EDUCATIONAL COMMENTARY – INTERPRETATION OF POTASSIUM RESULTS

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Learning Outcomes

Upon completion of this exercise, participants will be able to:

- list and discuss the symptoms of hypokalemia and hyperkalemia.
- list and discuss causes of hypokalemia and hyperkalemia.
- define and list causes of pseudohyperkalemia.

Potassium

Potassium, a positively charged electrolyte, is involved in regulating fluids, maintaining acid-base balance, and proper functioning of nerve and muscle cells. Although potassium is present in all body fluids, the highest concentration is in cells. Only 2% of total body potassium is found in plasma, and the erythrocyte potassium concentration is approximately 23 times higher than the plasma concentration. Although reference intervals may be laboratory-dependent, typical adult ranges have lower limits of 3.5 to 4.0 mEq/L (3.5-4.0 mmol/L) and upper limits of 5.0 to 5.3 mEq/L (5.0-5.3 mmol/L). With such a small plasma concentration and narrow reference interval, minor changes in potassium can have significant consequences. Laboratory measurement of potassium blood levels is essential for the differential diagnosis of potassium disorders because the symptoms of hypokalemia (decreased potassium in blood) and hyperkalemia (increased potassium in blood) are fairly similar and nonspecific.

Hypokalemia

Symptoms of hypokalemia include muscle fatigue, weakness, muscle cramps, paralysis, constipation, and potentially life-threatening arrhythmias. Although there are many causes of hypokalemia the most common are vomiting, diarrhea, or dehydration. Excess urinary excretion of potassium due to use of diuretics may also cause hypokalemia. The adrenal hormone, aldosterone, is essential for renal sodium retention and potassium excretion, and conditions resulting in hyperaldosteronism such as Cushing syndrome can cause hypokalemia. Diabetics may experience hypokalemia following insulin injection particularly if the diabetes had been out of control. Drugs shown to have caused hypokalemia include corticosteroids, beta-adrenergic agonists (such as isoproterenol), alpha-adrenergic antagonists (such as clonidine), antibiotics (such as gentamicin and carbenicillin), and the antifungal agent amphotericin B.

Hyperkalemia

Symptoms of hyperkalemia include muscle fatigue, weakness, paralysis, nausea, changes in breathing pattern, and potentially life-threatening arrhythmias. The kidneys regulate excretion of potassium, and the most common cause of hyperkalemia is impaired renal function caused by disorders such as acute or chronic kidney failure, glomerulonephritis, lupus nephritis, obstructive uropathy, or rejection of a kidney
transplant. Conditions resulting in hypoaldosteronism such as adrenal insufficiency or Addison disease can cause hyperkalemia. Other causes of hyperkalemia include excessive use of potassium supplements, excessive dietary intake, acidosis including diabetic ketoacidosis, and injury to tissue resulting from surgery, burns, gastrointestinal bleeding, and drug- or infection-induced rhabdomyolysis. Drugs that have been shown to cause hyperkalemia include potassium-sparing diuretics (such as triamterene, amiloride, and spironolactone), beta blockers (such as propanolol and atenolol), angiotensin-converting enzyme inhibitors (such as captopril, enalapril, and lisinopril), and nonsteroidal anti-inflammatory drugs containing ibuprofen.

Pseudohyperkalemia

Pseudohyperkalemia occurs when the potassium reported by the laboratory does not reflect the true physiological potassium concentration. This can not only cause a misdiagnosis of hyperkalemia in a patient with a normal potassium level but could mask hypokalemia if it increases the level into the normal range. The Table summarizes many of the causes of pseudohyperkalemia. Most instances of pseudohyperkalemia are due to preanalytical collection and processing conditions. One exception is use of an improper reference range. Serum potassium concentrations are approximately 0.4 mEq/L (0.4 mmol/L) higher than plasma ranges, presumably due to release of potassium during the clotting process. Therefore, use of the plasma reference range for a serum sample could result in pseudohyperkalemia.

TABLE. Causes of Falsely Elevated Potassium Levels (Pseudohyperkalemia).

| Inappropriate reference range (plasma/serum) | Elevated platelet count (>700,000/µL) |
| Elevated WBC count (>100,000/µL) | Fist clenching during collection |
| Incorrect order of collection tubes | Prolonged contact of serum with clot |
| Hemolysis induced during collection/processing | Improper use of gel-separator tubes |
| Crying and/or hyperventilation during collection* | Surfactant contamination from catheters |

* May also cause decreased potassium depending on duration.

Consideration of preanalytical causes of pseudohyperkalemia begins with the collection procedure. Any collection condition resulting in hemolysis due to rupture of RBCs and subsequent release of potassium results in pseudohyperkalemia. The most common cause of hemolysis during specimen collection is mechanical rupture of RBCs caused by actions such as use of excessive syringe suction, forcibly squirting blood from syringe to tube, drawing blood through a small needle or catheter (hemolysis rate is inversely proportional to the diameter), drawing through multiple devices with mismatched diameters, and inverting or mixing the tube too vigorously. Actions during the venipuncture may also cause pseudohyperkalemia. Fist clenching or pumping during the collection has been proven to result in increased potassium levels and this procedure should be avoided. Crying and hyperventilation can initially cause increased plasma potassium but this is followed by a decrease in potassium due to hydrogen/potassium exchange after about 30 minutes of hyperventilation. Incorrect order of collection tubes during specimen collection can result in falsely elevated potassium if blood from an EDTA tube (containing potassium) carries over into the serum or plasma tube used for potassium analysis. The recommended order of tube drawing is: blood culture tubes, sodium
citrate (blue stopper), serum or gel-separator tube (red, speckled, Tiger), heparin (green stopper), EDTA (lavender stopper), and NaF (gray stopper).

Pseudohyperkalemia is known to occur in conditions characterized by elevated platelets or WBCs, presumably due to release of potassium during the clotting process. Similarly prolonged contact of serum with clotted RBCs facilitates release of potassium from the cells. In this instance potassium release may be accompanied by a decrease in glucose due to cellular uptake. If multiple serum samples collected and/or processed at one location exhibit characteristics of increased serum potassium and decreased glucose, the laboratory professional should suspect prolonged clot contact. After collection the minimum time for adequate clot formation is 20 to 30 minutes and the maximum time between collection and separation of clot and serum is two hours. Refrigeration actually accelerates potassium release from the cells, so samples should be stored at ambient temperature between collection and centrifugation. Improper centrifugation of tubes containing gel barriers may result in increased potassium results. Manufacturer’s centrifugation instructions should be followed in order to obtain the correct relative centrifugal force and ensure proper barrier formation. Swinging head centrifuges generally cause formation of barriers with more uniform gel thickness compared with those of fixed-angle centrifuges. Re-spinning gel-separator tubes a second time to obtain more serum or plasma should be avoided, particularly if it has been >2 hours since collection.

One cause of pseudohyperkalemia can occur in the analytical phase of the testing cycle. The surfactant benzalkonium chloride coating vascular catheters often used in critical care areas interferes with ion-specific electrodes that require predilution of the sample prior to measurement. Flushing the catheter with approximately 10 mL of blood prior to the draw eliminates the interference. No such interference occurs with electrodes that measure potassium from whole blood or undiluted plasma.

Summary and Conclusions
Laboratory measurement of blood potassium levels is essential for the diagnosis of hypokalemia and hyperkalemia, conditions characterized by similar symptoms. Both hypokalemia and hyperkalemia have multiple causes, including renal or adrenal dysfunction and drugs. Improper sample collection or processing can cause pseudohyperkalemia or falsely elevated potassium results.

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