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PATIENT SAFETY NETWORK

Too Much, Too Fast

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The Case

A 68-year-old man with amyotrophic lateral sclerosis (ALS) was admitted to the intensive care unit (ICU) for fever, tachycardia, and increased respiratory secretions. His ALS was complicated by ventilator-dependence requiring a tracheostomy, along with comorbidities that included coronary artery disease and a prior bypass graft, insulin-dependent diabetes, hypertension, and hyperlipidemia. Initial physical examination and laboratory studies were suggestive of pneumonia with sepsis and poorly controlled hyperglycemia. His electrolytes were notable for sodium of 150 mEq/L, potassium of 3.7 mEq/L, and glucose of 421 mg/dL. He was treated with broad-spectrum antibiotics and fluid resuscitation while also being placed on an insulin infusion for his hyperglycemia.

Over the first few hours of hospitalization, his hemodynamics and glycemic control markedly improved. A repeat potassium level returned low at 2.7 mEq/L. Providers ordered 120 mEq of oral potassium replacement via a feeding tube and 60 mEq of intravenous potassium via a central line at 20 mEq/hour. While on the third bag of the potassium infusion, the patient went into cardiac arrest and advanced cardiovascular life support measures were delivered. Point-of-care testing showed potassium was critically elevated at greater than 9.0 mEq/L. Despite efforts to aggressively treat the hyperkalemia, resuscitation attempts were unsuccessful.

The Commentary

Potassium is integral to maintaining cellular function. As this case highlights, a thoughtful understanding of how our body manages potassium homeostasis can help providers avoid preventable adverse outcomes, some of which can be fatal.

All cells in the body have a sodium-potassium adenosine triphosphatase (Na-K ATPase), which pumps sodium out of the cell and potassium into the cell, creating a K+ gradient across cell membranes ($K+_{in} > K+_{out}$). This chemical gradient is critical for the function of excitable tissues such as nerve and muscle. Hence, the body has developed numerous mechanisms to prevent hyperkalemia and maintain 90% of total body potassium within cells.

The kidney is primarily responsible for maintaining total body potassium, matching K+ excretion with intake. Adjustments in renal potassium excretion occur over several hours. While renal handling of potassium is complex, the main determinants of K+ secretion include: mineralocorticoid activity, acidosis, urinary flow rate, and distal tubular delivery of Na+/water. The magnitude of each of these mechanisms depends on nephron mass and renal function. Acutely, changes in extracellular potassium concentration are mediated by movement of K+ into and out of skeletal muscle. Insulin, catecholamines, and acidosis are the most important factors regulating this movement under normal conditions. Through different mechanisms, insulin and beta-2 adrenergic stimulants increase Na-K APTase activity, which shifts K+ into cells. Acidosis, by contrast, leads to an increase in intracellular hydrogen ions, thereby leading to potassium efflux and hyperkalemia.(1)

Despite this elegant system to maintain potassium homeostasis both acutely and chronically, disorders of potassium balance are quite frequent among hospitalized patients. Hypokalemia, defined as a serum K+ concentration less than 3.6 mEq/L, has an estimated prevalence as high as 20%.(2) Hyperkalemia, defined as a serum K+ greater than 5.0 mEq/L, is less common, with a reported incidence among hospitalized patients ranging from 1.1%–10%.(3) Among hospitalized patients, certain conditions and medications can predispose to impairments of renal potassium excretion as well as skeletal muscle buffering. Impairment in renal function secondary to acute kidney injury or chronic kidney disease can decrease renal excretion of potassium, leading to hyperkalemia. Although clinicians typically use the serum creatinine level to estimate kidney function, there is a substantial misclassification, particularly in individuals with extremes of muscle mass. Estimated glomerular filtration rate (eGFR) by the four-variable MDRD [Modification of Diet in Renal Disease] equation, based on gender, race, age, and serum creatinine, is a more accurate estimation of kidney impairment, but still overestimates renal function among individuals with amputations or dystrophic muscular disorders. In these circumstances, it is important to recognize that a "normal" serum creatinine or eGFR overestimates the kidney's ability to excrete potassium.

Hospitalized patients may also experience difficulty acutely dealing with a potassium load. For example, such patients are often malnourished and have chronically low total body potassium stores. This depletion leads to low levels of Na-K ATPase expression, which in turn decreases the body's ability to shift potassium into cells when the need arises. Hypomagnasemia, also common among hospitalized patients, impairs cellular potassium intake as well. Commonly used medications can also predispose to hyperkalemia. Beta-blockers and digitalis directly decrease cellular intake of potassium and nonsteroidal anti-inflammatory medications, angiotensin converting enzyme inhibitors, trimethoprim, and heparin diminish mineralocorticoid activity. Disorders of skeletal muscle, such as amyotrophic lateral sclerosis, alter membrane potassium channels, which may impair the body's buffering capacity to prevent hyperkalemia.(4) Exacerbating these physiologic effects are the hidden sources of potassium among hospitalized patients. As an example, potassium is often added to large intravenous (IV) fluid solutions, where it can easily be overlooked as a source of potassium intake.

