PATHOPHYSIOLOGICAL ASPECTS IN HYPER-AND HYPOKALEMIA

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Abstract: *Potassium, the most abundent intracellular cation is essential for the life. Potassium is obtained through the diet. Gastrointestinal absorption is complete, resulting sometimes an excess intake of about 1mEq/kg/day (60-100 mEq). This excess is excreted through the kidneys (90%) and the gut (10 %). Potassium homeostasis is maintained predominantly through the regulation of renal excretion. The most important site of regulation is th cortical collecting tubule, where aldosteron receptors are present. The importance of potassium in the human body is reflected through the main role in the rest potential, in the ionic and fluid ballance and in the pH ballance. The potassium disorders can determine severe, sometimes life-threatening clinical situations. We propose to present the pathological mechanisme that appears in the potassium disordes.*

Cuvinte cheie: *potasemie, hiperpotasemie, hipopotasemie*

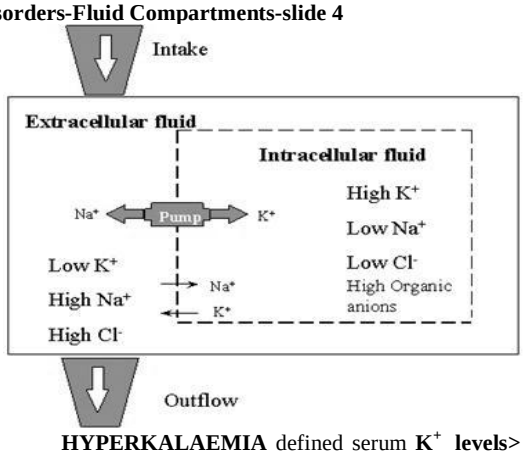
Rezumat: *Potasiul, cationul major intracelular, este esenţial pentru viaţă. Obţinut prin aport alimentar, potasiul este absorbit complet din tractul gastrointestinal, realizând uneori situatii cu exces de aport, mai mari decat necesarul zilnic de 1mEq/kg/zi (60-100 mEq). Excesul este eliminat apoi pe cale renală (90%) şi fecală (10 %). Homeostazia potasiului este menţinută în principal prin reglarea excreţiei renale, la nivelul corticalei tubilor colectori, unde există receptori pentru aldosteron. Importanţa potasiului în organism se reflectă prin rolul său principal în potenţialul membranar de repaus, în echilibrul ionic şi lichidian intracelular şi în realizarea echilibrului pH-ului. Dezechilibrele potasemiei determina situaţii clinice cu diferite grade de severitate, uneori ameninţătoare de viaţă. Articolul de faţă propune explicarea principalelor mecanisme fiziopatogenice întâlnite în dezechilibrele potasemiei.*

INTRODUCTION

Potassium is a major intracellular cation, with intracellular levels between 150 to 160 mEq / L. Extracellular, normal serum potassium values are 3,5-5,5 mEq / L, obviously, they do not reflect the total amount of body potassium. Total deposit of K^+ is about 50 mEq / kg. (1).

Adjustment is made by K^+ pump Na + / K^+ ATP-aza, controlled by insulin receptors or beta-2 adrenergic receptors.

Figure no. 1. EMPA Residency UTHSCSA- Electrolyte Disorders-Fluid Compartments-slide 4



HYPERKALAEMIA defined serum **K^+ levels> 5.5 mEq / L**, is caused by an excess of total K^+. Is explained by 3 mechanisms that are intricated: the increase intake of K^+ , the decreased excretion and the shift of K^+ from intracellular to extracellular space. Although the most common cause is a deterioration of renal excretion, hyperkalaemia may occur as a result of metabolic acidosis or uncontroled diabetes mellitus. (2)

THE EXCESSIVE INTAKE OF POTASSIUM is an unusual mechanism, because the shifting the K^+ intracellulary and the renal excretion, allow a person with intact homeostatic mechanisms to ingest virtually large quantities of potassium without changing its potasemia. Even the parenteral administration of potassium creates minimal increase in serum potassium concentration.

DECREASED EXCRETION OF POTASSIUM: most often associated with increased intake of potassium is the most common cause of hyperkalaemia. Is encountered in acute or chronic kidney failure, after administration of drugs (K^+ sparing diuretics, ACEI, NSAIDs), in Addison's disease, LES or because of inadequate response to aldosterone in the distal renal tubule (type IV of renal tubular acidosis) in DZ, or chronic partial urinary tract obstruction . (3)

SHIFT OF K^+ FROM INTRACELLULAR TO EXTRACELLULAR SPACE: a rare and isolated mechanism can exacerbate the hyperkalaemia caused by increased ingestion and / or decreased renal excretion. Clinical situations include hiperosmolarityty, hyperglycemia, moderate or severe physical exercises, digitalis intoxication, tumor lysis syndrome, acute intravascular hemolysis or rhabdomyolysis.

