MAYO CLINIC

REVIEW

Achieving the Benefits of a High-Potassium, Paleolithic Diet, Without the Toxicity

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Abstract

The average US dietary intake of K^+ is well below the current recommended nutritional requirements. This deficiency is even more striking when comparing our current intake with that of our ancestors, who consumed large amounts of dietary K^+. K^+ deficiency has been implicated in many diseases including cardiovascular disease, kidney stones, and osteoporosis. Importantly, dietary supplementation of K^+ has favorable effects on reducing blood pressure, decreasing the risk of stroke, improving bone health, and reducing the risk of nephrolithiasis. For this comprehensive review, we scanned the literature using PubMed and MEDLINE using the following search terms: *potassium intake*, *renal potassium excretion*, and *prevention of hyperkalemia*. Articles were selected for inclusion if they represented primary data or review articles published between 1980 and 2015 in high-impact journals. The normal kidney has the capacity to tightly regulate K^+ homoeostasis. We discuss new findings with respect to sensing mechanisms by which the kidney maintains K^+ homeostasis in the gastrointestinal tract and distal tubule. There are widely prescribed hypertensive medications that cause hyperkalemia and thus require dietary K^+ restriction. We conclude by discussing newly approved drugs capable of binding K^+ in the gastrointestinal tract and speculate that this new pharmacology might allow diet liberalization in patients at risk for hyperkalemia, affording them the numerous benefits of a K^+-rich diet.

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Potassium is an extremely important mineral, as supported by the recent Dietary Guidelines for Americans and the Food and Drug Administration designation that K^+ is a "nutrient of public health concern" because of its general underconsumption across the US population.[1] Underconsumption of K^+ is associated with hypertension and cardiovascular diseases, 2 common adverse diet-related health outcomes in the United States.[1] In 2004, the Food and Nutrition Board of the Institute of Medicine[2] recommended intake levels of 4700 mg/d. Despite these recommendations, data from the National Health and Nutrition Examination Survey (NHANES) 2007 to 2008 estimated mean intakes in the United States to be 2290 mg/d for women and 3026 mg/d for men, substantially lower than the suggested values.[3] This relative "deficiency" of dietary K^+ is even more noteworthy when one considers that the K^+ intake of prehistoric humans was estimated to be 15,000 mg/d, which actually exceeds the NHANES recommendations by a factor greater than 4.[4,5] Not only are diets of Western industrialized societies lower in K^+ intake, but they also differ from prehistoric cultures with respect to Na^+ intake. The daily intake of salt in Western industrialized societies is about 3 times higher than the daily intake of K^+ on a molar basis, whereas salt intake in primitive cultures is approximately 7 times lower than K^+ intake.[6]

The changes in K^+ and Na^+ intake over time reflect a shift from traditional plant-based diets high in K^+ and low in Na^+ (characterized by fruits, leafy greens, roots, and tubers) to processed foods high in Na^+ and low in K^+. The transition to processed foods began approximately 10,000 years ago with the onset of agriculture. This time period is short in comparison to the preceding several million-year period dating from the Stone Age to the onset of agriculture. Inadequate consumption of K^+ combined with excessive intake of Na^+ contributes to the pathophysiology of various chronic diseases such as obesity, hypertension, diabetes, kidney stones, and bone disease.

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ARTICLE HIGHLIGHTS

- Over several million years, physiology and metabolism of humans evolved to retain Na^+ and excrete K^+ in response to a diet that was low in Na^+ and high in K^+. With the onset of agriculture and industrialization, there has been a precipitous drop in dietary K^+ consumption and an equal rise in dietary salt consumption, contributing to disease onset. This is further supported by the fact that the newest Dietary Guidelines for Americans have listed K^+ as a "nutrient of public health concern" because of its inadequate consumption. Low K^+ intake is then implicated in various chronic diseases including hypertension, cardiovascular disease, osteoporosis, and nephrolithiasis.
- The ability to maintain K^+ homeostasis in the setting of high dietary intake is regulated by the normal kidney. In addition to the well-recognized role of aldosterone in renal K^+ secretion, recent findings have identified the presence of an enteric K^+ sensing mechanism that can initiate the renal secretory process upon K^+ entry into the gastrointestinal tract. In addition, the distal convoluted tubule has been identified as a K^+ sensor capable of initiating K^+ exertion independent of mineralocorticoid activity.
- Increased dietary K^+ intake has been linked to various health benefits including decreased blood pressure, reduced risk of stroke, improved bone health, and a reduction in the risk of renal stone disease. At the same time, drugs used to treat hypertension result in increased K^+ concentrations, requiring dietary restriction of K^+-enriched foods.
- A plant-based (K^+-enriched) diet offers benefits that include reduced phosphorus absorption and improvement in metabolic acidosis. A limitation of such a diet can be the development of hyperkalemia in patients with impaired renal K^+ excretion.
- New drugs designed to bind K^+ in the gastrointestinal tract are now available. These drugs have been shown to be effective in maintaining normokalemia in the setting of ongoing use of blockers of the renin-angiotensin-aldosterone system in patients previously intolerant of these drugs due to hyperkalemia. These drugs *may* allow patients to liberalize their diets so as to receive the benefits of a K^+-enriched diet without development of hyperkalemia.

One prevailing hypothesis is that our current diet represents a mismatch between what our body has the capability to metabolize and what we are actually consuming. The normal kidney has the capacity to maintain K^+ homeostasis in the setting of high dietary intake. As an example, serum K^+ levels are maintained in the normal range even when dietary K^+ intake is increased to approximately 15 g/d for 20 days.[7,8] This ability to maintain a normal serum K^+ concentration when challenged with large intake over a prolonged period of time suggests that humans are able to consume and excrete high K^+ loads (Table 1). The mechanism by which the kidney is able to maintain K^+ homeostasis in the setting of high intake is discussed below.

OVERVIEW OF RENAL K^+ HANDLING

K^+ is freely filtered by the glomerulus, and then mostly reabsorbed in the proximal tubule and thick ascending limb such that only a small amount reaches the distal nephron. Reabsorption in the proximal tubule is primarily through the paracellular pathway and is in rough proportion to Na^+ and water. The apical membrane Na^+-K^+-$2Cl^-$ cotransporter mediates transcellular K^+ transport in the thick ascending limb of Henle. In the early distal convoluted tubule (DCT), K^+ secretion begins and progressively increases in magnitude into the cortical collecting duct. As recently reviewed, the secretory component of K^+ handling is that which varies and is regulated according to physiological needs.[9]

The major K^+secretory mechanism in the distal nephron is electrogenic secretion through the ROMK (renal outer medullary K^+) channel. A second channel (maxi-K^+ or BK channel) also mediates K^+ secretion under conditions of increased flow. In addition to stimulating maxi-K^+ channels, tubular flow augments electrogenic K^+ secretion by diluting luminal K^+ concentration and stimulating Na^+ reabsorption through the epithelial Na^+ channel (ENaC). In part, this stimulatory effect can be traced to a mechanosensitive property by which shear stress increases the open probability of the ENaC.[10]

The biomechanical characteristics of Na^+ and K^+ transport in the distal nephron are ideally suited to buffer any increase in extracellular K^+ concentration following a K^+-rich diet. A protein-enriched meal high in K^+ content, typical of early humans, would lead to an increase in glomerular filtration rate and tubular flow.[11] Increased flow through the distal nephron increases distal Na^+

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