changes and/or changes in patient condition) in patients on potassium-wasting diuretic therapy or with conditions that predispose them to hypokalemia

Patient Education
1. http://www.hmc.psu.edu/healthinfo/h/hypokalemia.htm
References


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