Hypokalemia — Complications and Side Effects

Hypokalemia is defined as plasma potassium less than 3.5 mEq/L. Only 1% of the general population suffers from this disorder with the prevalence rising to 25% among hospitalized patients. Some risk factors of hypokalemia include elderly patients and people who rely on food poor in potassium content, women and patients recovering from bariatric surgery.

Definition

Hypokalemia is a metabolic/endocrine disorder that is characterized by a plasma potassium level of less than 3.5 mEq/L. A serum potassium level that is less than 2.5 mEq/L leads to life-threatening scenarios of arrhythmias and muscle paralysis. A normal level of potassium is necessary to maintain a charge difference between intracellular and extracellular environments which is the integral mechanism according to which muscles and nerves work.

Epidemiology of Hypokalemia

It is estimated that up to 1% of the general population have potassium levels less than 3.5 mEq/L. Among hospitalized patients, the incidence is higher, with 16% of
them having serum potassium levels between 3.0 and 3.5 mEq/L and 5 % having a level that is lower than 3.0 mEq/L. Conditions that are associated with affected people include:

- Elderly age due to the high prevalence of chronic diseases such as diabetes, and use of medication that may lead to hypokalemia;
- Low dietary intake of potassium in African Americans which predisposes them to hypokalemia;
- Female gender;
- Eating disorders;
- Alcoholic addiction compromises the potassium absorption mechanism;
- Recovery from bariatric surgery causes a reduced rate of potassium absorption.

Hypokalemia has no sex predilection.

Classification of Hypokalemia

Hypokalemia is classified into

1. Mild hypokalemia: 3.0–3.5 mEq/L;
2. Moderate hypokalemia: 2.5–3.0 mEq/L;
3. Severe hypokalemia: <2.5 mEq/L.

Etiology and Pathophysiology of Hypokalemia

Normal control of potassium levels

Potassium is the principal intracellular cation that is needed for maintenance of the membrane potential across the cells of nerves and muscles during transmission of impulses. One source of potassium can be a diet rich in potassium which includes intake of bananas, beans and meat or the intravenous/oral administration of supplemental potassium.

Upon intake or infusion, the cation is absorbed at a rate of 1mEq/Kg/day. Most of the absorbed ions (up to 90 %) is excreted via the kidneys. This is important in maintaining a normal serum level of potassium and a normal storage level.

The total body potassium stored in muscles is estimated to be 50mEq/kg. The cations are either intracellular (98 %) or extracellular (2 %). The extracellular potassium is the measurement in reference during laboratory testing and it is maintained at a range of 3.5–5.0 mEq/L via a homeostatic mechanism across the cell membrane aided by the Na+/K+/ATPase pumps.

Hypokalemia mainly results from disorders that lead to:

- Increased potassium excretion;
- Shift of potassium from the extracellular compartment to the intracellular compartment;
- Reduced potassium intake;
- Interplay of more than one of the above mechanisms.

Increased excretion of potassium

This is the most common pathogenic pathway in the causation of hypokalemia.
Mineralocorticoid excess, such as excess aldosterone, causes retention of salt and water. The retention of sodium dictates that potassium must be lost at the collecting tubules by function of the Na+/K+ pumps. The source of excess aldosterone may be endogenous, such as in Cushing’s syndrome, or exogenous, such as in steroid therapy.

Another way excess potassium is lost via the kidneys is the increase in diuresis. Diuretic drugs work by delivering more blood for ultrafiltration and thus more potassium is delivered for excretion. If the diuretics do not possess the ability to spare potassium, hypokalemia ensues. Such diuretics or diuretic-like drugs include: Lasix, theophylline and caffeine.

The other pathway of potassium loss is the gastrointestinal pathway where patients lose content that is rich in potassium and other minerals via vomit and diarrhea. Moreover, the rapid loss of gastric contents compromises absorption of dietary potassium thus leading to low potassium levels.

