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Relationship of Dietary Sodium, Potassium and The Sodium-to-Potassium Ratio to Blood Pressure

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ABSTRACT

Blood pressure (BP) is the major risk factor for cardiovascular diseases and is one of the leading causes of death in the US. Dietary modification, the cornerstone of lifestyle interventions, is recommended for prevention and treatment of hypertension. Current clinical guidelines recommend reducing dietary sodium and increasing potassium intake as effective interventions for BP management. Recent evidence suggests that the dietary sodium-to-potassium ratio may be a stronger and a more reliable determinant of BP, as this ratio takes into account both sodium and potassium intake. Dietary recommendations to decrease sodium-to-potassium ratio by modest reduction in sodium and increase in potassium intake may be more effective for BP management than reducing dietary sodium alone. The objectives of the current review were to evaluate the evidence studying the relationship of dietary sodium, potassium and sodium-to-potassium ratio with changes in BP, and to assess whether dietary sodium-to-potassium ratio would be a more effective and practical dietary factor to consider for prevention and treatment of hypertension.

Keywords

Dietary sodium-to-potassium ratio, Sodium, Potassium, Systolic blood pressure, Diastolic blood pressure.

Introduction

Hypertension is a major risk factor for cardiovascular diseases and is one of the leading causes of death in the US [1,2]. Healthful dietary modification is the cornerstone of lifestyle interventions and is recommended as the first line of treatment for lowering blood pressure (BP) [2,3]. The 2017 AHA clinical guidelines recommend reducing dietary sodium and increasing potassium intake as the most effective dietary interventions for BP management [2]. Emerging evidence [4-7] suggest that interventions focused on lowering dietary sodium-to potassium ratio (Na/K) with a modest decrease in sodium and an increase in potassium intake is more effective and practical for prevention and treatment of hypertension than restricting sodium alone. The purpose of this review is to evaluate and provide a summary of the evidence exploring the relationship of dietary sodium, potassium and sodium-to potassium ratio to BP.

Dietary Sodium Intake and BP

Reduced dietary sodium intake has been consistently shown to lower BP in adults with and without elevated BP [8-13]. The Intersalt [8] population study was one of the earliest studies to demonstrate a positive relationship between dietary sodium intake and BP. This study included 10,074 men and women aged 20-59 years from 32 countries. The mean 24-hr urinary sodium excretion was 156.0 mmol (range 0.2 to 242.1 mmol). The estimated dietary sodium intake range, based on 24-hour urinary sodium excretion, was 164.2 to 182.4 mmol/day (3,777 to 4,195 mg/day), assuming 90 to 95% of dietary sodium is excreted via the urine [9]. The 24-hour urinary sodium excretion has been validated as the most reliable indicator of dietary sodium intake [14]. 24-hour urinary sodium excretion was positively and linearly associated with elevated systolic BP (SBP, $p<0.05$), after adjusting for potential confounders. In this study, a reduction of 100 mmol (2,300 mg) urinary sodium was associated with a within-population reduction of 3.1 mm Hg SBP and 0.1 mm Hg diastolic BP (DBP), and a cross-population reduction of 4.5 mm Hg SBP and 2.3 mm Hg DBP [8].

The 2014 National Health and Nutrition Examination Survey (NHANES) study [9] investigated the association between urinary sodium excretion and blood pressure in 766 men and women aged

20-69 years. Of those included in the study, 51% had hypertension or elevated BP. The mean 24-hour urinary sodium excretion was 162.6 mmol for those with hypertension and 159.0 mmol for normotensive adults. The mean estimated dietary sodium intake range, based on 24-hour urinary excretion, was 171.2 to 180.7 mmol/day (3,938 to 4,156 mg/day) for hypertensive and 167.4 to 176.7 mmol/day (3,850 to 4,064 mg/day) for normotensive adults. A direct linear association ($p<0.05$) was observed between 24-hour urinary sodium excretion and elevated systolic and diastolic blood pressure, after adjusting for multiple confounders. A reduction of 4.58 mm Hg SBP and 2.25 mm Hg DBP was associated with each 43 mmol (1,000 mg) decrease in 24-hour urinary sodium excretion.

