Chapter 5 / Capítulo 5

Electrolyte and Internal Environment Imbalances in Emergencies (English Edition)
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Hyperkalemia and Hypokalemia

Hiperkalemia e hipokalemia

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Objectives:

- Describe the mechanisms involved in potassium regulation.
- Identify the causes of potassium disorders.
- Determine the diagnostic methods to identify potassium disorders.
- Describe the therapeutic options for potassium disorders.

INTRODUCTION

Potassium disorders, such as hypokalemia (low potassium) and hyperkalemia (high potassium), are common electrolyte disturbances in emergency settings and can have serious clinical consequences, particularly in the cardiovascular system (cardiac conduction system). It is important to note that serum potassium measurements are slightly higher (0,1–0,4 mEq/L) than plasma levels due to potassium release from platelets during coagulation.

Regulation of potassium homeostasis

Blood potassium concentration is determined by three main factors:

1. Intake: a daily intake of 3500 mg (90 mmol) is recommended.
2. Excretion: about 80 % of potassium is eliminated by the kidneys, 15 % through the gastrointestinal tract, and the remaining 5 % via sweat.
3. Transcellular Distribution: about 98 % of the body's potassium is inside the cells, while only 2 % is in the extracellular space. This distribution is crucial for maintaining the cell membrane potential, which is essential for neuromuscular function.

The movement of potassium between the intracellular and extracellular compartments is primarily regulated by the sodium-potassium ATPase pump (Na^+/K^+-ATPase), an enzyme that pumps 3 sodium ions out for every 2 potassium ions in.

Factors affecting potassium distribution

Several factors regulate the movement of potassium across cell membranes, modifying its concentration in the blood:

- Insulin: stimulates the Na^+/K^+-ATPase pump, promoting potassium entry into cells. For this reason, glucose administration can cause mild hypokalemia in healthy individuals.
- Adrenergic Stimuli: β_2-adrenergic stimulation (for example, with drugs such as salbutamol or epinephrine during stress) increases cellular potassium uptake, potentially causing hypokalemia.
- Aldosterone: this hormone, involved in water metabolism, not only increases renal potassium excretion but can also promote its entry into cells.
- pH Changes:
  - Metabolic acidosis tends to cause hyperkalemia. In this state, hydrogen ions enter the cells, and to maintain electrical balance, potassium exits.

- Metabolic alkalosis tends to cause hypokalemia. Here, hydrogen ions leave the cells, and potassium enters to compensate, which can lower its blood concentration.

- Hyperosmolality of the extracellular fluid: conditions such as severe hyperglycemia can passively draw water and potassium out of cells, increasing potassium concentration in the bloodstream.

