SHAHEED RAJAIE
CARDIOVASCULAR, MEDICAL & RESEARCH CENTER

HYPERKALEMIA

Zohreh Morshedizad

Shaheed Rajaie Cardiovascular, Medical & Research Center

zmorshedizad@gmail.com

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Overview

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CAUSES OF HYPERKALEMIA

Hyperkalemia is caused by excess potassium intake, impaired potassium excretion, or transcellular shifts . The etiology of hyperkalemia is often multifactorial, with impaired renal function, medication use, and hyperglycemia as the most common contributors. Because healthy individuals can adapt to excess potassium consumption by increasing excretion, increased potassium intake is rarely the sole cause of hyperkalemia, and underlying renal dysfunction is common.

IMPAIRED POTASSIUM EXCRETION

Renally mediated hyperkalemia results from derangement of one or more of the following processes: rate of flow in the distal nephron, aldosterone secretion and its effects, and functioning potassium secretory pathways. Hyperkalemia secondary to decreased distal delivery of sodium and water occurs with congestive heart failure, cirrhosis, acute kidney injury, and advanced chronic kidney disease. Conditions that cause hypoaldosteronism, such as adrenal insufficiency and hyporeninemic hypoaldosteronism (a common complication of diabetic nephropathy and tubulointerstitial diseases), can lead to hyperkalemia.

TRANSCELLULAR SHIFTS

Various mechanisms promote the exit of potassium from cells or impede its entrance, thereby raising the plasma potassium concentration (redistributive hyperkalemia). Increased plasma osmolality, such as with uncontrolled diabetes mellitus, establishes a concentration gradient wherein potassium follows water out of cells. Relative insulin deficiency or insulin resistance, which also occurs in persons with diabetes, prevents potassium from entering cells. In response to acidosis, extracellular hydrogen is exchanged for intracellular potassium, although the net result is highly variable and depends in part on the type of acidosis; metabolic acidosis produces the greatest effect. Because 98% of total body potassium is intracellular, any process that increases cell turnover, such as rhabdomyolysis, tumor lysis syndrome, or red blood cell transfusions, can result in hyperkalemia.

MEDICATION-INDUCED HYPERKALEMIA

Medication use is a common cause of hyperkalemia, particularly in patients with baseline renal dysfunction or hypoaldosteronism. Medication-induced hyperkalemia is most often a result of the medication interfering with potassium excretion. Also, the administration of potassium to treat or prevent hypokalemia can inadvertently cause hyperkalemia. ACE inhibitors contributed to one-half of all cases of drug-induced hyperkalemia in one sample, and approximately 10% of outpatients who start an ACE inhibitor or an ARB will develop hyperkalemia within one year.

The incidence of hyperkalemia associated with use of potassium-sparing diuretics has risen since adding spironolactone to standard therapy was shown to reduce morbidity and mortality in patients with congestive heart failure. Dual treatment with an ACE inhibitor and an ARB increases the risk of harmful adverse effects, including hyperkalemia, and should be avoided. Other commonly used medications known to cause hyperkalemia include trimethoprim, heparin, beta blockers, digoxin, and nonsteroidal anti-inflammatory drugs.

EVALUATION AND MANAGEMENT

GENERAL PRINCIPLES

As with hypokalemia, the immediate danger of hyperkalemia is its effect on cardiac conduction and muscle strength, and initial efforts should focus on determining the need for urgent intervention. The absence of symptoms does not exclude severe hyperkalemia, because hyperkalemia is often asymptomatic. Because of their increased risk of developing hyperkalemia, patients with underlying renal dysfunction merit special attention.

HISTORY AND PHYSICAL EXAMINATION

Severe hyperkalemia (more than 6.5 mEq per L [6.5 mmol per L]) can cause muscle weakness, ascending paralysis, heart palpitations, and paresthesias. Chronic kidney disease, diabetes, heart failure, and liver disease all increase the risk of hyperkalemia. Clinicians should review patients' medications to identify those known to cause hyperkalemia, and ask patients about the use of salt substitutes that contain potassium. The physical examination should include assessment of blood pressure and intravascular volume status to identify potential causes of kidney hypoperfusion, which can lead to hyperkalemia. Neurologic signs of hypokalemia include generalized weakness and decreased deep tendon reflexes.

LABORATORY ANALYSIS AND ECG

Repeat measurement of serum potassium can help identify pseudohyperkalemia, which is common and typically results from potassium moving out of cells during or after sample collection. Other laboratory studies include measurement of serum blood urea nitrogen and creatinine, measurement of urine electrolytes and creatinine, and assessment of acid-base status. Further evaluation may include measurement of serum glucose to evaluate for hyperglycemia, and measurement of serum renin, aldosterone, and cortisol to further investigate kidney and adrenal function.

ECG should be considered if the potassium level is greater than 6 mEq per L; if there are symptoms of hyperkalemia; if there is suspicion of rapid-onset hyperkalemia; or among patients with underlying kidney disease, heart disease, or cirrhosis who have a new case of hyperkalemia. Findings on ECG are neither sensitive nor specific for hyperkalemia. Therefore, although ECG changes should trigger urgent treatment, treatment decisions should not be based solely on the presence or absence of ECG changes. Peaked T waves are the prototypical, and generally the earliest, ECG sign of hyperkalemia. Other ECG changes include P-wave flattening, PR-interval prolongation, widening of the QRS complex, and sine waves. Hyperkalemia-induced arrhythmias include sinus bradycardia, sinus arrest, ventricular tachycardia, ventricular fibrillation, and asystole.

