Potassium, Magnesium and Calcium: Their Role in both the Cause and Treatment of Hypertension

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Introduction

Hypertension remains the leading cause of cardiovascular disease (CVD) affecting approximately 1 billion individuals worldwide (1). More than 72 million Americans, or nearly 1 in 3 adults, are estimated to have hypertension but only 34 percent achieve BP control (2). Nearly 70 million more adults are at risk of developing pre-hypertension, and 90 percent of adults will probably develop hypertension, especially systolic elevations by age 65 (3). Hypertension is associated with an increased risk of mortality and morbidity from stroke, coronary heart disease, heart failure (HF), and end-stage renal disease. Over the past several years there have been minimal changes in BP diagnostic thresholds, treatment targets or in therapeutic approaches. The major focus of research remains the poor control rates of hypertensive individuals. Although evidence suggests that goals set by JNC-7 are attainable, only about one third of patients are meeting them (4,5). Poor BP control is even more of a challenge for patients with diabetes and chronic kidney disease due to the lower recommended BP goals (6). Due to its high prevalence, hypertension remains the most common reason for visits to physician’s offices and the primary reason for prescription drug use.

Diet in the Prevention and Treatment of Hypertension

Several epidemiological studies (7,8,9,10) suggest that diet plays an important role in determining BP. Dietary therapies known to lower BP include a reduced sodium intake, increased potassium intake and a diet rich in fruits and vegetables. The landmark Dietary Approaches to Stop Hypertension (DASH) trial (11,12,13,14), demonstrated that modification of diet significantly lowered BP in patients with stage 1 hypertension and high-normal BP. The DASH diet, which emphasizes fruits, vegetables, and low-fat dairy products, also lowers BP in persons with isolated systolic hypertension (15). The Seventh Report of the Joint National
Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) guidelines (16) as well as the recent American Heart Association (AHA) recommendations for the prevention and management of hypertension (17) also recognize the role that various foods and nutrients play in lowering BP. Increased potassium intake and the DASH diet are also current recommendations of the European Society of Hypertension (ESH)(18), the World Health Organization (WHO)/International Society of Hypertension (ISH)(19), and the British Hypertension Society Guidelines (20) for lowering BP.

**Potassium in the Prevention of Hypertension**

Cardioprotective effects of dietary potassium have been hypothesized as the basis for low CVD rates in populations consuming primitive diets and in vegetarians in industrialized countries (21). In isolated societies consuming diets high in fruits and vegetables, hypertension affects only 1 percent of the population, whereas in industrialized countries which consume diets high in processed foods and large amounts of dietary sodium, 1 in 3 persons have hypertension (22). In primitive diets, the daily intake of potassium is much higher while that of sodium is much lower than in the modern diet. The rates of intake for primitive cultures range from 20 to 40 mmol/day for sodium and from 150 to 290 mmol/day for potassium. In comparison, the daily rates of intake of potassium and sodium for members of industrialized societies consuming large amounts of processed foods are 80-250 mmol/d for sodium and 30-70 mmol/d for potassium. In the modern Western diet, the potassium-to-sodium intake ratio on a molar basis is usually <0.4, whereas in primitive cultures the intake ratio is >3 and closer to 10 (7).

Low potassium intake in the U.S. (<3.5 mg/d) is considered a major contributor to the prevalence of hypertension (23). Geleijnse et al.(23) calculated the population attributable risk (PAR) percentages of a low potassium intake at 17 percent for hypertension (SBP >140 mm Hg).
Therefore, if Americans were able to increase their potassium intake alone, the number of adults with known hypertension could decrease by 17 percent and increase life expectancy by 5.1 years for 12 million Americans (24). Hypertension mortality was documented at 54,707 for 2008 and 300,000 reported hypertension as an underlying cause (total mention mortality). Conservatively, over the next decade, an increase in potassium intake could save 510,000 lives.

In individuals for industrialized countries, high rates of potassium intake have been reported to be inversely related to BP (25, 26, 27, 28, 29, 30, 31, 32, 33,34) and to the incidence of stroke (27) and other cardiovascular diseases. An increase in dietary intake from approximately 60 to 80 mmol/day has been shown to be inversely and significantly related to the incidence of stroke mortality in adult women (27). A significant inverse relationship between potassium intake and the risk of stroke was also demonstrated among a study of 43,738 US men, aged 40 to 75 years old, followed up for 8 years (p = 0.007)(35). In both studies, increasing potassium intake appeared to have a direct effect on preventing strokes independent of its effect on BP (27, 35).