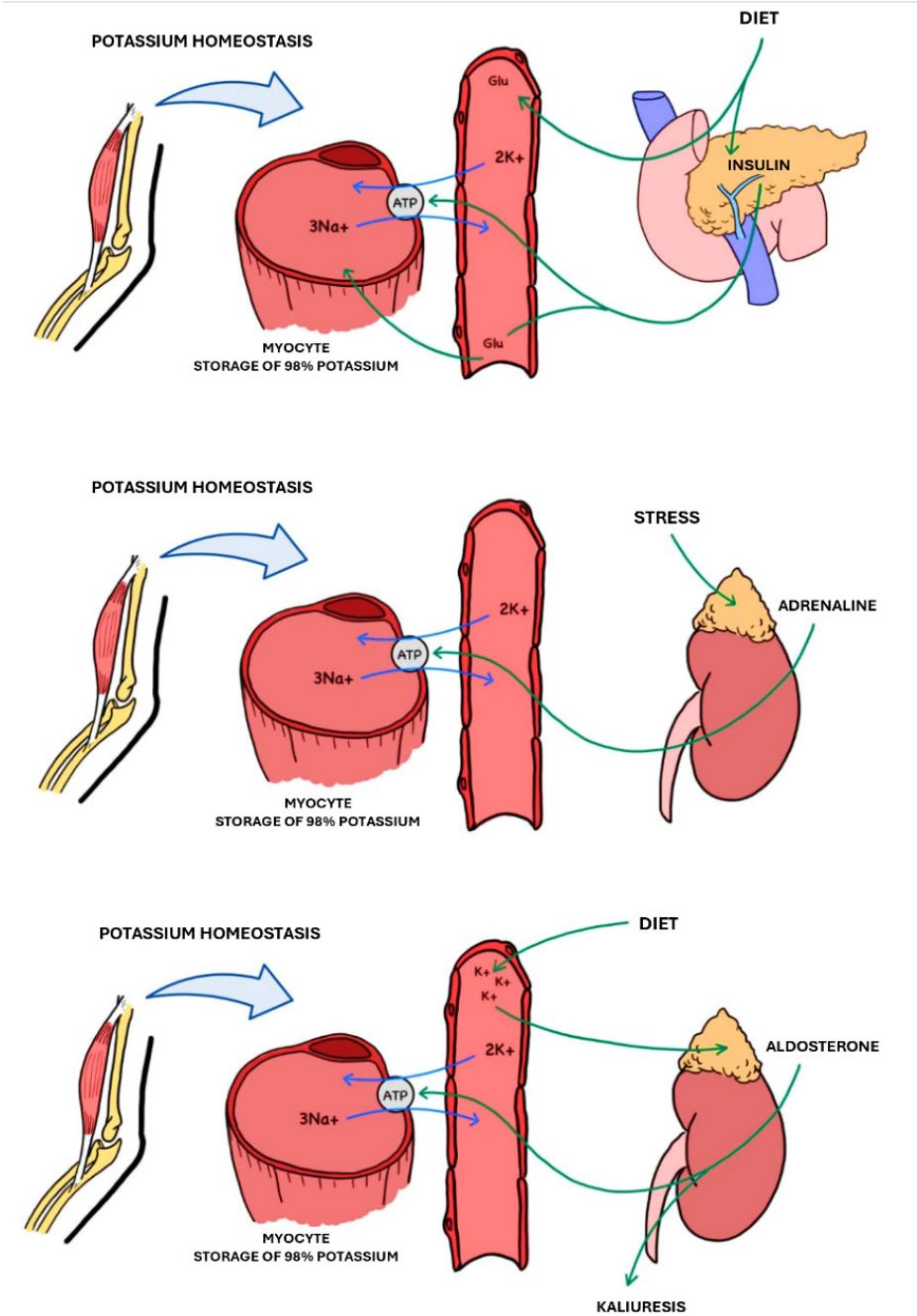

Figure 5.1. Factors affecting potassium distribution

Regulation of renal potassium excretion

The kidney plays a crucial role in regulating potassium in the body. About 90 % of filtered potassium is reabsorbed in the early part of the renal tubule, while the final adjustment of potassium excretion occurs in the late distal tubule and the collecting duct (self-regulation mechanism).

Cells in these regions of the kidney have a polarized structure that allows efficient sodium reabsorption and potassium secretion.

- The sodium-potassium ATPase pump (Na^+/K^+-ATPase) is located only on the basolateral membrane (facing the blood), pumping potassium into the cell.
- On the luminal membrane (facing the tubules), there are specific potassium channels (ROMK and BK) that allow potassium to exit into the urine.
- There is also a specific sodium channel known as ENaC, which reabsorbs sodium from the urine into the cell, creating a negative electrical gradient that facilitates potassium secretion.

Potassium excretion in the kidneys is a highly regulated process, influenced by several key factors:

- Tubular flow and sodium delivery: increased fluid flow and higher sodium content in the distal tubule enhance potassium elimination.
- Mineralocorticoids (Aldosterone): this hormone is essential for regulation. Aldosterone is released in response to hyperkalemia (high potassium) and acts by increasing sodium reabsorption and potassium secretion. It does so by stimulating the Na^+/K^+-ATPase pump and increasing the number and activity of ENaC and ROMK channels.
- Non-reabsorbable anions: the presence of anions such as bicarbonate or phosphate in the distal tubule increases the negative charge of the fluid, attracting and facilitating potassium secretion.
- Entero-renal signaling: recent studies suggest that a communication axis between the intestine and the kidney may rapidly regulate potassium excretion in response to intake, even before blood potassium levels change significantly.