It is important to keep these factors in mind when repleting potassium levels, as the most common cause of hyperkalemia among hospitalized patients is physician-ordered K+ supplementation.(5) Electrolytes, including but not limited to potassium, have been implicated in up to 3.5% of preventable adverse events or medication errors in hospitalized patients.(6) Injectable potassium products are considered among the top five high-alert medications identified by the Institute for Safe Medication Practices.(7)

Despite the well-recognized safety issues associated with potassium repletion, institutional practices and potassium repletion protocols have not been widely studied.(8) Nonetheless, principles and guidelines for K+ repletion do exist for individuals with normal renal and muscular function (Table).(9,10) They generally recommend repletion with oral potassium chloride for mild–moderate hypokalemia (K+ 3.1–3.5 mEq/L) and IV repletion via central line with cardiac monitoring for hospitalized patients with severe hypokalemia (K+

In the absence of a cardiovascular emergency, the guidelines emphasize slow repletion with frequent monitoring, (i.e., after administration of 60 mEq of potassium chloride), to ensure appropriate cellular uptake and avoidance of hyperkalemia. As this case illustrates, rapid administration of potassium can be dangerous, even among patients with severe hypokalemia. Administration of 80 mEq/h, for example, has been associated with electrocardiogram changes and complete heart block.(11) Despite these guidelines, however, physicians are often quite aggressive with potassium repletion. One 2003 study in an academic medical center noted that 83% of potassium doses prescribed to patients on medical, surgical, and intensive care units were not consistent with replacement guidelines and 69% of patients receiving IV potassium repletion were eligible for oral replacement therapy.(6) Although the reasoning behind these practices were not ascertained, possibilities include a perception that IV formulations have superior efficacy over oral products or that IV replacement is needed promptly to avoid adverse events, the ease of administration of IV products, and the general desire for shorter hospital stays for patients.

Numerous studies have evaluated efforts to improve medication prescribing in the hospital setting. These efforts have focused on the distribution of prescribing guidelines, linkage of pharmacy and laboratory data in electronic medical record systems (12), and use of health information technology. Computerized physician order entry (CPOE), with clinical decision support system in particular, has been shown to increase appropriate prescription of medications, though there is a paucity of data examining its effect on electrolyte prescriptions.(13) CPOE is being integrated into hospital medicine on an international scale, and studies are needed to identify which features can enhance safe potassium repletion. Such features could include the following: a hard stop when a certain dose of potassium has been ordered, thus preventing another physician initiated repletion order until a new potassium level is obtained; automatic identification of patients whose eGFR is not likely an accurate representation of renal clearance, perhaps based on existing diagnoses (i.e., amputation, cancer, cachexia, muscle disorder); and displays of cumulative doses of potassium that a patient has already received in the previous 24 hours, including any potassium in IV fluids and nutritional supplements. While we don't know if any of these systems were utilized or available to the providers in the case presented, each of these has the potential to enhance patient safety and prevent adverse outcomes from repleting too much potassium, too fast.

Take-Home Points

- Most institutional protocols for potassium repletion have not been studied.
- A "normal" serum creatinine or eGFR may overestimate the kidney's ability to excrete potassium.
- Common medications can predispose to hyperkalemia, including: beta-blockers, digitalis, nonsteroidal anti-inflammatory medications, angiotensin converting enzyme inhibitors, trimethoprim, and heparin.
- Oral potassium repletion is considered first-line therapy; intravenous repletion should be saved for patients who cannot take oral medications or who have symptomatic severe hypokalemia (K+

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Table

Table. Principles of Potassium Replacement.

Potassium deficit

- Assessment of the physiology effects of hypokalemia: ECG, muscle strength
- Serum potassium concentration

Preparation of potassium salts

- Potassium chloride: most effective and first line treatment
- Potassium bicarbonate or citrate: effective for patients with mild hypokalemia and metabolic acidosis
- Potassium phosphate: useful to replace phosphate losses

Route of administration

- Oral: preferred if there are bowel sounds; should be considered first-line
- Intravenous: necessary when the patient cannot take oral medicines or for cases of severe hypokalemia causing cardiac arrhythmias, quadriplegia, respiratory failure or rhabomyolysis

*Rate of administration***

- Oral: 60–80 mEq/day initially
- Intravenous: usual rate of 10–20 mEq/h with preference for cardiac monitoring; emergency rate of 5–10 mEq over 20 min with mandatory cardiac monitoring in an ICU setting

***frequent monitoring is advised, especially after doses of 60 mEq PO or 40 mEq IV)*

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