

Practice Point

Potassium Replacement in Hypokalemia

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Hypokalemia is defined as plasma potassium (K⁺) concentration of < 3.5 mEq/l. It is a common electrolyte abnormality with a wide range of presentations. Hypokalemia is reported in < 1% of healthy adults. However, about 20% of hospitalized patients requiring care in medical wards and nearly 50% of patients on either loop/thiazide diuretics exhibit hypokalemia. Hypokalemia is associated with a nearly tenfold increase in-hospital mortality due to its adverse cardiovascular effects.¹

Severity of Hypokalemia:

1. Mild hypokalemia: 3 to 3.4 mEq/l
2. Moderate hypokalemia: 2.5 to 2.9 mEq/l
3. Severe hypokalemia: <2.5mEq/l

Treatment

Managing hypokalemia aims to prevent/treat life-threatening complications (arrhythmias, paralysis, rhabdomyolysis, and diaphragmatic weakness), replace potassium deficit, and correct underlying cause. The urgency of treatment depends upon the severity of hypokalemia, associated comorbid conditions and rate of decline in serum potassium concentration. The risk of arrhythmia from hypokalemia is more in older patients, patients with organic heart disease, and patients on drugs like digoxin and antiarrhythmics.²

Potassium replacement is the mainstay of therapy in hypokalemia. It is indicated in patients with hypokalemia due to renal or gastrointestinal losses. It should also be considered when hypokalemia is due to redistribution of

potassium from the extracellular fluid into the cells (e.g. hypokalemic periodic paralysis, insulin therapy) and if serious complications such as paralysis, rhabdomyolysis, or arrhythmias are present or imminent.

The aetiology of hypokalemia should be identified as quickly as possible. Patients having hypokalemia with concurrent hypomagnesemia due to causes like diarrhea or diuretic therapy can be refractory to potassium replacement alone. Thus, measurement of serum magnesium should be considered in patients with hypokalemia, and, if present, hypomagnesemia should be addressed.

Potassium deficit

Estimation of potassium deficit assumes a normal distribution of potassium between the cells and extracellular fluid. The most common settings where this estimation does not apply are diabetic ketoacidosis, nonketotic hyperglycemia and redistributive causes of hypokalemia like hypokalemic periodic paralysis.

Potassium deficit varies proportionately with the severity of hypokalemia. In different studies, serum potassium concentration decreased by approximately 0.27 mEq/l for every 100 mEq decrease in total body potassium. In chronic hypokalemia, a potassium deficit of 200-400 mEq lowers the serum potassium concentration by 1.0 mEq/L.^{3,4,5} However, these estimates only approximate the amount of

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potassium replacement required to normalize the serum potassium concentration, and careful monitoring is needed.

Potassium preparations

Potassium can be administered as potassium phosphate, potassium chloride, potassium gluconate and potassium bicarbonate or its precursors (potassium citrate, potassium acetate). However, the choice among these preparations varies with the clinical setting.

Potassium chloride can be given both via oral as well as intravenous routes. Oral potassium chloride can be given as crystalline (salt substitutes), liquid formulations, or slow-release tablets/capsules. Intravenous potassium chloride is indicated in patients who cannot take oral therapy or as an adjunct to oral therapy in patients who have severe symptomatic hypokalemia.

Mild to moderate hypokalemia

Most hypokalemic patients have a serum potassium concentration of 3.0-3.4 mEq/L. This severity of hypokalemia usually does not produce any symptoms; however, exceptions include patients with heart disease or patients with cirrhosis for whom mild hypokalemia may lead to complications. Treatment of mild to moderate hypokalemia depends upon the underlying cause of the hypokalemia and acid-base status of the patient.

1. Patients with gastrointestinal causes are treated with potassium chloride if they have metabolic alkalosis (as usually seen with vomiting) or a normal serum bicarbonate concentration and with potassium bicarbonate (or potassium citrate or acetate) in the presence of metabolic acidosis (as seen with diarrhoea or renal tubular acidosis). Treatment is usually started with 10 to 20 mEq of potassium given two to four times/day (20 to 80 mEq/day), depending upon the severity of the hypokalemia.
2. In contrast, potassium replacement at usual doses produce only modest elevations in serum potassium in patients with hypokalemia secondary to renal potassium wasting (e.g., chronic diuretic therapy, primary aldosteronism). With the increase in serum potassium levels, there is less hypokalemia-induced potassium retention, and most of the administered potassium is excreted in the urine. Thus, a potassium-sparing diuretic is likely to be more effective.

Amiloride, a mineralocorticoid receptor antagonist, is usually better tolerated and preferred. Primary aldosteronism is an essential exception since spironolactone or eplerenone is chosen to block apparent adverse effects of excess aldosterone on the cardiovascular system.