Definition and causes of hypokalemia

Hypokalemia is defined as a serum potassium concentration below 3,5 mEq/L. It is classified as: mild (3-3,5 mEq/L), moderate (2,5-3 mEq/L), severe (less than 2,5 mEq/L).

This electrolyte disorder is more common than hyperkalemia and can be caused by:

- Transcellular redistribution: potassium shifts from the extracellular to the intracellular space. This occurs in conditions such as hypokalemic periodic paralysis or with the use of certain medications (β-adrenergic agents, insulin).
- Extrarenal losses: potassium is lost through the gastrointestinal tract (e.g., diarrhea, fistulas), the skin (e.g., excessive sweating), or due to insufficient intake, although the latter is rarely a sole cause.
- Renal losses: the most common cause is the use of diuretics. Other causes include hyperaldosteronism, licorice consumption, and genetic disorders such as Bartter, Gitelman, and Liddle syndromes.

It is important to differentiate pseudohypokalemia, a falsely low potassium measurement that can occur in patients with extremely high white blood cell counts or if the blood sample is processed with delay.

Clinical Manifestations and Diagnosis

Symptoms of hypokalemia correlate with its severity and the speed of onset. Moderate to

severe hypokalemia may cause:

- Neuromuscular symptoms: muscle weakness, cramps, and in severe cases, paralysis starting in the lower limbs.
- Cardiac symptoms: arrhythmias and characteristic electrocardiogram (ECG) changes, such as the appearance of a U wave.

Diagnosis begins with measuring urinary potassium to determine whether the loss is renal or non-renal in origin.

- If urinary potassium excretion is low (<15–20 mmol/day), the cause is usually insufficient intake, extrarenal losses, or transcellular redistribution.
- If urinary potassium excretion is high (>15–20 mmol/day), the cause is renal, such as diuretic use or excess mineralocorticoids.

Other markers, such as the transtubular potassium gradient (TTKG) and the urinary potassium-to-creatinine ratio, can also be used to help identify the cause.