**Cardiovascular Benefits of Potassium**

A consistent body of evidence from observational studies (8, 27,31,36,37,38,39,40,41) and clinical trials (23,42,43,44) indicates that high levels of potassium are associated with low BP. Although the results from observational trials are relatively consistent, data from individual clinical trials have been less consistent and compelling. This may be due to the fact that most trials have been of short duration, type of potassium used may vary as well as the dose of potassium used.
Epidemiological Evidence Showing Link Between Potassium and BP

Epidemiological studies have indicated that BP is lower in populations consuming primitive (Paleolithic) diets and in vegetarians in industrialized countries. This increase in potassium intake can reduce BP and related CVD (7,8,41). For example, a population study in St. Lucia (45) suggested that an increase of only 20 to 30 mmol/d (742-1173 mg/d) of potassium in the diet could result in a 2-3 mmHg reduction of BP in a population. This potassium intake is equivalent to an increase of three servings of either fruits or vegetables per day.

The Yanomamo Indians in Brazil which consume very little sodium and follow mostly a vegetarian diet are also known for having low average BP and no hypertension. As part of the INTERSALT study, this population was found to have a very low urinary sodium excretion (0.9 mmol/24h), a mean SBP of 94.5 mm Hg and a mean DBP of 61.4 mm Hg. In addition, urinary sodium excretion showed a positive correlation and urinary potassium excretion a negative correlation to SBP (46). In the presence of low sodium intake among the Yanomamo, potassium, which was found to be related to BP in the overall INTERSALT study, was not consistently related to BP in this population. Furthermore, the Yanomamo had the lowest urinary sodium excretion (0.2 mmol.24 h) and had no increase of SBP with age (8).

Observational Data Showing Link Between Potassium and BP

Although most observational studies have demonstrated an inverse relationship between potassium intake and BP (8,27, 31,36,37,38, 39, 40,41) not all studies are consistent (25,47,48,49, 50). This may be due to the high degree of inter-correlation (multicollinearity) among dietary factors, such that it is difficult to separate the effect of potassium from other nutrients found in potassium rich foods (31). In addition, since many studies have lasted approximately four years and include populations with diverse dietary patterns, observational
data provides insight into the long term effects of habitually consuming a diet high or low in potassium.

The INTERSALT study (51) also provided evidence that potassium intake (as measured by 24h urinary potassium excretion), is an important determinant of population BP, independent to that of sodium. In INTERSALT, an inverse association between urinary excretion and BP levels was found across diverse populations. More specifically, a 1173-1564 mg increase in potassium intake was associated with an approximately 2-3 mmHg reduction of SBP on a population level (51).

While most intervention studies have focused on high levels of potassium intake, observational studies show that even increasing potassium by 750 - 1000 mg/d can lower BP by 2-3 mmHg (8, 27,31,36,37,38,39,40,41). This translates into an important cardiovascular benefit in terms of reducing stroke and other CVD events.

**Meta-Analyses and Dose Response**

Several meta-analyses (23,42,43,44) show a significant reduction in BP with potassium supplementation (Table I). An earlier meta-analysis by Cappuccio and MacGregor (42) of 19 clinical trials examining the effect of potassium supplementation on BP found that oral potassium supplements significantly lowered both systolic blood pressure (SBP) and diastolic blood pressure (DBP) (5.9 mm Hg and 3.4 mm Hg, respectively). The average amount of potassium given was 86 mmol/day (primarily as potassium chloride, KCl) with an average duration of 39 days. The magnitude of BP lowering was greater in patients with hypertension (8.2/4.5 mm Hg) and more pronounced the longer the duration of treatment (p<0.05 and p<0.01 for systolic and diastolic BP, respectively).
A meta-analysis of 33 randomized controlled trials (RCTs) performed by Whelton et al. (43) also documented that potassium supplementation significantly lowered BP. This meta-analysis included 12 trials in normotensive individuals and 21 in hypertensive patients, with a duration ranging from 4 days to 3 years (median 5 weeks). On average, a typical dose of 60 to 120 mmol/day (2.5 to 5.0 grams/day) (median 75 mmol/d) of supplemental potassium reduced systolic and diastolic BP by 4.4 and 2.5 mm Hg in hypertensives and by 1.8 and 1.0 mm Hg in normotensives. Although most studies used potassium chloride, some used diet and potassium citrate and bicarbonate as a source of potassium (60 mmol of potassium is equivalent to 4.5 grams of potassium chloride, 6 grams of potassium bicarbonate or 20 grams of potassium citrate). The BP lowering effect was more pronounced in blacks compared with whites and those consuming a diet high in sodium chloride.