Some congenital disorders manifest as defects in the pathways that control the amount of sodium and potassium in circulation thus leading to derangements—most commonly to hypokalemia due to failure of the Na+/K+ pump. If the pump fails, then more sodium remains intracellular and hypokalemia ensues. Such disorders include the barter syndrome that is characterized by hypokalemic metabolic alkalosis and hypotension. Another genetic abnormality is the Gitelman syndrome which is an autosomal recessive disorder characterized by hypokalemic metabolic alkalosis and low blood pressure.

Shift of potassium into the intracellular compartment

An increase of insulin in the circulation triggers an increase of water in the cells causing a shift of potassium in the cells and a reduction of potassium efflux leading into a net increase in the intracellular potassium level. The rise in insulin levels could be endogenous, following a rise in blood glucose, or exogenous, following erratic administration of insulin in high doses.

A high β-sympathomimetic activity in the body causes a similar effect. The effect may result from endogenous β-adrenergic agonists administration or endogenous hormones such as those secreted in thyrotoxicosis.

Reduced bodily intake of potassium

Potassium is usually absorbed via the gastrointestinal system at a rate of 1 mEq/kg/day, and 90 % of this is excreted in the kidneys every day. Therefore, any reduction in intake with no proportional reduction in loss leads to a deficit in potassium. Good example is the reduced intake of potassium rich foods, such as in patients with eating disorders or poor patients who may not afford a balanced diet. The elderly population is also at risk due to neglect and are thus forced to depend on poor quality food such as bread and tea which have low potassium content.

Interplay of more than one mechanism

In the majority of patients suffering from hypokalemia, an interplay of more than one pathway is incriminated with increased loss of potassium being almost always present. In most cases, it is coupled with a shifting of potassium into the intracellular compartment.
Clinical Features of Hypokalemia

Mild hypokalemia occurs as an incidental finding during routine workup or during workup for other diseases. The patient is asymptomatic.

**Potassium is the cation required for membrane stability and signal transmission in muscles and nerves.** Therefore, if the membrane is destabilized by deficits, the patient complains of compromised muscle function such as:

- Weakness and fatigue as muscles in the extremities are unable to contract.
- Continued compromise of the function leading to frank paralysis.
- Later muscle pains set in with onset of rhabdomyolysis.
- Compromised gut muscles may lead to reduced bowel movements and constipation.

Other symptoms occur due to associated conditions

- Poor feeding habits are observed with eating disorders that could be the cause of hypokalemia.
- Socio-economic problems, such as poverty and neglect, may be the presetting history in patients with poor intake of potassium.
- Polyuria and poor glucose control may be the presenting symptoms in a patient whose causative mechanism is diuresis or a shift of potassium due to high insulin levels.
- Vomiting and diarrhea indicate gastrointestinal losses which are the cause behind the deficit of potassium.
- Increase in β-sympathomimetic activity **may be seen in patients with thyrotoxic symptoms** or patients with a history of β-adrenergic agonist use, such as C.O.P.D patients.

Likely findings on examination include:

- Absent deep tendon reflexes due to muscle paralysis;
- Hypoactive/absent bowel sounds;
- Tachycardia due to the heart’s attempt to compensate the compromised respiratory system;
- Bradycardia due to compromise of the heart muscle function;
- Hypotension in association with diuresis;

*Image: “Abdominal stretch marks,” by Martinez-Valles MA, Palafox-Cazarez A, Paredes-Avina JA. License: CC BY 3.0*
Hypertension if disease process is associated with suprarenal disease.

Investigations of Hypokalemia

**Laboratory investigations are done mainly to define the severity of hypokalemia**, to rule out other medical conditions and as a baseline before the initiation of therapy. They include:

**Serum potassium level**
- Less than 3.5 mEq/l (usually the initial test if hypokalemia is suspected) is a sign of hypokalemia.

**Electrocardiogram (ECG)**
- Establish ECG findings in hypokalemia that include Tachyarrhythmias such as PVCs and ventricular fibrillation.
- ST wave depression, T wave flattening and appearance of U waves.
- Reduced amplitude of P waves.