Treatment of Hypokalemia

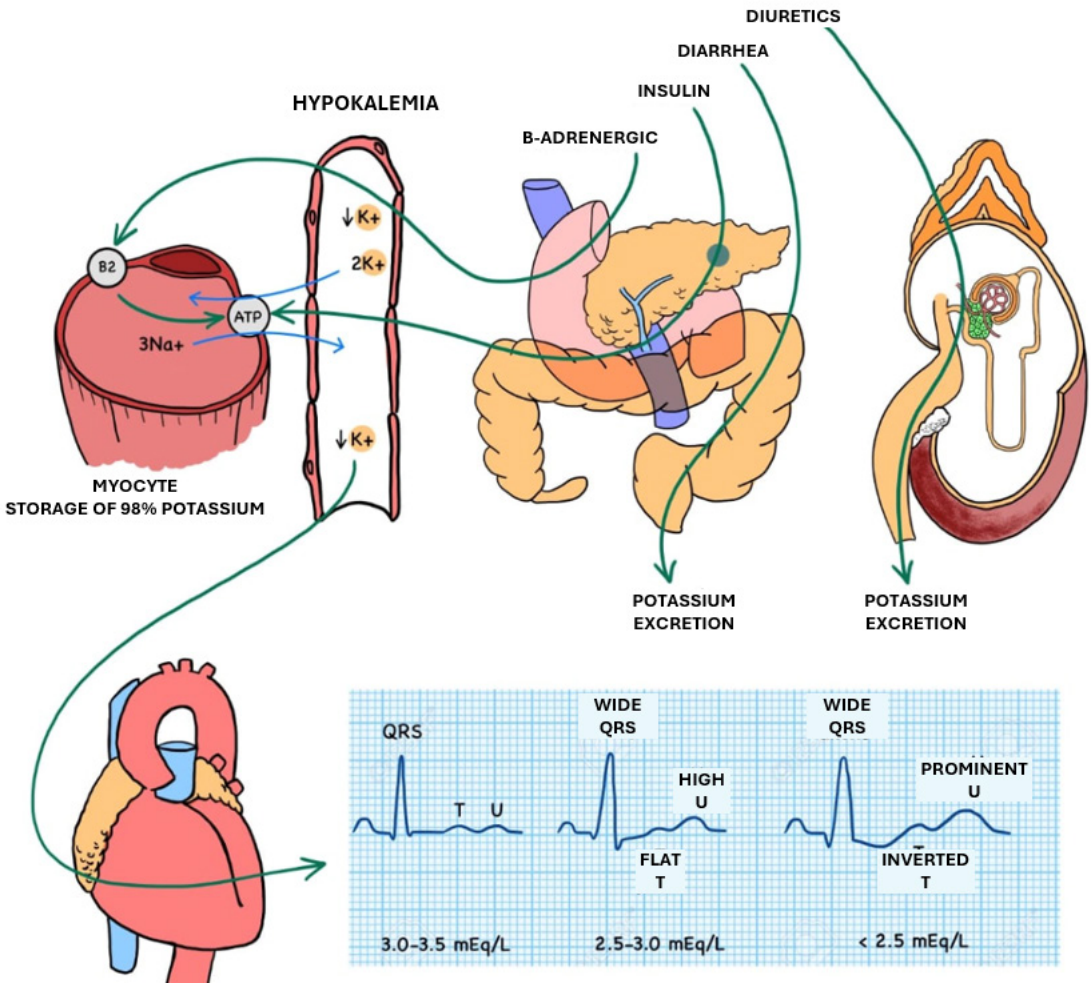

Figure 5.2. Hypokalemia and electrocardiographic disorders

Treatment should be individualized based on severity and underlying cause. A serum potassium deficit of 1 mEq/L may indicate a total body loss of 200–400 mEq.

- Acute treatment: intravenous administration is prioritized in cases of severe hypokalemia (K <2,5 mEq/L), or when cardiac or neuromuscular symptoms are present. Administration must be cautious, with controlled concentrations and infusion rates to avoid overcorrection.
- Chronic treatment: potassium replacement is preferably given orally. Increasing the intake of potassium-rich foods is recommended. In cases of chronic renal losses, potassium-sparing diuretics such as spironolactone or amiloride may be necessary.

Additionally, it is crucial to correct hypomagnesemia, a condition that often accompanies hypokalemia and can render potassium replacement treatment ineffective if not addressed simultaneously. It is fundamental that acute hypokalemia treatment be planned and adjusted daily, monitoring serum potassium and urinary excretion.

Severity of hyperkalemia

Hyperkalemia is defined as a serum potassium concentration greater than 5,0 or 5,5 mEq/L. It is considered the most serious electrolyte disturbance due to its potential to cause fatal ventricular arrhythmias. Severity is classified based on its effects on the electrocardiogram (ECG) (figure 5.3):

- Levels around 6,5 mEq/L: peaked T waves.
- Levels above 7 mEq/L: prolongation of the PR interval, loss of the P wave, and widening of the QRS complex.
- Levels greater than 8 mEq/L: formation of a sine wave, which is a sign of imminent risk of fatal arrhythmia.

Etiology and risk factors

Hyperkalemia can be caused by a variety of factors, but the main causes are:

- Pseudohyperkalemia: false elevations of potassium in the blood sample due to hemolysis or potassium release from white blood cells or platelets in cases of extreme leukocytosis or thrombocytosis.
- Decreased renal excretion: this is the most common cause. It occurs in renal failure (RF), especially when kidney function has declined below 10–15 mL/min, or in patients with hyporeninemic hypoaldosteronism (common in diabetics and elderly individuals).
- Medications: this is an iatrogenic and therefore preventable cause. Drugs that inhibit the renin-angiotensin-aldosterone system (ACE inhibitors, ARBs), potassium-sparing diuretics, and NSAIDs are the main culprits.
- Cellular redistribution: massive release of potassium from cells into the extracellular space, which occurs in cases of tissue lysis (trauma, chemotherapy) or metabolic acidosis.