Three well-controlled meta-analyses including randomized control trials (RCT) [10-12] investigated the effects of lowering dietary sodium on BP. He et al. [10] included 34 RCTs, which had a total of 3,230 participants. The median age was 50 years and the study duration ranged between 4 weeks and 3 years. The mean decrease in urinary sodium excretion after intervention was 75 mmol/day or 1725 mg/day (range 40 - 118 mmol/day). A decrease of 100 mmol (2,300 mg) urinary sodium was associated with a reduction of 5.8 mm Hg SBP, after adjusting for confounders. In the sub-group analysis with hypertensive patients (999 participants; 22 trials) and normotensive individuals (2,240 participants; 12 trials), a decrease of 100 mmol (2,300 mg) urinary sodium was associated with a greater reduction of 10.8 mm Hg SBP in hypertensive compared to 4.3 mm Hg SBP in normotensive individuals. DBP was not significantly associated with change in urinary sodium excretion in this study.

The meta-analysis study by Aburto et al. [11] included 36 RCT with a total of 5,508 participants. The duration of the studies ranged from 4 weeks to 3 years. The meta-regression analysis showed a decrease in SBP by 3.47 mm Hg and diastolic BP by 1.81 mm Hg, when dietary sodium intake was < 87 mmol/day (< 2,000 mg/day) compared with intakes ≥ 87 mmol/day (≥ 2,000 mg/day), after adjusting for confounders. Subgroup analysis showed a greater reduction of 4.06 mm Hg SBP in hypertensive patients (n=1,487) compared with a reduction of 1.38 mm Hg in normotensive (n=3,263) individuals, with lower sodium intake. In this meta-analysis, dietary sodium effect on BP was determined based on only two levels of sodium intake (less or greater than 87 mmol/day).

The third meta-analysis included 133 RCT [12] and demonstrated the effects of dietary sodium reduction on BP based on baseline BP stratification. This study included normal, pre-hypertensive, and hypertensive individuals; and showed a linear, dose-response reduction in BP only in hypertensive participants with baseline BP in the highest 25th percentile (BP >131 mm/78 mm Hg). The dose response reduction was 7.7 mm Hg SBP and 3.0 mm Hg DBP for each 100 mmol sodium reduction. Sodium reduction did not have a significant effect on SBP (-1.46 mm Hg/100 mmol) or DBP (-0.07 mm Hg/100 mmol) when baseline BP was <75th percentile (≤ 130/78 mm Hg).

An interventional study by Juraschek et al. [13] investigated the impact of reduced dietary sodium intake on blood pressure in adults with elevated BP, who were not taking any anti-hypertensive medications. The 412 adult participants were randomized to a control diet or the Dietary Approaches to Stop Hypertension (DASH). Both groups had three sodium levels: low (50 mmol or 1,150 mg), intermediate (100 mmol or 2,300 mg) and high (150 mmol or 3,450 mg) at 2,100 kcal/day. The mean age of the participants was 48 years and the duration of the study was 4 weeks. The results showed a significant reduction of SBP when sodium intake was reduced from high to low sodium (a reduction of 100 mmol or 2,300 mg sodium), in both the control and DASH diet groups. The reduction in SBP was stratified by baseline BP, and were -3.20, -8.56, -8.99 and – 7.04 mm Hg for individuals with baseline SBP of <130, 130-139, 140-140 and >150 mm Hg, respectively in control diet. With DASH diet, the reduction in SBP were -0.88, -3.29, -4.90, and -10.41 in the above strata of baseline SBP. The magnitude of reduction in SBP with reduced sodium intake in control and DASH diet was greater when baseline SBP was > 130 mm Hg.

These studies [8-13] demonstrate that a modest dietary sodium reduction can lead to a clinically significant reduction in SBP. The effect of sodium reduction on BP was more pronounced in hypertensive adults with elevated baseline BP (> 130 mm Hg SBP) compared to those with BP < 130 mm Hg. There is insufficient evidence to recommend restricting dietary sodium intake to < 100 mmol/day (<2,300 mg/day) for BP control.

Dietary Potassium Intake and BP

Increased dietary potassium intake has been consistently shown to lower BP [15-17]. The Intersalt study [15] showed a significant inverse relationship ($p<0.05$) between dietary potassium intake (estimated based on validated 24-hour urinary potassium excretion) and BP. The mean 24-hour urinary potassium excretion was 55.2 mmol (range 23.4 – 81.1 mmol) and estimated mean dietary potassium intake was 69.0 mmol/day (2,698 mg/day), assuming 80% of dietary potassium is excreted via urine [9]. In this study, an increase of 15 mmol (600 mg) dietary potassium intake was associated with a significant reduction of 1.0 mm Hg SBP ($p<0.05$).