**Urine potassium levels**
- Necessary to find out the causative mechanism of the disease.
- Levels higher than 40mEq/L suggest a renal cause for the losses, while a level that is less than 20mEq/L suggests the loss is due to gastrointestinal mechanisms such as vomiting and diarrhea.
- This test, however, is inaccurate, especially with concentration of urine.
- Therefore, a second test is applied to rule out this confounding factor.

**Trans-tubular potassium gradient (TTKG)**
- Obtained by urine (K+) x Serum osmolality divided by serum (K+) x Urine osmolality.
- Gradient higher than 7 indicates that losses are renal and high levels of urinary potassium are not secondary to concentration of urine.

**Tests to rule out differential diagnoses**
- Thyroid function tests;
- 24-hour urinary cortisol levels to rule out suprarenal tumors;
- Drug screen to rule out diuretic and sympathomimetic use;
- Insulin levels and C-peptide to determine the level and source of high insulin level if detected;
- Enzyme assays such as dexamethasone suppression tests and ACTH stress test.

**Differential Diagnosis of Hypokalemia**

<table>
<thead>
<tr>
<th>Pseudo hypokalemia</th>
<th>• Results from poor sampling of a venipuncture site, such as drawing blood from a vein that has a distal infusion of saline running.</th>
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<tbody>
<tr>
<td>Congenital disorders</td>
<td>• Differentiated by the presence of associated features such as hypotension in Gitelman syndrome and identifiable genetic mutation.</td>
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<tr>
<td>Metabolic acidosis</td>
<td>• Has features of ketoacidosis polyuria, increased thirst and vomiting.</td>
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Cushing syndrome

- Has associated increase in pituitary hormones or identifiable mass on imaging.

Treatment of Hypokalemia

Approaches to the management of hypokalemia are:

1. Reduction of potassium losses;
2. Replenishment of potassium stores;
3. Avoiding recurrences.

Reduction of potassium losses

This is achieved by reducing the amount of potassium reaching the renal tubules. Non-potassium sparing diuretics such as thiazides and thiazide-like agents must be discontinued.

If that is not possible (diuresis is still needed) an introduction of potassium-sparing diuretics such as spironolactone can be used, especially in patients with normal kidney function. Watch out for rebound hyperkalemia.

Replenishment of potassium stores

Dietary modification and introduction of low sodium but potassium rich foods are of great value in treatment of mild hypokalemia. Success is achieved especially if potassium losses are reduced concurrently. The foods include leafy vegetables, avocados, tomatoes and oranges.

Oral potassium chloride is indicated in mild to moderate hypokalemia with a goal of achieving serum potassium levels of > 3.5mEq/L or > 4.0 mEq/L in CAD and CHF patients. To achieve this, the total potassium requirement is estimated based on the assumption that to raise the potassium level by 1 mEq/L, 200–400 mEq of potassium must be administered.

Intravenous administration of potassium chloride via peripheral veins is indicated if the level of potassium is below 2.5 mEq/L and ECG findings are present. With a similar target, estimate the deficits and replenish at a rate of 20-40 mEq per day to avoid irritation of the veins.

Intravenous administration of potassium chloride via a central line is indicated to rapidly correct ECG changes. The rate is as high as 10 mEq/hr. This can be done but the total dose should not exceed 80 mEq in a day.

Avoiding recurrences

Surgical treatment is carried out to cure causative diseases such as adrenal adenoma or renal artery stenosis.

Magnesium replacement is indicated for refractory cases in the setting of low magnesium levels.

Complications of Hypokalemia

Due to low potassium levels, cardiac arrhythmias manifest as dysfunctional heart muscles that lead to tachycardia and ventricular fibrillation.

Paralysis that may be life-threatening is common, especially in situations of
elevated thyroid function tests (thyrotoxic periodic paralysis). Rebound hyperkalemia is also seen with aggressive replacement.

References


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