

Hyperkalemia

Margaret Roberson, MD

Potassium is a major intracellular cation with only 2% found in the extracellular space. Ninety percent is intracellular and 8% can be found in bone and cartilage. Although only a small percent is extracellular, its flow is carefully regulated. Acid-base balance, insulin, hormones like aldosterone and catecholamines, and other factors moderate potassium. Metabolic acidosis leads to high potassium because the potassium exits the cell to provide a buffer for the hydrogen ion. Metabolic alkalosis has the opposite response with a fall in serum potassium, but to a lesser degree than seen in acidosis. In respiratory acidosis there is a loss of potassium as pCO₂ and serum bicarbonate rise. Respiratory alkalosis has little effect on potassium. Insulin enhances uptake by the cell and quickly reduces serum potassium. Lack of insulin, as in some forms of diabetes, can limit cell uptake especially if renal insufficiency is present. Because of hyperosmolarity, hyperglycemia will also shift potassium out of cells. The effect of catecholamine agonist and antagonists on potassium depends on the type of catecholamine. Beta agonists block potassium uptake while beta-adrenergic antagonists will increase uptake of potassium. The opposite response is seen with the alpha-adrenergic system.

In the balanced state, the kidneys provide the major mechanism for potassium excretion. The majority potassium regulation occurs in the distal kidney. Sodium concentration, urine flow and aldosterone combine to determine the amount of excreted potassium. In turn, the secretion of aldosterone by the adrenal cortex is determined by renin, angiotension II and presence of hyperkalemia.

The minimal dietary potassium requirement is 1600-2000 mg (40mg = 1mEq) per day. The amount in a daily diet varies according to a person's age, race and diet. Elderly patients tend to have a low potassium intake compared with teenagers. Patients who consume large amounts of fresh produce will have the highest level. Blacks tend to have lower potassium intake than urban whites.⁴

Causes of Hyperkalemia

By definition hyperkalemia is serum potassium > 5.5 milliequivalents per liter. Any level over 6 mEq/L can be life-threatening, depending on the clinical setting.¹⁻⁷ Pseudohyperkalemia may be seen following an artificial rise in potassium values due to potassium exiting from cells immediately before and after venipuncture. This can be occur with

hemolysis or prolonged use of a tourniquet. It can also be found when there is significant leukocytosis or thrombocytosis. Pseudohyperkalemia can be ruled out by checking a plasma as opposed to serum potassium level. The plasma level should be normal if pseudohyperkalemia is present.

True hyperkalemia may occur as a result of insufficient elimination, medications² or excess intake. Hyperkalemia due to inadequate removal of potassium may be viewed in several ways. In renal insufficiency, potassium filtration is decreased due to a reduction in the glomerular filtration rate (GFR). Hyporeninemic hypoaldosteronism is seen in mild renal insufficiency, diabetes and patients with chronic tubulointerstitial nephritis. The lack of aldosterone leads to hyperkalemia. Aldosterone synthesis is also decreased in primary adrenal disease or Addisons disease. This should be suspected if the sodium is low or if there are orthostatic blood pressure changes. Elevated potassium levels can occur due to renal tubules being unresponsive to aldosterone. Aldosterone levels will frequently be in the normal range. This is seen with sickle cell anemia, amyloidosis and renal transplantation.

Medications can affect potassium levels, especially if the patient has renal disease or hypoaldosteronism. The percent affected ranges from 1.3 – 10%. Medications that affect potassium can be separated into four groups:

- Potassium sparing diuretics
- Nonsteroidal anti-inflammatory agents (NSAIDs)
- ACE inhibitors
- Miscellaneous

Spirolactone is an aldosterone antagonist and competes with aldosterone for binding sites. Amiloride and triamterene work by diminishing the intracellular electrical gradient and decreasing sodium reabsorption and this decreases potassium secretion. ACE inhibitors (ACEI) block the conversion of angiotension I so that aldosterone is not released. About 10 % of out patients will develop hyperkalemia from ACEI. Angiotension II receptor antagonists compete for binding sites and decrease adrenal production of aldosterone. It is not clear is this is a clinically significant cause of elevated potassium. However caution should be used especially in high-risk patients receiving these medications.

Potassium levels need to be watched closely in patients with a decreased GFR such as diabetics or elderly patients especially if using ACEI or potassium sparing diuretics. Given the known benefits of ACEI in diabetics and in patients with proteinuria and renal insufficiency, the additional attention to laboratory monitoring is clearly justified. Patients should be educated about low potassium diets if their levels rise. If the potassium level cannot be controlled with dietary changes alone, Angiotension II receptor antagonists may be tried if the potassium level is below 6 mEq/L with close follow up.

NSAIDs will block production of renal prostaglandins. The prostaglandins stimulate renin production and thus aldosterone.

