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Family Medicine and Medical Science Research

Mini Review

Potassium Intake Overview: Are We Chronically Hypokalemic?

Frederico Sassoli Fazan*

Department of Pharmacology and Physiology, Federal University of São Paulo, Brazil

ABSTRACT

Potassium is the most abundant intracellular ion with about 98% of all potassium residing inside the Intracellular Fluid (ICF) with a concentration of 140 mEq/L. Only 2% is found in the Extracellular Fluid (ECF) with a concentration about 4 mEq/L. The high potassium concentration in the ICF is crucial for intracellular functions such as regulation of cell volume, protein synthesis, nucleic acid polymerization, and regulation of the intracellular acid-base status. Additionally, the potassium concentration gradient between the ICF and ECF promote the maintenance of the resting membrane potential, consequently modulating the activity of all excitable cells. Therefore, the muscles, brain, glands, and vasculature are all influenced by the potassium difference across the membrane, which can be greatly influenced by the amount of potassium intake. The adequate intake for potassium has been defined as 4.7 g (120 mmol)/day for adults of both males and females. It was demonstrated that potassium intake is related to lower blood pressure, attenuation of renovascular hypertension, lowering renin release and reducing vascular resistance. Potassium intake also has diuretic effects, reducing the adverse effects of sodium chloride intake on blood pressure. Despite that, several past studies suggested that many countries do not meet an adequate potassium intake goal. Thus, increasing potassium intake is desirable as it has been proven to help in the hypertension control, a disease that affects almost one third of the world population. However, increasing potassium intake can be a potentially dangerous task, especially for individuals with reduced renal function. Elevated potassium in the ECF can promote hyperkalemia ($[K^+]$>5 mEq/L), presenting a potential cardiovascular risk. Therefore, in this mini-review we will present and discuss the possible consequences of potassium intake in the healthy and diseased kidney population presenting evidences of potassium overload consequences through high potassium intake in experimental models.

Keywords: Potassium intake; Renovascular hypertension; Nutrition

INTRODUCTION

Potassium is the most important intracellular cation. Various processes for life maintenance require high potassium concentration inside the cells, such as nucleic acid polymerization, protein synthesis, cell volume, and intracellular pH regulation. Without intracellular potassium, the efficiency of these processes would be much lower and insufficient to maintain life. The total amount of potassium in the adult body is about 45 millimole (mmol)/kg body weight (about 140 g for a 175 pound adult; 1 mmol=1 milli Equivalent [mEq] or 39.1 mg potassium) [1]. The potassium, however, is not evenly distributed in the body. Around 98% of this ion resides in the Intracellular Fluid (ICF) retaining around 3435 mmoles, while only 2% is in the Extracellular Fluid (ECF) retaining around 65 mmoles [1,2]. This difference in concentration is generated by the activity of the Na/K ATPase, that constantly pumps potassium from the ECF to the ICF. This creates a potassium concentration gradient across the cell membrane (140 mEq/L in the ICF and 4 mEq/L in the ECF) [3]. Since potassium has a very high conductance across the cell membrane, it is particularly important for generating and maintaining the resting membrane potential. Hence, alterations in this gradient can cause severe consequences for excitable cells in the heart, nervous system,

***Correspondence to**: Frederico Sassoli Fazan, Department of Pharmacology and Physiology, Federal University of São Paulo, Brazil, E-mail: frederico.fazan@usp.br

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glands, vasculature, and muscles [4]. For this reason, many redundant mechanisms coexist to promote a stable and reliable concentration gradient across the cell membrane protecting the fluids from reaching dangerous potassium concentrations as the consequences can be fatal. The ECF is strictly maintained between 3.5 and 5 mEq/L [5].

POTASSIUM HOMEOSTASIS

Potassium balance is achieved by the relation between intake and excretion. If the dietary potassium intake is of 100 mmol/day, then the same amount must be excreted in order to prevent accumulation or depletion of this ion [1]. The kidneys play a major role in the regulation of potassium homeostasis by the excretion, when potassium intake is high, or reabsorption, when potassium intake is low. In the same 100 mmol of potassium/day diet, around 92 mmol are excreted in the urine, and the remaining 8 mmol are excreted in the stool [1]. However, if we consider that the individual makes 4 meals a day, he would ingest 25 mmol of potassium for each meal, which if totally transferred to the blood could raise the concentration of potassium from 4.0 to 8.0 mEq/L, causing major hyperkalemia and possibly death [6,7]. The extracellular potassium, however, does not rise significantly after each meal. There is a rapid cumulative internalization of potassium into the ICF immediately after ingestion that buffers the potassium rise in the ECF. This mechanism is related to the Na/K ATPase globally expressed in our tissues. The activity of this pump is secondarily stimulated after potassium overload by the primary rise and action of insulin and aldosterone release. Therefore, the renal excretion of potassium begins after 3 hours of high potassium intake [7].

The renal excretion of potassium occurs mainly in the distal nephron where the distal convoluted tubule connects to the collecting tubule; this region contains the connecting tubule and the cortical collecting duct. In this segment of the nephron, two cells are responsible for the presence of potassium in the urine: principal cells and intercalated cells. Both these cells express a Renal Outer Medullary Potassium channel (ROMK) that is highly conductive for potassium and promotes the net secretion of potassium from the ICF to the tubule lumen [8]. Additionally, the principal cells express the Epithelial Sodium Channels (ENaC) that is aldosterone inducible. This channel reabsorbs sodium promoting negative-lumen trans-epithelial potentials, increasing the driving force of potassium excretion through ROMK [9-12].