TREATMENT OF HYPERKALEMIA

The goals of acute treatment are to prevent potentially life-threatening cardiac conduction and neuromuscular disturbances, shift potassium into cells, eliminate excess potassium, and resolve the underlying disturbance. Patients with chronic hyperkalemia should be counseled to reduce dietary potassium. Although redistributive hyperkalemia is uncommon, a cautious approach is warranted because treatment may not involve attempts to eliminate potassium, and correction of the underlying problem can provoke rebound hypokalemia. Indications for prompt intervention are symptoms of hyperkalemia, changes on ECG, severe hyperkalemia (greater than 6.5 mEq per L), rapidonset hyperkalemia, or underlying heart disease, cirrhosis, or kidney disease.

URGENT TREATMENT

Intravenous Calcium. Intravenous calcium, which helps prevent life-threatening conduction disturbances by stabilizing the cardiac muscle cell membrane, should be administered if ECG changes are present. Intravenous calcium has no effect on plasma potassium concentration. If after five minutes, follow-up ECG continues to show signs of hyperkalemia, the dose should be repeated.37 Clinicians should be aware that intravenous calcium has a short duration, ranging from 30 to 60 minutes.

Insulin and Glucose. The most reliable method for shifting potassium intracellularly is administration of glucose and insulin. Typically, 10 units of insulin are administered, followed by 25 g of glucose to prevent hypoglycemia. Because hypoglycemia is a common adverse effect even with the provision of glucose, serum glucose levels should be monitored regularly. Patients with a serum glucose level of more than 250 mg per dL (13.9 mmol per L) typically do not require coadministration of glucose.

Inhaled Beta Agonists. Albuterol, a beta2 agonist, is an underutilized adjuvant for shifting potassium intracellularly. All forms of administration (i.e., inhaled, nebulized, and intravenous where available) are effective. It should be noted that the recommended dose of nebulized albuterol (10 to 20 mg) is four to eight times greater than the typical respiratory dose. There is an additive effect when albuterol is combined with insulin. Albuterol's potassium-lowering effect is mitigated in some patients, particularly those with end-stage kidney disease; therefore, albuterol should not be used as monotherapy.

Sodium Bicarbonate. Although sodium bicarbonate is often used to treat hyperkalemia, the evidence to support this use is equivocal, showing minimal to no benefit. Therefore, sodium bicarbonate should not be used as monotherapy. It may have a role as adjuvant therapy, particularly among patients with concurrent metabolic acidosis.

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Hyperkalemia is defined as a serum potassium level which exceeds the normal blood potassium level of 5.5 mEq/L. Excessive administration of potassium enriched cardioplegic solutions is one of the causes for hyperkalemia during CPB. One of the most common causes of hyperkalemia is poor kidney function. Kidneys are responsible for measured serum potassium levels and removing excess amounts. When the kidneys are dysfunctional or not functioning well, it will lead to high levels of K+.

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Hyperkalemia can also occur with the use of older units of blood or packed cells, and in patients with uncontrolled diabetes. Aged blood products lead to hyperkalemia with longer periods of storage, K+ leaks into the supernatant as a result of fracture red blood cell membranes from aging and decreased synthesis of adenosine triphosphate (ATP). The magnitude of this leak increases with duration of storage. Irradiation of blood to inactivate T-lymphocytes and minimize the risk for graft vs. host disease enhances K+ leakage from red cells as a result of subtle membrane injury.

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Depending on the conditions, the supernatant of stored red blood cell units may contain greater than 60 mEq/L K+. When fresh PRBCs are unavailable, the risk for post -transfusion hyperkalemia can be minimized by washing the cells and decreasing the amount of additive solution. In addition, uncontrolled diabetes will cause hyperkalemia because diabetic patients lack the insulin required to breakdown the excess glucose in the blood.

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High glucose levels affect the body negatively in two ways. The lack of insulin facilitates the breakdown of fat cells releasing ketones into the blood, making it acidic (ketoacidosis). The ketoacidosis coupled with high glucose blood levels cause potassium to shift out of the cells into the extracellular space. High glucose levels also hinder the kidneys ability to excrete potassium in the urine. Potassium being forced out of the cells and the kidneys not removing the excess potassium via urine leads to hyperkalemia.

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Prevention is first step in making sure hyperkalemia does not occur on CPB. Maintaining renal function on CPB, being attentive during cardioplegia delivery, giving fresh blood when possible or using a cell washers to wash cells, and making sure a diabetic patient is properly medicated before surgery are all preventative measures that should always be taken. These preventative measures are helpful but it cannot always prevent hyperkalemia from occurring and treatment needs to be initiated. Pharmacological treatment is usually the first step taken to correct hyperkalemia. Normal pharmacological treatment of hyperkalemia is as follows:

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1. 20 units of insulin which is used to drive the potassium into the cell, thus insulating the myocardium from high potassium levels, and 25 g of dextrose or glucose to replace the glucose driven off with administration of insulin. The glucose will further promote the movement of K+ from extracellular to intracellular compartments.

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2. 500 mg to 1 g of calcium chloride which is used to activate the receptor sites of the potassium pumps on the cell membranes and to replace the serum calcium which will be driven into the cell upon administration of insulin.

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3. 50 mEq sodium bicarbonate which will provide intracellular binding sites for the potassium in the form of potassium carbonate. This will correct the acidosis resulting from the shift of hydrogen ions from inside the cell to the extracellular space as electrical equilibrium is maintained. When pharmacological treatment fails during CPB, alternatives such as zero-balance ultrafiltration (ZBUF) can be used. The following is a case report that shows the successful treatment of hyperkalemia during CPB, after failed pharmacological treatment, with the use of Z-BUF.

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