Miscellaneous medications include trimethoprim-sulfamethoxazole, pentamidine, heparin and succinylcholine. Succinylcholine can induce hyperkalemia when cell membranes are depolarized and the intracellular negative charge is reduced, thus causing potassium to exit. Trimethoprim-sulfamethoxazole and pentamidine's methods of action resemble amiloride. Patients being treated for *Pneumocystis carinii* should have potassium levels followed, especially if they have renal insufficiency. Nonselective beta-blockers may increase potassium by suppressing renin release and secondarily aldosterone. Beta-blockers also reduce the shift of potassium into cells. Heparin can also suppress aldosterone and lead to decreased elimination of potassium but to be clinically significant additional factors are usually necessary such as underlying kidney disease or use of ACEI. Salt substitutes have a significant amount of potassium up to 10 – 13mEq/g and low sodium canned food may also lead to high potassium since NaCl is replaced by KCl. Finally nutrient supplements and herbal juices can also be a silent source of potassium. When evaluating patients for hyperkalemia all sources of potassium should be evaluated including parenteral nutrition, potassium salts, and intravenous fluids.

Patients can also receive a potassium load from tissue breakdown, dietary noncompliance in renal patients or intracellular potassium shifts. Tumor lysis syndrome or rhabdomyolysis can provide a high potassium load. As long as urine output is adequate and renal function is preserved, hyperkalemia usually does not occur. Exercise and trauma can lead to high potassium due to release of potassium from tissue. Shifts of potassium can also be found in acidosis or digoxin toxicity. Hemolysis is

another source of potassium and in significant hemolysis acute renal failure can develop further decreasing the excretion of potassium. Red cell transfusions using older units of blood can be a significant load of potassium. This is usually only significant with a decrease in renal function. However, transfusion on hemodialysis does not require "fresh" units as was once thought to be necessary for patients with end-stage renal disease.

Effects of Hyperkalemia

Potassium's effect of skeletal and cardiac tissue leads to its toxicity. Potassium is a significant factor in determining the transmembrane potential. The action potential is decreased due to increased repolarization. The resting membrane potential and threshold potential become less negative thus depolarization is more likely. As depolarization continues sodium becomes less permeable and the sodium influx slows and excitability is decreased. Hyperkalemia should be considered in chronic renal insufficiency patients with complaints of muscle weakness.

Cardiac disturbances include sinus bradycardia, slow idioventricular rhythm, ventricular tachycardia, ventricular fibrillation, and asystole. The EKG changes seen include peaked T waves³, prolongation of PR interval, second-degree AV block, loss of p waves and intraventricular conduction defects. Lastly T wave and widened QRS complexes form a "sine-wave" pattern that can precede asystole. EKG changes however do not develop in a characteristic pattern. Clinically significant arrhythmias including ventricular arrhythmias can occur at any time. The EKG is an insensitive test to identify hyperkalemia.

Treatment of Hyperkalemia

Urgent treatment is indicated for any patient with EKG changes and any patient with a potassium greater than 6 mEq/L. Treatment focuses on three areas:

1. Antagonizing the effect of potassium on the cell membrane
2. Rapidly forcing potassium into the cell
3. Eliminating it from the body

Calcium works in minutes to antagonize potassium effect on membranes and reverse EKG changes. It will last 30 – 60 minutes. Calcium gluconate or calcium chloride can be used. Calcium is sclerosing on the vessels and can lead to skin necrosis if it extravasates.

If a peripheral line is used, then calcium gluconate should be chosen. If calcium is given through a central line, either form is acceptable. Since the majority of potassium is intracellular, shifting a small amount will cause a significant clinical effect and have little effect on the intracellular concentration. Insulin and glucose will decrease potassium 0.6 to 1.0 mEq/L. The insulin moves glucose into cells and potassium follows. Do not give glucose alone as hyperosmolarity can shift potassium out of cells. Ten units of insulin intravenously is given with 50 cc of 50% Dextrose. Careful attention should be paid to the blood sugar since patients may develop hypoglycemia. In hyperglycemic patients, insulin alone may be sufficient. Bicarbonate can be used but is unreliable and is more helpful to correct accompanying acidosis. Albuterol can be used to shift potassium into cells but cardiac effects limit the use. These measures will help to stabilize the patient but elimination of the excess potassium is needed.

A renal consultant should be called early into treatment especially in patients with renal insufficiency. Dialysis will cause a fall in intracellular and extracellular levels. The potassium levels tend to rebound after dialysis. Do not immediately repeat potassium levels after dialysis. Nephrologists may check this level to be certain that the potassium is down. If post dialysis potassium is below 3.5 do not treat as levels tend to rebound. A potassium level drawn several hours after hemodialysis is reliable.

Exchange resins such as sodium polystyrene sulfonate (Kayexalate) binds gut cations in exchange for sodium. In order to eliminate potassium from the body it should be given with a laxative such as sorbitol. Oral Kayexalate tends to be more effective than enemas. Enemas should be avoided due to the risk of rectal perforation. Kayexalate should be used with caution in patients with CHF due to the sodium load.

Summary

When a patient presents with hyperkalemia it may be clinically silent or explosive. Regardless careful attention should be paid to a thorough evaluation of the patient. In particular the clinician needs to determine the etiology of the hyperkalemia and review all medications and nutritional supplements. An EKG should be reviewed and treatment begun to correct the potassium level and prevent recurrence.

References

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