European Journal of Internal Medicine 26 (2015) 106–111

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Review Article

Postoperative hyperkalemia

Taha Ayach [a], Robert W. Nappo [b], Jennifer L. Paugh-Miller [a], Edward A. Ross [c,*]

[a] Division of Nephrology, Hypertension and Renal Transplantation, University of Florida, USA
[b] University of Florida Shands Hospital, Gainesville, FL, USA
[c] University of Central Florida, Orlando, FL, USA

ARTICLE INFO

Article history:
Received 18 November 2014
Received in revised form 8 January 2015
Accepted 23 January 2015
Available online 17 February 2015

Keywords:
Hyperkalemia
Postoperative
Rhabdomyolysis
Transfusions
Drug adverse effect

ABSTRACT

Hyperkalemia occurs frequently in hospitalized patients and is of particular concern for those who have undergone surgery, with postoperative care provided by clinicians of many disciplines. This review describes the normal physiology and how multiple perioperative factors can disrupt potassium homeostasis and lead to severe elevations in plasma potassium concentration. The pathophysiologic basis of diverse causes of hyperkalemia was used to broadly classify etiologies into those with altered potassium distribution (e.g. increased potassium release from cells or other transcellular shifts), reduced urinary excretion (e.g. reduced sodium delivery, volume depletion, and hypoaldosteronism), or an exogenous potassium load (e.g. blood transfusions). Surgical conditions of particular concern involve: rhabdomyolysis from malpositioning, trauma or medications; bariatric surgery; vascular procedures with tissue ischemia; acidosis; hypovolemia; and volume or blood product resuscitation. Certain acute conditions and chronic co-morbidities present particular risk. These include chronic kidney disease, diabetes mellitus, many outpatient preoperative medications (e.g. beta blockers, salt substitutes), and inpatient agents (e.g. succinylcholine, hyperosmolar volume expanders). Clinicians need to be aware of these pathophysiologic mechanisms for developing perioperative hyperkalemia as many of the risks can be minimized or avoided.

1. Introduction

Hyperkalemia occurs frequently in hospitalized patients, and its reported incidence has a wide range due to inconsistent definitions of an elevated serum potassium level. High concentrations have been described in approximately one to ten per 100 inpatients, depending on whether the inclusion threshold is >5.9 [1,2] or ≥5.3 mEq/L [3]. It is most commonly caused by drug therapy or underlying renal insufficiency [1,4]. Surgery, however, is frequently associated with a multitude of perioperative factors that can lead to significant hyperkalemia, with an increased risk of morbidity and mortality. The purpose of this review is to identify and explain how these diverse conditions disrupt the normal physiologic mechanisms for potassium homeostasis, and are broadly divided into: reduced urinary excretion, altered distribution, and exogenous loads. Clinicians caring for these patients need to be aware that some pre-, intra- or postoperative causes are well-known (e.g. massive transfusions) while others are under-appreciated (e.g. certain volume expanders or anesthetic agents). It is important to identify individuals at high risk so as to avoid exacerbating factors, serially monitor potassium levels, and initiate therapy before there are adverse outcomes.

* Corresponding author at: Department of Internal Medicine, University of Central Florida, 6850 Lake Nona Blvd, Orlando, FL 32827, USA. Tel.: +1 407 266 1060.
E-mail address: Edward.ross@ucf.edu (E.A. Ross).

2. Physiology: normal homeostatic mechanisms

The physiological regulation of potassium, the most abundant cation in the body, requires achievement of two goals. First, high concentrations of potassium in the cytosol are necessary for many cells to function normally. Second, sizable concentration gradients of potassium across cell membranes are required for nerve excitation and muscle contraction. The vast majority of potassium is contained by cells; only a very small fraction, 1–2% of total potassium, is located in the extracellular fluid [5].

Although man has a remarkable ability through renal and non-renal mechanisms to maintain normal plasma levels of potassium [6], the postoperative state can have a single overwhelming factor or a "perfect storm" of multiple conditions that lead to critical hyperkalemia. A patient's physiologic response [7] may be inadequate to maintain homeostasis in the setting of various surgical and pharmacologic scenarios that increase potassium load or impair excretion.