In case of metabolic acidosis, hyperkalaemia appeares more common in acidosis caused by mineral acids (HCl,

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NH4Cl), than that caused by organic acids (βhidroxibutiric, lactic acid). HCI determine the release of K^+ from the cells through intracellular proton intake, resulting membrane depolarisation, which favors the exit gradient of K^+ from the cell . (4)

Increasing extracellular osmolarity determine the increase of extracellular K^+ from 1 to 2mEq / l, when administering mannitol or in case of unbuffered hyperglycaemia with insulin or in diabetes mellituswith ketoacidosis.

Hyperkalaemia may also be caused by IV administration of EACA (epsilonaminocaproic acid), a synthetic amino acid, because of a similarity of structure of EACA to arginine and lysine. These amino acids enter the muscle cells in exchange for potassium, thus leading to increased extracellular potassium. (5)

PSEUDOHIPERKALEMIA is due to lab error, but appears also in leukocytosis or thrombocytosis. (6)

HYPOKALEMIA defined serum level of **K^+ <3.5 mEq / L**.

Hipokalemia causes are low intake, excessive loss of K^+ through the gastrointestinal tract and kidneys, excessive penetration of K^+ in the intracellular space, diluting the blood or administration of β-blockers. All these cases causes neuromuscular irritability, cardiac effects, acid-base imbalance, or effects on renal metabolism.

Hypokalemia can be explained by 3 mechanisms:

THE LOW INTAKE OF K^+ which is rare and occurs in the elderly who are unable to eat properly, or due to parenteral nutrition for a prolonged period without adequate additional potassium.

INCREASE LOSSES OF K^+ the second pathophysiological mechanism, explained by the renal losses due to chronic diuretic therapy (thiazide, loop diuretics) or osmotic diuresis.These drugs most commonly causing hypokalemia. It's blocking Na + reabsorption in the distal nephron.

Hyperaldosteronism decreases K^+ by direct effect of mineralocorticoids on secretion K^+ in the distal nephron (Cushing's syndrome, primary aldosteronism or, rarely, renin-secretant tumors). Congenital adrenal hyperplasia, causes hypokalemia by training in excess of mineralocorticoid.

Liddle syndrome is an autosomal dominant disease characterized by severe hypertension and hypokalemia.It is caused by increased reabsorbtion of Na in the distal nephron, with hypertension and renal loss of K^+ (8)

The Bartter and Gitelman syndromes are genetic disorders characterized by renal loss of K^+ and Na +, excessive production of renin and aldosterone, but normal values of arterial pressure. (9)

In renal tubular acidosis and Fanconi syndrome, loss of K^+ will join those of glucose, phosphate, uric acid and amino acids.

Other causes of renal potassium losses are consecutive administration of medications (amphotericin, carbenicillin) or administration of high doses of penicillin, theophylline lithium thaliu, dopamine.

Gastrointestinal losses by chronic diarrhea, chronic use of laxatives or intestinal diverticulosis, vomiting and malabsorption are common causes of hypokalemia. In vomiting, the mechanism is complex: the gastric juice contains potassium, approx. 10 mEq / L. The vomiting causes volemic depletion and metabolic alkalosis and is associated with increased renal excretion of K^+.Volemic depletion produce secondary hyperaldosteronism with increased secretion of K^+ in the tubular collectors, so the increase of Na + reabsorbtion. Metabolic alkalosis increases K^+ secretion in the tubular collectors, by decreasing the availability of hydrogen ions in response to Na + reabsorption. Gastrointestinal losses may be simultaneous with the kidney by metabolic alkalosis and stimulation of aldosterone due to depletion volemice. (10)

Trauma and excessive sweating also causes increased loss of K^+.

SHIFT OF K^+ FROM EXTRACELLULAR TO INTRACELLULAR SPACE is frequently associated with increased excretion of K occurs in metabolic alkalosis or if increasing the dosage of insulin in diabetes mellitus. Intracellular penetration of potassium are often episodic and self-limited (eg insulin therapy in acute hyperglycaemia). On the pathophysiological, to increase the pH in the extracellular space, potassium enters the cell. Increase with 0.10 in pH, cause decreases by 0.5 mEq / L of serum potassium.

Stimulation of the sympathetic nervous system, particularly by β2-agonists cause hypokalemia. (eg, albuterol, Terbutaline) due to increased cellular potassium acquisition. Similarly, in patients with thyrotoxicosis, hypokalaemia appears excessive stimulation β-sympathomimetics (thyrotoxicosis, hypokalemia periodic paralysis). Periodic familiar paralisis is a rare disease of autosomal dominant, characterized by transient episodes of severe hypokalemia due to high intracellular penetration of K^+. In these episodes occur at different stages of paralysis. Are precipitated by high carbohydrate diet and intense exercise, but may occur without precipitating factors. (11)

Since potassium is predominantly an intracellular cation, regulated by different mechanisms, may encounter severe cases of increases or decreases of K^+, without a franc hypo / or hyperkalaemia. Arguably, the serum potassium imbalances do not always reflect real excess or deficit of total deposit of K^+ in the body.

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