A metaregression analysis by Geleijnse et al. (23) provided further evidence of increased BP sensitivity to potassium in hypertensives. In this analysis, an increased potassium intake (median: 44 mmol/d, or 1.7 g) resulted in a mean BP lowering of 2.4 mm Hg for SBP and 1.6 mm Hg for DBP. These estimates are somewhat conservative compared to the earlier meta-analyses by Whelton et al. (43) (3/2 mm Hg) and Cappuccio and MacGregor (42) (6/3 mm Hg) and may be due to the exclusion of short-term trials (<2 weeks duration) from this study. As with the previous meta-analyses, the BP response was greater in hypertensives than normotensives (3.5/2.5 mmHg vs. 0.97/0.34 mmHg, respectively) which was of borderline statistical significance.

A more recent meta-analysis of 5 randomized controlled trials (RCTs) conducted by Dickinson et al. (44) showed that potassium supplementation resulted in large, but statistically non-significant reductions in both SBP (3.9 mm Hg) and DBP (1.5 mm Hg). Overall reductions
in BP were smaller when one trial in an African population was excluded due to a very high baseline BP. Further sensitivity analysis limited to two high quality RCTs also showed non-significant reductions in BP. Due to the small number of participants in these two trials, the short duration of follow-up (≥ 8 weeks), and substantial heterogeneity between trials, evidence concerning the effect of potassium supplementation on BP was found to be inconclusive (44).

All of these meta-analyses reveal the dose response relationship between BP lowering and potassium intake. Significant BP lowering with doses of potassium in the range of 1900-4700 mg/d (49-122 mmol/d) resulted in BP lowering of approximately 2-6 mm Hg for DBP and 2-4 mm Hg for SBP. The high variability between these results reflects the variability observed in different studies. In addition, the effect of potassium on BP is influenced by pretreatment BP level, age, race, gender, comorbid conditions, intake of sodium, magnesium, calcium or other ions, diet, exercise, weight, type of potassium used, concomitant medications and duration of use. A summary of the findings of all meta-analyses on the effects of potassium on BP to date is given in Figure 1.

**DASH Eating Plan**

The Dietary Approaches to Stop Hypertension (DASH) study (11) was a controlled feeding study of 11-weeks duration designed to assess the effects of modifying whole diets on BP. The DASH trial demonstrated that a diet rich in fruit and vegetables and low-fat dairy products and reduced saturated and total fat can result in a clinically significant reduction in BP, compared to the typical American diet (14). The reduction in BP began within two weeks of feeding and was maintained for the following six weeks. Among normotensive individuals, this diet reduced SBP and DBP by 3.5 and 2.1 mmHg, respectively (Figure 2). A subgroup analysis of the DASH trial also found that the BP lowering effects were more pronounced in
hypertensives (11.4 and 5.5 mmHg) and in blacks (12). Although potassium intake was increased by 1447 - 2776 mg/d through increased consumption of fruit and vegetables, reductions in BP cannot be attributed to potassium alone, as the diet was also rich in calcium, magnesium and other nutrients.

In a subgroup analysis of patients with Isolated Systolic Hypertension (ISH)(15), the DASH diet was found to be as effective as first-line antihypertensive therapy for the treatment of ISH. Svetkey et al.(3) further demonstrated that patients with stage 1 hypertension, a reduced sodium intake in combination with the DASH diet improved BP control. Among DASH-Sodium trial participants, sustained reductions in BP were observed over a one year period despite increased sodium intake (52).