Maintenance of a normal serum potassium concentration depends to a large extent on renal function, as more than 80% of the ingested potassium is excreted in the urine. Although potassium is freely filtered by the glomerulus, approximately 90% of filtered potassium is reabsorbed by the proximal tubule and the loop of Henle. The majority of potassium excretion is regulated normally through active secretion and absorption in the distal tubule and collecting duct mainly by principal and intercalated cells respectively [8]. Several factors regulate principal cell

http://dx.doi.org/10.1016/j.ejim.2015.01.010
0953-6205/

Table 1
Major causes of postoperative hyperkalemia.

Mechanism	Causes
Reduced urinary potassium excretion	Reduced aldosterone production:
	Renal disease
	NSAIDs
	Calcineurin inhibitors
	ACE-I, ARBs and direct renin inhibitors
	Heparin (unfractionated) and low molecular weight heparin
	Adrenal insufficiency
	Reduced response to aldosterone:
	Potassium-sparing diuretics:
	Spironolactone, eplerenone, amiloride, triamterene
	Antibiotics:
	Trimethoprim, and pentamidine
	Reduced distal sodium delivery and tubular flow as in prerenal states
	AKI
	CKD
Increased potassium load	Exogenous sources:
	Potassium supplements
	Salt substitutes
	Medications: penicillin G and citrate
	Blood transfusions
	Endogenous sources:
	Extensive tissue dissection
	Rhabdomyolysis
	Trauma
	Operative malpositioning of patient
	Ischemia
	Propofol
	Hemolysis
Altered potassium distribution	Increased potassium release from cells:
	Hyperosmolality: hyperglycemia, mannitol, radiocontrast
	Succinylcholine
	Transcellular shift and impaired cellular uptake:
	Beta blockers
	Acidosis
	Digitalis
	Intravenous amino acids
	Malignant hyperthermia
	Ritodrine
	Epsilon-aminocaproic acid

potassium secretion. These mainly are extracellular potassium, aldosterone, luminal flow rate, distal sodium delivery, and extracellular pH. An increase in plasma potassium stimulates the secretion of aldosterone, which causes increased expression of basolateral Na–K-ATPase and apical sodium channel ENaC with a net effect of enhanced potassium secretion. Increasing extracellular potassium directly stimulates Na–K-ATPase activity, leading to higher potassium secretion. Many surgical patients are at risk of becoming acidotic, so it is important to be aware that metabolic acidosis has both direct effects on potassium channels and changes in interstitial ammonia concentration, which then decreases potassium secretion [9].

There has been much research to explain the preservation of potassium homeostasis and maintenance of normal plasma potassium concentrations in chronic kidney disease (CKD), even with glomerular filtration rate (GFR) as low as 10 to 20 ml/min [6]. Both aldosterone and an increase in serum potassium contribute to the increased potassium excretion per nephron at the collecting duct; however, with advancing renal insufficiency there are also important non-renal, principally gastrointestinal, pathways. Patients with CKD have difficulty handling an acute potassium load, which is secondary to decreased nephron number and a constellation of endogenous and iatrogenic factors that impair the Renin–Angiotensin–Aldosterone-System (RAAS) axis. Importantly, much of the pathophysiology that leads to breakthrough hyperkalemia in CKD overlaps with, and is exacerbated by, perioperative conditions. Many of these patients are routinely treated preoperatively with medications that alter renal potassium handling, such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and β-adrenergic receptor blockers [6]. After surgery they are often volume depleted, acidotic, transfused or exposed to agents that further impair RAAS and the sympathetic nervous system (SNS). Table 1 lists the renal and non-renal pathophysiologic mechanisms for postoperative hyperkalemia, which are described in more detail below.

3. Pathophysiology: inadequate urinary potassium excretion

Both CKD and acute kidney injury (AKI) limit maximal renal potassium excretion, secondary to reduced number of nephron mass and functional collecting ducts. In addition, a number of non-renal, endocrine and pharmacologic causes can contribute to inappropriately low urinary potassium losses.

3.1. Renin–Angiotensin–Aldosterone System (RAAS) pathway

The RAAS axis is the primary hormonal system regulating renal potassium excretion. There are multiple factors that can interfere with this pathway and lead to hypoaldosteronism and the predisposition for hyperkalemia. This can be secondary to reduced aldosterone production or to aldosterone resistance.

3.1.1. Reduced aldosterone production

3.1.1.1. CKD. Surgical patients may already suffer pre-operatively from the hyporeninemic hypoaldosteronism commonly seen in renal disease, most often due to diabetic nephropathy [10].