Hyperkalemia

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Hyperkalemia, defined as a serum potassium level greater than 5.0 mmol/L, may cause life-threatening cardiac and neuromuscular alterations, and it is associated with high mortality rates. Its treatment includes a multifaceted approach, guided by potassium levels and clinical presentation. In general, treatment of hyperkalemia may be directed towards stabilizing cell membrane potential, promoting transcellular potassium shift and lowering total K^+ body content. The latter can be obtained by dialysis, or by increasing potassium elimination by urine or the gastrointestinal tract

Keywords: Hyperkalemia

1. Definition

Hyperkalemia is defined as a serum potassium level greater than 5.0 mmol/L, while severe hyperkalemia is defined as a level greater than 6.0 mmol/L.

2. Introduction

Hyperkalemia is a very common disorder. The actual incidence and prevalence of hyperkalemia in the general population are unknown, but studies based on large cohorts have reported incidence rates between 1 and 3 per 100 persons per year, rising to 10% in hospitalized patients[1]. Moreover, hyperkalemia prevalence may be significantly high in the presence of certain predisposing conditions. So, an analysis of a large geographically diverse population showed basal potassium values of ≥ 5.0 mmol/L in 9.1% of patients with chronic heart failure (CHF), in 11.5% of chronic kidney disease (CKD) stage 3–5 patients, in 8.3% of patients with diabetes, and in 13.1% of those patients with all these conditions[2]. In addition, among CKD patients, those requiring dialysis represent a group at particularly high risk of hyperkalemia [3]. Clinical complications and death in hyperkalemia patients are mainly determined by the cardiac electrophysiological effects of elevated K^+ levels [4]. The treatment of hyperkalemia may involve the recognition of different time-points and goals, guided by potassium levels and the severity of the clinical presentation. In general, the first aim is to prevent cardiac consequences and lower serum potassium to safe levels as soon as possible; then it is important to reduce the K^+ body content, aiming to maintain serum potassium at normal values [5]. The latter can be obtained by dialysis, or by increasing potassium elimination via urine or the gastrointestinal tract.

3. Hyperkalemia: Physiopathology, Risk Factors, Clinical Consequences

Hyperkalemia may be caused by several conditions that may alter K^+ homeostasis. First, it could be the consequence of an increased K^+ body content due to excessive K^+ intake, or, more commonly, due to reduced renal excretion. Renal K^+ excretion may be impaired as a result of advanced renal damage. Indeed, while the normal kidney presents adaptation mechanisms that preserve potassium homeostasis, the diseased kidney has a much lower capacity for handling acute potassium loads. Failures of the kidneys in regulating the potassium balance may result from multiple factors, including a reduced glomerular filtration rate, decreased distal delivery of sodium, intrinsic abnormalities of the distal nephron, and decreased mineralocorticoid activity (e.g., hypoaldosteronism), which impair the capacity of the distal nephron to eliminate K^+ from the urine. Moreover, concomitant metabolic alterations, such as acidemia and hyperglycemia, may also concur [6]. Hypoaldosteronism, in turn, may be caused by diabetes, adrenal disease, numerous drugs (e.g., nonsteroidal anti-inflammatory drugs, beta-blockers, inhibitors of the renin-angiotensin-aldosterone system-RAASi, mineralocorticoid receptor blockers, calcineurin-inhibitors, etc.) and old age. Beyond an increase of K^+ body content, alterations in the K^+ distribution across cell compartments can also lead to hyperkalemia. These conditions determine the net release of potassium from damaged cells, such as in cases of trauma, rhabdomyolysis, or hemolysis. Moreover, an impaired distribution of K^+ between the intracellular and extracellular spaces can also be due to metabolic acidosis, decompensated diabetes, or dysfunctions of the autonomic nervous system. The early recognition and treatment of hyperkalemia are essential, because this condition, although often clinically silent, may have severe consequences.

Indeed, hyperkalemia, by diminishing the K^+ intracellular/K^+ extracellular ratio, reduces the membrane potential, causing a partial depolarization of the cell membrane, which results in an initial increase in conduction velocity. Then, if persistent and profound, hyperkalemia also decreases membrane excitability by the inactivation of the voltage-gated sodium channels, making the cell refractory to excitation, and thus leading to arrhythmias and heart block [7]. Moreover, besides cardiac effects, hyperkalemia can also cause other physiologic perturbations, such as muscle weakness progressing to flaccid paralysis, and metabolic acidosis, which in turn may contribute to the progression of CKD [8]. Hyperkalemia is associated with poor outcomes and high mortality rates, both in the general population and in different clinical settings, including patients with cardiac and renal diseases and critically ill patients[9] [10].

4. Hyperkalemia: Treatment Strategies

From the pathophysiological point of view, the therapeutic approaches to hyperkalemia can have three different targets: i) cell membrane potential stabilization; ii) shifting potassium from extracellular spaces into the cells (i.e., acting on internal K^+ balance); and iii) lowering K^+ levels and enhancing potassium elimination (i.e., acting on external K^+ balance). Membrane stabilization may be achieved through the administration of intravenous calcium (calcium chloride or calcium gluconate), while potassium redistribution may be promoted using insulin/glucose, beta-adrenergic agonists (such as albuterol and salbutamol, both intravenous and inhaled) and sodium bicarbonate [11]. These treatments are often preferred in emergency interventions since they can reduce K^+ levels within a few minutes. However, while they act rapidly, their effects also fade very rapidly. So, complementary to the strategies that promote the shifting of potassium into cells, the reestablishment of potassium homeostasis should include the reduction of body K^+ content. This can be achieved through the limitation of potassium intake and the use of medications that increase potassium elimination via urine or the gastrointestinal tract (GI), such as loop diuretics or cation-exchanging resins, or alternatively, by use of hemodialysis, which can reduce body K^+ content but usually require more time to act [12] In particular, the use of drugs increasing GI potassium elimination is valuable in patients with advanced CKD, who present significant fecal K^+ excretion. For a long time, the only therapeutic option for increasing fecal K^+ excretion has been represented by sodium polystyrene sulfonate, a cation-exchanging resin the efficacy and safety of which have been questioned. Recently, new drugs able to promote gastrointestinal potassium elimination, namely patiromer and sodium zirconium cyclosilicate, have been developed and studied in large trials, proving their efficacy and safety in different clinical contexts. Several studies are ongoing and others should be designed to define the potentiality offered by the applications of these new potassium binders in specific clinical settings and elucidate their role in improving long-term clinical outcomes.[13]

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