

Case: You are called on cross-cover to evaluate a 47 year old man. The laboratory has called to alert you of a K^+ of 6.3.

What do you want to do first?

What diagnostics are in order?

What underlying conditions might predispose him to hyperkalemia?

What will your orders be and how will you follow him?

Hyperkalemia

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Demographics

In the hospitalized patient, reported incidence varies between 1.4 and 10%. The vast majority of cases are related to pre-existing or new renal insufficiency or failure. Most other cases are related to K^+ supplementation and K^+ -sparing diuretics.

Etiologies

1. Transcellular shift

- Acidosis *
- Insulin deficiency due to fasting or DM
- Hypoadrenergic state (beta blockers, peripheral neuropathy), Hyperosmolarity (hyperglycemia, mannitol)
- Drugs (beta blockers - rarely cause hyperkalemia alone, in absence of another cause, hypertonic solutions, succinylcholine, arginine, digitalis)
- Hyperkalemia periodic paralysis

2. Renal causes

- Decreased GFR *
- Addison's disease
- Hypoaldosteronism/pseudohypoaldosteronism
- Hyperkalemic renal tubular acidosis (Type IV) *
- Defects in renal K^+ secretion
- Tubulointerstitial disease
- Drugs that interfere with K^+ excretion (amiloride, triamterene, spironolactone, cyclosporine, trimethoprim - more common at higher IV doses, pentamidine, lithium, tacrolimus, mitomycin C) *
- Drugs that interfere with renin-angiotensin system (ACE inhibitors, ARBs, NSAIDs, heparin) *

(* = most common)

SIDE NOTE: We often wonder how high the K^+ should get before stopping or withholding ACE inhibitor therapy. One author recommends 5.5. You can use loop diuretics or low potassium diet in attempts to control the potassium level.

3. Increased circulating potassium - exogenous or endogenous

- Exogenous (K^+ supplementation, salt substitute, potassium penicillin, e.g. ticarcillin-clavulanic acid, penicillin G)
- Endogenous (tumor-lysis syndrome, drug-induced hemolysis, rhabdomyolysis/trauma, cellular necrosis, active GI bleeding (pathogenesis unclear))

Initial questions

1. **Is hyperkalemia really present?** Always assume that an elevated K^+ is real and check an EKG, but repeat test to verify. Causes of *pseudohyperkalemia* include: hemolysis from lab mishandling or prolonged tourniquet time, leukocytosis ($>70K$) or thrombocytosis ($>1M$) - K^+ is released from WBCs and platelets after they have formed clots - or abnormal K^+ permeability of RBCs (familial, cold agglutinins, infectious mono). By contrast, hyperkalemia is usually real in renal failure.
2. **Is there an emergency related to hyperkalemia?** Any value over 6 OR hyperkalemia in the setting of EKG changes (see below) require urgent management.
3. **Did this hyperkalemia develop acutely?** Acute changes are more strongly associated with development of cardiac conduction disturbances.
4. **What is the cause?** Often obtainable from history. In situations where no obvious cause is identified, you can be aided by use of the *transtubular K^+ gradient* (although rarely used on the wards and not useful acutely):
 - Divide the ratio of urinary K^+ to serum K^+ by the ratio of urinary osmolality to serum osmolality.
 - A value of >5 indicates a non-renal cause for hyperkalemia (i.e. increased intake or cellular shift)
 - The formula is unreliable in very dilute urine or urine with little sodium.

Questions to ask upon assessing the patient

1. **What is the patient's medical history and what medications has he or she been given?**
Often, your cause will be obvious after this step.

2. **Is the patient having any symptoms/physical exam findings?** These may include fatigue, weakness, palpitations, paresthesias, muscular weakness, flaccid paralysis (usually when $K^+ >7.5$). Severe symptoms often do not occur until level is >7 .

3. **Are there EKG abnormalities?** The EKG does not always demonstrate findings even in the presence of high K^+ , so a normal reading does not obviate the need for therapy. However, the presence of findings should be a strong impetus for urgent action. These findings may include: *peaked T waves, decreased or absent P waves, PR prolongation, QRS widening, sine wave or asystole*. May also present as *bradycardia* and *AV block*.

Management

1. **Protect the cardiac membrane.** Give *calcium gluconate* (1-2 amps of 10% solution IV). Calcium chloride is more damaging to tissue in extravasation. Give calcium regardless of the serum calcium level. EKG improvement should be seen within the first 1-3 minutes, and if not, can redose after five minutes. The effect should last $\frac{1}{2}$ -1 hour. **NOTE: if the patient is on digoxin, should give calcium SLOWLY over 20-30 minutes mixed in 100ml of D5W, as Ca^{2+} can precipitate myocardial digoxin toxicity.**

2. **Shift the potassium from the blood into the cell.**

Insulin. 10 U of regular insulin IV with 1 amp of D50 (DO NOT give D50 if the patient already has a glucose >250). This should work within <20 minutes and lasts 4-6 hours. Giving the dextrose 5 minutes before the insulin may prevent hypoglycemia, but will take longer. Follow chemsticks frequently.

Beta adrenergic therapies. *Nebulized albuterol* (standard dose) may work within 30 minutes, but many patients are on beta blockers which will antagonize its effects and other patients (40% of patients on dialysis, in one study) may be resistant in the absence of these agents. Not recommended as a single agent, but may be used additively (albuterol plus insulin and dextrose causes less hypoglycemia)

Bicarbonate. Previously used frequently, but now falling out of favor. Multiple studies have demonstrated failure to lower K^+ in dialysis patients. May also cause volume and sodium overload, hypertension and CHF, particularly in oliguric ESRD patients.

The interventions cited above can be repeated multiple times if the K^+ remains elevated while you pursue other measures

3. Remove potassium from the body. Three options:

Use the kidneys. Loop diuretics (particularly furosemide 40-80mg IV) increase urine flow Na^+ delivery to the distal nephron, thereby increasing K^+ excretion. Not as useful in patients with renal failure, acute OR chronic.

Use the gut. Kayexalate releases sodium in the gut, and in doing so, binds K^+ . Can be given PO (15g qid) or in an enema (30-60g PR q6H). Oral dosing works slowly (4-6 hours), and other measures should be employed in the meantime. Technically, there is no maximum dose of Kayexalate, but it removes 0.5-1 mmol of K^+ by substituting 203 mmol of Na^+ → this can result in issues with hypervolemia.

Use dialysis. Most effective and definitive, but invasive and not without risks. Use if hyperkalemia is severe (level debated, >6.5) and other first-line agents have been unsuccessful, or if there is ongoing tissue damage and you expect there will be continued release of intracellular potassium. A 2-3 hour run is necessary. Enlist the help of nephrology early if you think your patient is headed this way.

4. As always, treat the underlying cause.

Case follow-up. You ask them to repeat the sample, but in the meantime, you check an EKG, which is normal. You also give calcium gluconate. On your review of the patient's chart, you find that he was admitted for elective ankle surgery. None of his previous K^+ levels have been elevated. He is without symptoms. Interestingly, the repeat value is 4.5; it is determined that the specimen was mislabeled.

Clinical pearls.

1. Always repeat the test if it is inconsistent with previous values.
2. The EKG can be negative in the setting of hyperkalemia, and a negative EKG does not negate the need for calcium and maneuvers such as insulin/dextrose.
3. Don't forget about Kayexalate enemas.
4. Do not give D50 with insulin if glucose is over 250.
5. Calcium and insulin are not definitive therapies; they simply buy you time. Kayexalate, diuretics and dialysis are the only ways to remove potassium from the body.
6. Don't forget to turn off K^+ -containing fluids!

References

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