Hyperkalemia is particularly common in elderly patients and those with chronic kidney disease (CKD), heart failure (HF), and diabetes mellitus (DM).

Treatment

The treatment of hyperkalemia depends on its severity and on the presence of symptoms or ECG abnormalities.

Treatment of severe and symptomatic hyperkalemia:

- Antagonize cardiac effects: the first measure is the intravenous administration of calcium gluconate to stabilize the cardiac membrane. This does not lower potassium

levels, so it must be followed by other interventions.

- Shift potassium into the cells: salbutamol (nebulized or IV) and IV insulin with glucose are used. These treatments promote the entry of potassium into the cells. Sodium bicarbonate is reserved for patients with concomitant metabolic acidosis.
- Insulin and glucose, or insulin alone in patients with hyperglycemia, will drive potassium back into the cells, effectively reducing serum potassium. A common regimen consists of administering ten units of regular insulin with 50 ml of a 50 % dextrose solution IV over 20 minutes.
- Remove potassium from the body: in patients with severe renal impairment, hemodialysis is the fastest and most effective method. In patients without renal impairment, loop diuretics can be used to increase renal excretion.

Treatment of chronic asymptomatic hyperkalemia:

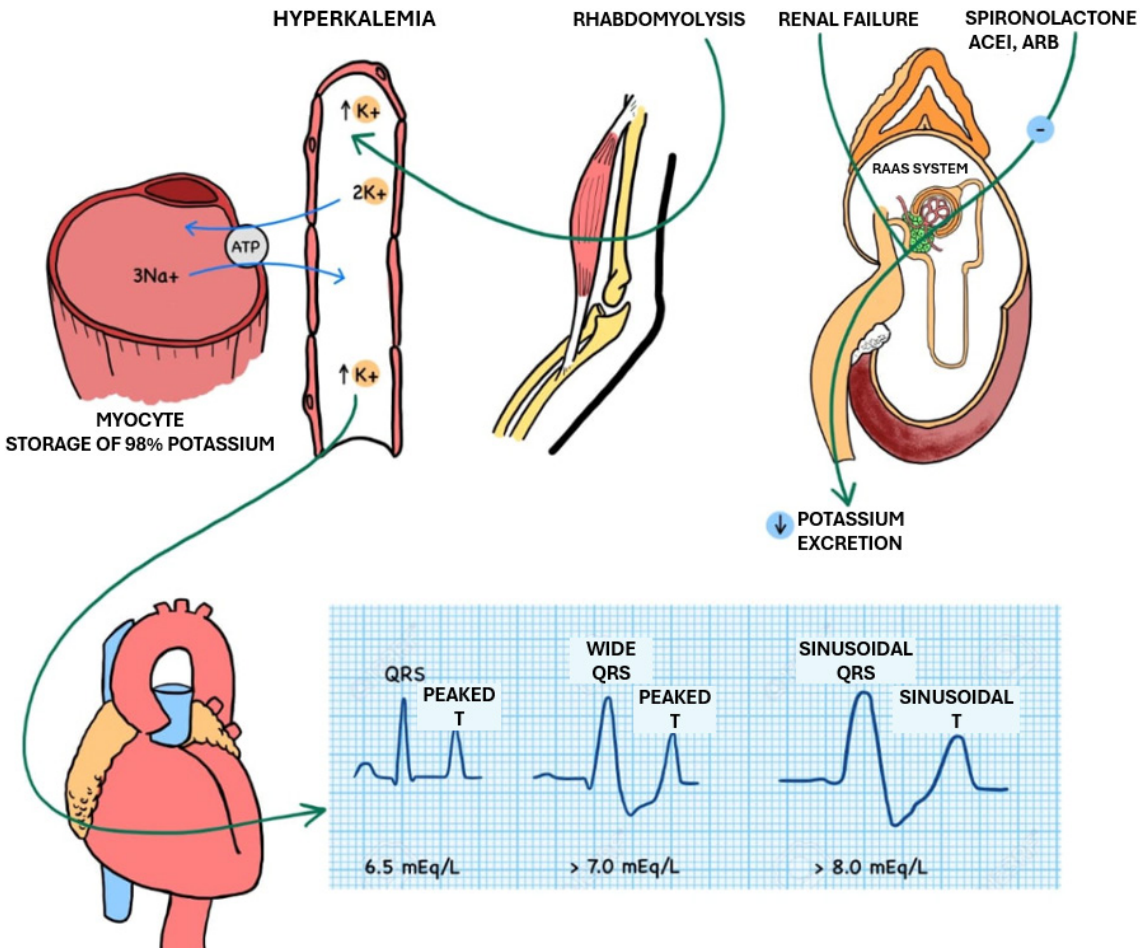

Figure 5.3. Hyperkalemia and electrocardiographic alterations

- Medication review and adjustment: drugs that contribute to hyperkalemia should be discontinued or adjusted. However, in patients with heart failure, maintaining therapy with renin–angiotensin system inhibitors should be prioritized, as interruption is associated with worse outcomes.

- Dietary modification: potassium restriction in the diet may be considered, although recommendations vary and evidence is limited.
- Potassium binders: these agents remove potassium from the body by binding it in the gastrointestinal tract. Newer binders such as patiromer and sodium zirconium cyclosilicate have proven to be more effective and better tolerated than traditional ion-exchange resins.