The 2014 NHANES study [9] also demonstrated the benefits of increased dietary potassium intake on BP. The mean 24-hr urinary potassium excretion was 51.0 mmol/day for hypertensive and 55.1 mmol/day for normotensive adults. The mean estimated dietary potassium intake was 63.8 mmol/day (2,493 mg/day) for hypertensive and 68.9 mmol/day (2,694 mg/day) for normotensive adults. This study showed a significant inverse relationship ($p<0.05$) between 24-hr urinary potassium excretion and BP. A significant reduction ($p<0.05$) of 3.72 mm Hg SBP for each 25 mmol (1,000 mg) increase in urinary potassium excretion was seen.

A meta-analysis study of RCT by Aburto et al. [16] provided further evidence for the positive effects of increased dietary

potassium intake on BP. This large, comprehensive study included 22 RCTs (1,606 participants) and looked at the effect of dietary potassium supplementation on BP. The achieved potassium intake in the intervention group ranged from <90 mmol to >155 mmol/day and the achieved difference in potassium intake between intervention and control groups ranged from <30 mmol to >60 mmol/day. Increased potassium intake in the intervention group significantly reduced mean SBP by 3.49 mm Hg and mean DBP by 1.96 mm Hg, compared to control group. Subgroup analysis based on achieved potassium intake showed that 90-120 mmol/day (3,500 – 4,700 mg/day) potassium intake resulted in the largest reduction of 7.2/4.0 mm Hg (SBP/DBP) compared to achieved potassium intakes of <90 mmol/day (3.7/1.4 mm Hg reduction), 120-155 mmol/day (1.7/0.83 mm Hg reduction) and >155 mmol/day (3.0/1.8 mm Hg reduction). Further, potassium supplementation resulted in greater reduction of 5.3/3.1 mm Hg in adults with hypertension (N=818) compared to 0.09/0.56 mm Hg reduction in normotensive adults (N=757). Based on these data, dietary potassium intake of 90-120 mmol (3,500 – 4,700 mg/day) would be the optimal intake for BP management.

A meta-analysis study by Binia et al. [5] explored the effect of dietary potassium supplementation in normotensive and hypertensive participants, who were not taking antihypertensive medications. This study included 15 RCTs and a total of 917 participants; 329 participants were normotensive, 400 were hypertensive and 188 were mixed population (either normotensive or hypertensive). The duration of the trials ranged from 4 weeks to 12 weeks. Potassium supplementation ranged from 40 – 120 mmol/day with most of the studies having 60-65 mmol/day potassium intervention. Potassium supplementation significantly reduced SBP by 4.7 mm Hg and DBP 3.5 mm Hg, compared to baseline in all participants. The effect was greater in hypertensive participants with a reduction 6.8 mmHg SBP and 4.6 mm Hg DBP. Further, urinary potassium excretion of 60 – 120 mmol (2,300 – 4,700 mg/day), corresponding to dietary potassium intake between 75 mmol (2,900 mg) and 125 mmol (4,900 g), resulted in highest BP reduction. Based on these estimates, an increase of each 75 mmol (2,900 mg) of urinary potassium, corresponding to 90 mmol (3,500 mg) dietary potassium, would reduce SBP by 2.25 mm Hg.

Filipini et al. [17] performed a meta-regression analysis to investigate the effect of potassium supplementation on BP in hypertensive subjects. The study included 25 RCTs with 1,163 participants with hypertension. The duration of the RCT included were ≥ 4 weeks. The median amount of supplemented potassium was 64 mmol/day (2,500 mg/day) with a range of 25 – 250 mmol/day (1,000 – 9,800 mg/day). SBP decreased by 4.48 mm Hg and DBP decreased by 2.96 mm Hg after potassium supplementation. Sub-group analysis showed a greater reduction of SBP and DBP with potassium supplementation when sodium intake was higher; SBP and DBP decreased by 6.13 and 5.30 mm Hg, respectively, when sodium intake was ≥ 4 g/day, compared to a decrease of 3.06 mm Hg SBP and 1.60 mm Hg DBP when sodium intake was < 4g/day.