When potassium intake is low, these excretory mechanisms are inhibited and urine potassium is very low, as it is mostly reabsorbed in the proximal and Thick Ascending Limb (TAL) of the nephron [1].

ADEQUATE POTASSIUM INTAKE AND ITS BENEFITS

The adequate intake for potassium has been defined as 4.7 g (120 mmol)/day for adults of both males and females according to the Dietary Reference Intakes from the National Academics of Sciences Engineering and Medicine [3]. This intake amount has been shown to reduce blood pressure and attenuate the hypertensive effect of sodium chloride in rats. For two centuries certain potassium salts have been used as diuretics in clinical medicine. In 1679 Thomas Willis recommended the use of potassium nitrate in the treatment of edema [13]. Wilks and Taylor used it successfully in 1863 [14]. In 1921 Blum and Magnus-Levy were able to show that potassium chloride could be administered safely orally in relatively large doses and that it produced frequently a satisfactory diuresis [15,16]. This increase in urinary volume can partially explain the positive effect of potassium in reducing the progression and the developed renovascular in two-kidney, one clip Goldblatt hypertension [10]. Dietary potassium depletion raises blood pressure in normal humans [11], and this is associated with a blunted ability to handle acute sodium load and sodium retention [12]. Potassium chloride is also vasoactive; for example, when infused into the arterial supply of a vascular bed, flow increases [17]. Additionally, potassium-magnesium citrate has been shown to lower renal stone risk in humans [18].

Therefore, these studies suggest that adequate potassium intake is a goal that the overall population should strive for. If the necessary potassium intake is reached, it is possible that an overall prevalence in salt intake related hypertension will lower, bringing a healthier life for millions of individuals and lowering the cost with the treatment and care for this widespread condition.

POTASSIUM INTAKE STUDIES

In 2010, a study involving 21 countries shockingly revealed that none of the studied countries met the adequate intake for potassium [19]. In the same study, it was shown in China, the average potassium intake was only 36% of the adequate intake amount [19]. Earlier, more localized studies, for example, in Evans County, Georgia, showed that African American subjects consumed less potassium than Caucasian subjects and that high blood pressure in African American subjects is associated with low potassium intake [17]. In Portugal, it has been reported that 83% of the adolescents aged between 13-18 years exceed the recommended sodium intake and that 96.1% did not meet recommendations for potassium intake [20]. Furthermore, in the same study, it was shown that on average, urinary Na^+/K^+ ratio did not differ between boys (1.7) and girls (1.6); although these values are much higher than Na^+/K^+<0.59 mg/mg the World Health Organization recommends [21]. High Na^+/K^+ ratio has been associated with an increase in the commercialization and popularization of processed foods with high sodium contents and low potassium [22].

It is evident that the most frequent potassium related problem is associated with suboptimal intake. Surprisingly, the main sources of potassium among the Portuguese study participants were milk and milk products (21%) and meat products (17%), as explained by the low intake of fruit and vegetables (2% and 9%, respectively). These data reflect the low proportion of adolescents who follow the recommendation of 400 g of fruit and vegetables intake daily [23].

To increase the potassium intake in order to achieve the daily recommended intake, it is necessary to promote nutritional and

education strategies that increase public awareness for fruit intake and stimulate the development of technologies to control the amounts of potassium salts in processed foods.

POSSIBLE RISKS

Despite the evident necessity of increasing potassium intake in the overall population, the rise of K^+ concentration in the ECF has potentially fatal consequences [6]. It is understood, however, that hyperkalemia induced by potassium ingestion is extremely rare and almost never happens in individuals with healthy kidneys taking natural potassium food sources. Despite that, fatal hyperkalemia has been reported from potassium chloride supplementation tablets massive overdose [24]. The renal excretion of potassium is immensely greater than what any possible source of natural dietary potassium could offer on a daily basis. It has been shown experimentally that potassium excretion can reach up to 180% of the filtered amount, which shows the overwhelming capacity for kidney's tubular secretion of potassium [25].

Nonetheless, there are risk groups that must be taken into consideration. Individuals with acute or chronically impaired kidney function with a very low (<20 mL/min) estimated glomerular filtration rate are at risk of developing hyperkalemia. Diabetes mellitus can impair aldosterone secreting by a condition called hyporeninemic hypoaldosteronism which increases the likelihood of mild hyperkalemia [26]. It has been shown that chronic inhibition of the angiotensin-converting enzyme by captopril can raise serum potassium levels [27]. Primary or secondary adrenal insufficiency can also impair potassium excretion leading to dangerous potassium levels in the blood [28].

All these conditions, however, require close monitoring of ingested water and salts (sodium and potassium). Therefore, the risk is not exclusively related to potassium, although fast serum K^+ rise usually brings more immediate consequences such as arrhythmias and asystole [6].

CONCLUSION

In the attempt to elucidate ways to increase the quality of life and possibly decrease the burden of one of the most frequent chronic diseases, hypertension, this mini-review proposes that nutrition should be one of the major priorities for public health programs. It offers a view that, at populational level, conscious and well-thought potassium ingestion may be a tool that can reduce the threat of the global epidemic of hypertension.

Additionally, the strategies for potassium intake adjustments must involve, to some extent, the regulation of the salt contents in processed foods together with health awareness provided through health programs in community and family medicine motivating healthier diets, aiming for the goal of the adequate potassium intake and reducing the consequences in low potassium intake.

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CONFLICT OF INTEREST

The author has no conflict of interest to declare.

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