Other Clinical Trial Evidence

Overall, conflicting results regarding the effects of potassium supplementation on BP have been reported in clinical studies (53, 54,55,56,57). More recent trials, however, have demonstrated results consistent with that of the meta-analysis by Whelton et al.(43) (Table II). Gu et al. (58) found that moderate potassium supplementation (60 mmol KCl) taken for 12 weeks resulted in a substantial reduction in SBP, but not DBP, in a Chinese population. Similarly, Kawano et al. (59) documented that a 4-week potassium supplementation period (during which 64 mmol/d of potassium was given as slow-release KCl) resulted in small but significant reductions in office, home and 24-h BP in Japanese men and women. Naismith and Braschi (60) further examined the effect of low dose potassium supplementation on BP and found that 24 mmol/d of slow-release KCl administered for six weeks resulted in significant reductions in mean arterial pressure (MAP), and DBP in healthy volunteers.
Beneficial Effects of Potassium on CVD

High potassium intake may have other beneficial effects independent of its effect on BP, such as reducing the risk of stroke and cardiac arrhythmias. For example, an increase in dietary intake of potassium, from approximately 60 to 80 mmol/d, has been shown to be inversely and significantly related to the incidence of stroke mortality in women (27). A similar pattern was demonstrated in U.S. men, where the multivariate relative risk of stroke of any type for men in the top fifth of potassium intake (median intake, 4.3 g/d) versus those in the bottom (median, 2.4 g/d) was 0.62 (35).

Since increasing potassium intake lowers BP, it is difficult to distinguish between the effects of potassium on BP mediated by BP lowering alone from those mediated by a direct effect of potassium. A direct protective effect of potassium on stroke is suggested by studies in the rat model, in which a high potassium intake was associated with a large reduction in stroke mortality (61) . This was observed even when BP was precisely correlated with high and low potassium intakes. Epidemiologic studies further demonstrate that a high potassium intake is related to a lower risk of stroke and some of this effect may be independent and additive to the effect of potassium on BP (62).

Several observational studies have also found a link between potassium intake and risk reduction in stroke. In a 12 year prospective study by Khaw and Barret-Connor, an increase in potassium intake of 10 mmol/d among 859 men and women resulted in a 40 percent reduction in stroke mortality (27). This association was found to be independent of other dietary variables and CVD risk factors, such as BP. In two additional studies with much larger cohorts, the US health professional men (43,738 men) (35) and the US nurses (85,764 women) (63), a high potassium intake also resulted in a lower risk of stroke. Moreover, the US professional men
study (35) demonstrated a dose-response relationship between potassium intake and risk of stroke, whereas the US nurses study (63) showed a borderline significant association between the intake of potassium and stroke after adjusting for confounding variables.

For arrhythmias, hypokalemia results in prolonged repolarization, which underlies the pathologic mechanism of torsade de points, especially in patients with ischemic heart disease, HF, and left ventricular hypertrophy. Increasing serum potassium concentrations improves repolarization in patients with inherited or acquired long QT syndromes (64). The risk of arrhythmia is further increased in hypertensive patients taking non-potassium sparing diuretics. In the Multiple Risk Factor Intervention Trial (MRFIT) (65), among the 1403 hypertensive men taking diuretics, a 28 percent increase in ventricular arrhythmia was observed for every one mmol/d decrease in serum potassium.

**Mechanisms by which Potassium Lowers BP**

The homeostasis of sodium and potassium plays an important role in endothelium-dependent vasodilatation (66). Sodium retention decreases the synthesis of nitric oxide, an arteriolar vasodilator elaborated by endothelial cells, and increases the plasma level of asymmetric dimethyl l-arginine, an endogenous inhibitor of nitric oxide production (67). Sodium restriction induces the opposite effects.

A diet rich in potassium as well as increases in serum potassium, even within the physiologic range, cause endothelium-dependent vasodilation by hyperpolarizing the endothelial cell through stimulation of the sodium pump and opening potassium channels (68,69). Endothelial hyperpolarization is transmitted to the vascular smooth-muscle cells, resulting in decreased cytosolic calcium, which in turn promotes vasodilatation. In contrast, experimental potassium depletion inhibits endothelium dependent vasodilatation (68).
In addition to increased vasodilatation, other proposed mechanisms by which potassium can influence BP include natriuresis, modulation of baroreceptor sensitivity, reduced vasoconstrictive sensitivity to norepinephrine and angiotensin II, increased serum and urinary kallikrein, increased sodium/potassium ATPase activity and alteration in DNA synthesis and proliferation in vascular smooth muscle and sympathetic nervous system cells (70,71,72,73).