Mild to moderate hypokalemia is typically treated with oral potassium supplementation. Patients who cannot take oral therapy require intravenous replacement, and serial monitoring of serum potassium is essential to determine the response.

Severe or symptomatic hypokalemia

In severe or symptomatic hypokalemia cases, potassium replacement needs to be rapid and monitored. Serum potassium concentration can transiently rise by 1 to 1.5 mEq/l after an oral dose of 40-60 mEq and by nearly 2.5-3.5 mEq/l after 135-160 mEq.^{6,7} However, serum potassium levels tend to fall back to baseline over a few hours, as most of the exogenous potassium is taken up by cells⁸. In severe hypokalemia, potassium chloride can be given orally in doses of 40 mEq, three to four times a day or, particularly in patients treated with intravenous potassium, 20 mEq every two to three hours.

Potassium supplements at usual doses produce only modest elevations in serum potassium in hypokalemia due to renal potassium wasting (e.g., chronic diuretic therapy, primary aldosteronism). Thus, a potassium-sparing diuretic is likely to be more effective.

Intravenous potassium replacement

Potassium chloride can be given intravenously as an adjunct to oral replacement in patients with severe symptomatic hypokalemia and in patients with less severe hypokalemia who cannot take oral medications. Potential concerns to intravenous therapy for severe hypokalemia include the risk of volume overload in susceptible patients and hyperkalemia due to excessive depletion. Saline rather than dextrose solution should be used for initial therapy. Although isotonic saline is often the initial replacement fluid used in treating diabetic ketoacidosis or nonketotic hyperglycemia, the addition of potassium makes it a hypertonic fluid, thereby delaying the reversal of the hyperosmolality. Thus, 40-60 mEq of potassium per litre in one-half isotonic saline is preferred.

In contrast to patients with marked potassium depletion, patients with hypokalemia due to potassium redistribution (e.g., hypokalemic periodic paralysis) have no potassium deficit. However, even low rates of potassium replacement can result in hyperkalemia once the redistributed potassium returns to the extracellular fluid.

The recommended approach for intravenous potassium chloride

For patients with severe hypokalemia due to gastrointestinal or renal losses, the recommended maximum rate of potassium administration is 10-20 mEq/hour in most patients. However, initial infusion rates as high as 40mEq/hr are used for life-threatening hypokalemia. Infusion rates of more than 20 mEq/hour irritate peripheral veins. Therefore, such higher rates of infusion should be given into a large central vein or multiple peripheral veins.

Potassium can be given intravenously via a peripheral or a large central vein (preferably femoral vein). The maximum amounts of potassium that should be added in an infusion container to decrease the risk of inadvertent administration of a large absolute amount of potassium are as follows 9,10:

- 10 mEq of potassium per 100 to 200 ml of non-dextrose fluid to be infused into a peripheral line.
- 40 mEq of potassium per 100 ml of non-dextrose fluid to be infused into a large central vein.

Intravenous potassium is most often infused in a peripheral vein at concentrations of 20-60 mEq/l in a non-dextrose-containing saline solution. Use of an infusion pump is preferred to prevent rapid potassium administration in any intravenous container with more than 40 mEq of potassium or if the desired rate of potassium administration is greater than 10 mEq/hour.

Adverse effects of intravenous potassium

Phlebitis and pain can occur with potassium infusion into a peripheral vein. This primarily occurs at rates >10 mEq/hour but can be seen at lower rates. Extravasation, a known complication of potassium infusions, is characterized by severe local pain that can progress to significant tissue necrosis.

Monitoring of severe hypokalemia

Monitoring for effects of severe hypokalemia like ECG abnormalities, muscle weakness, and paralysis is essential.

Continuous ECG monitoring is warranted in patients with arrhythmias caused by hypokalemia, prolonged QT and/or other ECG abnormalities attributable to hypokalemia, underlying cardiac issues that predispose to arrhythmia in the setting of hypokalemia (digoxin toxicity, myocardial infarction, underlying long QT syndrome), intravenous potassium infusion at a rate more than ten mEq/hour, and patients at risk of rebound hyperkalemia (as in thyrotoxic periodic paralysis). Hypokalemia once corrected to non-severe levels, the rate of intravenous potassium repletion should be reduced or changed to oral therapy.

Serum potassium should initially be measured every two to four hours to ascertain the response to therapy. If tolerated, this regimen should be continued until the serum potassium concentration is persistently above 3.0-3.5 mEq/L and features attributable to hypokalemia have resolved. After that, the dose and frequency of potassium replacement can be reduced to that used to treat mild to moderate hypokalemia.

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