- Other treatments: in specific cases, diuretics and fludrocortisone may be used.

SPECIAL CONSIDERATIONS

- Diabetes: diabetic patients may develop hyperkalemia due to insulin deficiency, acidosis, and renal impairment. In diabetic ketoacidosis, although the initial serum potassium may be elevated, total body potassium is decreased.
- Heart failure (HF): hyperkalemia in patients with HF increases the risk of mortality and complicates the administration of cardioprotective medications.
- Kidney disease: the risk of hyperkalemia rises as renal function declines. However, the intestine compensates for part of potassium excretion in these patients. During dialysis, potassium fluctuations are a constant risk for arrhythmias.

BIBLIOGRAPHY

1. Li T, Vijayan A. Insulin for the treatment of hyperkalemia: a double-edged sword? Clin Kidney J. 2014 Jun;7(3):239-41. https://doi.org/10.1093/ckj/sfu049

2. González Gómez JM, Milano Manso G. Trastornos hidroelectrolíticos. Equilibrio ácido-base en pediatría. An Pediatr Contin. 2014;12(6):300-11. https://doi.org/10.1016/S1696-2818(14)70208-2

3. Segado Soriano A, Sánchez Sendín D, Martínez Larrull E, Fernández Herranz J. Alteraciones hidroelectrolíticas en urgencias. Med (Barcelona). 2015;11(90):5379-88. https://doi.org/10.1016/j.med.2015.11.004

4. Hernández JC, Solano A, Zecua Y. Líquidos y electrolitos en medicina interna. 2ª ed. Editorial. Benemérita Universidad Autónoma de Puebla; 2020.

5. De la Cal Ramírez MA, coord. Manejo agudo de los trastornos electrolíticos y del equilibrio ácido-base. 2ª ed. Córdoba.

6. Guzmán F, Carrizosa E, Vergara A. Líquidos y electrolitos en cirugía: fisiopatología celular y bioquímica. Colombia: Editorial Médica Panamericana S.A.; 2004. ISBN 958-9181-77-5.

7. Sociedad Española de Nefrología. Diuréticos y alteraciones electrolíticas. 2019. https://www.nefrologiaaldia.org/es-articulo-diureticos-y-alteraciones-electroliticas-218

8. Sociedad Española de Nefrología. Trastornos electrolíticos. 2019. https://www.senefro.org/modules.php?idwebstructure=23&name=webstructure