**Dietary Guidelines for Potassium**

Recognizing a high potassium intake has the potential to lower BP, several national and international guidelines have incorporated an increased dietary intake of potassium as part of their recommendations for the prevention and treatment of hypertension. Maintaining an adequate intake of dietary potassium (>90 mmol [3500 mg] per day) has been recommended for the primary prevention of hypertension by the National High Blood Pressure Education Program Coordinating Committee (JNC 7) (16). The Institutes of Medicine have recommended a sodium intake below 65 mmol/d (3.8 g per day) and an increase in potassium to 120 mmol per day (74). In 2006, the American Heart Association (AHA) issued new guidelines suggesting an increase in potassium intake to 120 mmol/d (4.7 g/d), which is the level provided in the DASH diets (17).

International guidelines have followed suit. The Canadian Hypertension society recommends that the daily dietary intake of potassium should be 60 mmol or more, since this intake has been associated with a reduced risk of stroke-related mortality (75,76). The most recent European Society of Hypertension guidelines also support an increased potassium intake based on the DASH diet (18). In addition, the 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement recommends a diet high in fruits and vegetables, a reduction of dietary sodium intake, and increased dietary potassium intake for
reducing the incidence of hypertension (19). Current sources of potassium in the diet are listed in Table III.

**Effect of Magnesium on BP**

Epidemiologic, observational, and clinical trial data show that a diet high in magnesium (at least 500 to 1,000 mg/d) lowers BP, but the results are inconsistent (57,71,77,78,79,80,81,82,83,84,85,86). In most epidemiologic studies, an inverse relationship has been shown between dietary magnesium intake and BP (70,79,83,84,87,88,89,90,91,92). In a study of 60 patients with essential hypertension given magnesium supplements over eight weeks, significant reductions in ambulatory, home and office BP were observed (82). However, in the Trials Of Hypertension Prevention (TOHP) -1 trial, magnesium was found to have a small and insignificant effect on BP (57).

Witteman et al (93) further demonstrated that treatment of 91 middle-aged to elderly women with mild to moderate hypertension using magnesium asparate -HCl (20 mmol/d or 485 mg of magnesium) for six months significantly decreased SBP and DBP by 2.7 mm Hg (p<0.18) and 3.4 mm Hg (P<0.003), respectively. In addition, BP response was not associated with baseline magnesium level.

The mechanism by which magnesium lowers BP is by acting like a natural calcium-channel blocker (CCB). Specifically, magnesium competes with sodium for binding sites on vascular smooth muscle cells, increases prostaglandin E, binds to potassium in a cooperative manner, and induces endothelial-dependent vasodilation and BP reduction (77,80,87,92,94,95). Magnesium is more effective in reducing BP when administered as multiple minerals in a natural form as a combination of magnesium, potassium and calcium than when given alone (71). Also,
administration of magnesium chelated to an amino acid improves absorption and reduces diarrhea.

Magnesium is also an essential co-factor for the delta-6-desaturase enzyme, which is the rate-limiting step for the conversion of linoleic acid (LA) to gamma-linolenic acid (GLA) (87,96,97,98). GLA in turn elongates to form DGLA (dihomo-gamma-linoleic acid), the precursor for prostaglandin E\textsubscript{1} (PGE\textsubscript{1}), both a vasodilator and platelet inhibitor (87,96). Low magnesium states lead to insufficient amounts of PGE\textsubscript{1}, causing vasoconstriction and increased BP (87; 97).

In addition to BP, magnesium regulates intracellular calcium, sodium, potassium and pH as well as left ventricular mass, insulin sensitivity and arterial compliance (91,92). Research involving new imaging techniques such as P-Nuclear Magnetic Resonance (NMR) and Magnesium-specific ion-selective electrodes (ISE), which measure intracellular and extracellular free concentrations of magnesium, will further enhance our understanding of the role of magnesium in hypertension (91,92).

**Calcium**

Population studies (77,79) show that high intakes of calcium from the diet are linked to low BP, whereas clinical trials (78,99,100) using calcium supplements are less compelling. A high dietary intake of calcium has been shown to be associated with both a decrease in BP and risk of developing hypertension (79,101). In two studies, individuals taking more than 800 mg/d of calcium versus 400 mg/d achieved a 23 percent reduction in risk of developing hypertension (79,93). Ascherio et al. (36) also demonstrated in over 30,000 normotensive male health professionals aged 40 to 75 years old, that those consuming less than 250 mg/d of magnesium
had a 50 percent greater chance of developing hypertension than men who consumed 400 mg/d or more.

In addition, a meta-analysis of the effects of calcium supplements on BP showed a reduction in SBP and DBP of 4.3 mm Hg and 1.5 mm Hg, respectively, in hypertensive patients (102,103, 104). Calcium containing foods were found to be more effective in lowering BP than calcium supplements (102,104). Karanja et al. (105) compared the effects of calcium carbonate to calcium in the diet and found that significant increases in magnesium, riboflavin and vitamin D correlated with calcium intake in the dietary group. Like magnesium, a synergistic effect on BP reduction occurs when calcium is administered in combination with other minerals and vitamins compared to calcium alone (11,13,106).

In contrast, TOHP-1 tested the separate effects of micronutrients on BP in hypertensive patients with a DBP of 80-89 mm Hg. Increases in dietary calcium and magnesium had only a small effect on BP, whereas restriction of sodium intake and weight reduction resulted in significant decreases in BP (57).

The BP lowering response to calcium depends on the hypertensive subtype being studied (71,101,107). Patients demonstrating the greatest reduction in BP with calcium supplements include blacks, the elderly, women with pregnancy-induced hypertension, postmenopausal women, patients with low-renin hypertension, sodium-sensitive hypertensives, those with a high sodium intake and type II diabetes mellitus (71,101,107).

Resnick (108) has offered two possible mechanisms for the various responses to calcium supplementation. One is a salt-sensitive, low renin and calcium-antagonist sensitive, dependent upon impaired uptake of calcium from the extracellular space. The second is a salt-sensitive, renin-dependent and calcium-antagonist insensitive, dependent on increased calcium released
from intracellular sites. A reduction in calcium in the diet may cause calcium depletion from all membrane storage sites, resulting in less stability of the vascular smooth muscle cell membrane (108, 109).

When present in optimal concentrations, calcium stabilizes vascular cell membranes, inhibits its own entry into cells, and reduces vasoconstriction (70,97,110). Calcium works in combination with other ions such as sodium, potassium and magnesium to provide an ionic balance to the vascular membrane, vasodilation and resulting reduced BP (87,111).

**The “Ionic Hypothesis” of Resnick**

The “ionic hypothesis” of hypertension and other metabolic disorders by Resnick (112) is characterized by the following: (1) increased intracellular free calcium and reduced intracellular free magnesium determine the amount of vasoconstriction or vasodilation (113,114); (2) an elevated glucose and low density lipoprotein - cholesterol (LDL-C) increase the intracellular calcium and/or lower intracellular magnesium in vascular smooth muscle cells (115,116); (3) hypertension, insulin resistance and type II diabetes mellitus are associated with an increased intracellular calcium and decreased intracellular magnesium, which all respond to weight loss (108,117,118) (4) weight loss also decreases intracellular calcium levels (119); (5) dietary calcium suppressible hormones like PTH, 1,25 vitamin D are vasoactive and promote calcium uptake in vascular smooth muscle cells and cardiac muscle (120,121,122); (6) the higher the PTH concentration, the greater the fall in BP, and the greater the reduction in PTH and 1,25 vitamin D, the greater the BP reduction)(106); (7) individuals with salt-sensitive and calcium-sensitive hypertension have elevated intracellular calcium PTH and 1,25 vitamin D, but low intracellular magnesium (123); (8) dietary calcium reverses abnormal calcium indices and lowers
BP (124); and (9) dietary potassium reduces urinary calcium excretion and 1,2 vitamin D plasma levels (125); and (10) magnesium intake reduces tissue calcium accumulation (126).

In summary, the overall effect of diet on BP is determined by the net contribution of various nutrients on cytosolic free minerals such as potassium, calcium and magnesium. Steady-state mineral concentrations are determined by both the direct ionic effects on glucose or calcium and the ionic effects on hormones (PTH, 1,25 vitamin D) (106).

Conclusion

Americans consume double the sodium and about half of the potassium that is recommended by current guidelines. In fact, the average US dietary intake of potassium is 45 mEq/d with a potassium to sodium ratio of less than 1:2 (77). This is far less than the recommended intake of 650 mEq/d of potassium, with a potassium/sodium ratio of over 5:1 (77). As epidemiologic studies in the Yanomamo Indians suggest, if we were to achieve the correct potassium/sodium ratio through dietary means, there would be less hypertension and CVD in the population as a whole. A high intake of potassium, magnesium, and calcium through increased consumption of fruits and vegetables is important for the prevention of hypertension and major public health problems such as coronary heart disease and stroke.
References


(65) Cohen JD, Neaton JD, Prineas RJ, Daniels KA. Diuretics, serum potassium and ventricular arrhythmias in the Multiple Risk Factor Intervention Trial. Am J Cardiol 1987 September 1;60(7):548-54.


Table I. Summary of Meta-Analyses of Potassium Trials.

<table>
<thead>
<tr>
<th>Meta-analysis</th>
<th>n trials</th>
<th>Intervention</th>
<th>Average Duration</th>
<th>Mean BP lowering SBP/DBP 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cappucio and McGregor, 1991 (42)</td>
<td>19</td>
<td>100 mmol/d diet; 48-120 mmol/d KCl; 66 mmol/d K Glu + Cit</td>
<td>39 d</td>
<td>5.9/3.4 [-6.6 to -5.2] [-4.0 to 2.8]</td>
</tr>
<tr>
<td>Whelton et al., 1997 (43)</td>
<td>33</td>
<td>100-200 mmol/d diet; 60-120 mmol/d KCl; 120 mmol/d K Cit + Bicarb</td>
<td>5 wk</td>
<td>3.1/2 [-1.9 to -4.3] [-0.5 to -3.4]</td>
</tr>
</tbody>
</table>
Forms of K⁺ include KCl, citrate (Cit), gluconate (Glu), and bicarbonate (Bicarb). One milliequivalent (Meq) or millimole (mmol) of K⁺ equals 39.09 milligrams (mg).  

BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure, CI = confidence interval.

### Table II. Other Clinical Trial Evidence of the Effect of Potassium on Blood Pressure.

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Subjects</th>
<th>Intervention</th>
<th>Avg Duration</th>
<th>Mean BP Lowering SBP/DBP (mm Hg)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appel et al., 1997[11]</td>
<td>459</td>
<td>DASH diet</td>
<td>8 wk</td>
<td>3.5/2.1 Non-HTN 11.4/5.5 HTN</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Dickinson et al., 2006[44]</td>
<td>5</td>
<td>&gt;100 mmol/d diet; 48-120 mmol/d KCl; 120 mmol/d - K Cit + Bicarb</td>
<td>≥8wk</td>
<td>11.2/5.0 to 25.2 to 2.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.0 to 12.5 to 2.4</td>
<td>&lt;.001</td>
</tr>
</tbody>
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**Table III. Major Dietary Sources of Potassium.**

<table>
<thead>
<tr>
<th>Source</th>
<th>mg/kg potassium</th>
</tr>
</thead>
<tbody>
<tr>
<td>milk</td>
<td>1.4 - 1.5</td>
</tr>
<tr>
<td>Food</td>
<td>Percentage</td>
</tr>
<tr>
<td>--------------</td>
<td>------------</td>
</tr>
<tr>
<td>Fruit and vegetables</td>
<td>0.8 - 4.4</td>
</tr>
<tr>
<td>Fish</td>
<td>1.9 - 3.5</td>
</tr>
<tr>
<td>Shellfish</td>
<td>0.3 - 4.2</td>
</tr>
<tr>
<td>Beef</td>
<td>2.0 - 3.5</td>
</tr>
<tr>
<td>Chicken and turkey</td>
<td>3.0</td>
</tr>
<tr>
<td>Liver</td>
<td>2.5 - 4.2</td>
</tr>
</tbody>
</table>

Ref: Food and Nutrition Board, Institute of Medicine, National Academies of Science. (74)
Figure 1. Overview of meta-analyses of studies investigating the blood pressure lowering effects of potassium. SBP = systolic blood pressure; DBP = diastolic blood pressure.
Figure 2. Mean Systolic and Diastolic Blood Pressures at baseline and during each intervention week, according to diet, for 379 subjects with complete sets of weekly blood-pressure measurements. Reprinted with permission from Apple LJ, Moore, Obarzanek, et al. N Engl J Med 1997;336:1117-1124.