Two interventional studies [18,19] compared BP reduction from using potassium supplements provided as chloride or citrate. Most RCT used potassium chloride as the source for potassium supplementation. However, potassium in most foods occurs in the citrate salt form [18]. He et al. [18] performed a randomized crossover study in which 14 hypertensive individuals consumed 96 mmol/day (3,700 mg/day) potassium in the form of potassium chloride or potassium citrate for one week in a cross-over design. After both interventions, potassium chloride and potassium citrate had similar, significant effects on BP, with a mean SBP and DBP reduction of 1.6 mm Hg and 0.6 mm Hg reduction, respectively ($p<0.05$). However, another randomized, placebo-controlled, crossover study [19] showed that potassium chloride was more effective than potassium citrate supplement for BP reduction. In this study, 30 patients with pre-hypertension and stage 1 hypertensive were provided three forms of potassium supplements: potassium chloride, potassium citrate, or potassium magnesium citrate. Each supplement provided 40 mEq (40 mmol or 1,600 mg) of potassium over 4 weeks in a cross-over design. After intervention, potassium chloride significantly reduced 24-hour ambulatory SBP by 5 mm Hg ($p<0.05$), whereas potassium citrate and potassium magnesium citrate had no effect on BP.

These studies demonstrate that increasing potassium intake to achieve a dietary potassium intake in the range of 75 to125 mmol (2,900 – 4,700 mg/day) can effectively lower BP. However, the effect of potassium on BP reduction was influenced by sodium intake, baseline BP status, and the form of potassium supplemented.

Dietary Sodium-to-Potassium Ratio and BP

Emerging evidence shows that the ratio of dietary sodium-to-potassium may be a strong and a robust predictor of BP as it takes into account both the important electrolytes that regulate blood pressure. The combined effect of increasing dietary potassium and reducing sodium intake exert synergistic effects on reducing BP and would be a more effective and practical approach to achieve optimal BP than reducing sodium or increasing potassium intake alone.

The Intersalt study [15] was one of the earliest to demonstrate the relationship between the Na/K and BP reduction. In this study, a decrease in urinary Na/K from 3.09 (typical dietary ratio in the US) to 1.0 resulted in a reduction of 3.36 mm Hg SBP ($p<0.05$). These results showed that dietary Na/K was a reliable predictor of SBP.

The INTERMAP (International Study of Macro- and Micronutrients and Blood Pressure) study [4,20] used a nutrient-wide approach to identify and validate nutrients that significantly improved BP. The INTERMAP study included data from 4,680 participants aged 40-59 years and validated it against the NHANES in order to study the association of individual nutrients with changes in BP. In this study, Na/K was significantly and linearly associated with SBP and DBP ($p<0.05$). SBP and DBP decreased by 3.1 and 1.7 mm Hg respectively, for each 2 standard deviation (SD) decrease in the urinary Na/K. Further, the Na/K ratio relationship with BP was

independent of BMI or other dietary factors. Urinary sodium alone was also positively associated with BP, but its effect was attenuated by BMI. Urinary sodium was not associated with SBP (0.8 mm Hg reduction in SBP for every 2 SD decrease in urinary sodium, $p>0.05$), when adjusted for BMI. These findings showed the Na/K to be a stronger and a more reliable predictor of BP compared to urinary sodium alone.

The 2014 NHANES study [9] also demonstrated a significant association of urinary Na/K with BP. In this study, each 0.5-unit reduction in the molar ratio of Na/K was associated with a reduction of 1.72 mm Hg SBP and 0.30 mm Hg DBP ($p<0.05$). In the meta-analysis study of 15 RCTs by Binia et al. [5], decreased urinary Na/K was associated with reduced SBP. In this study, an estimated one unit decrease in the molar ratio of urinary Na/K was associated with a reduction of 2.1 mm Hg SBP ($p<0.05$).

The ELSA-Brasil longitudinal study [21], included 15,505 men and women aged 35-74 years of age, followed over 3.8 years in Brazil. The mean Na/K ratio in men and women were 4.1 and 3.6, respectively at baseline, and 3.9 and 3.4, respectively at follow up. The findings from this study demonstrated a strong and a linear association ($p<0.05$) between 24-hr urinary Na/K and BP. Participants in the fourth and fifth quintiles of urinary Na/K had significantly higher SBP and DBP compared to lowest quintile ($p<0.05$). Men had an increase of 2.36/1.18 mm Hg (SBP/DBP) at fifth quintile of Na/K ratio compared to 1.19/0. 69 mm Hg at lowest quintile. Women had an increase of 3.30/2.13 mm Hg at fifth quintile compared to 0.40/0.28 mm Hg in the lowest quintile. The study did not report the median Na/K ratios corresponding to the quintiles. The authors reported that the association of urinary Na/K with BP was stronger than the associations of urinary sodium or potassium alone, but did not report regression coefficients for the effects of urinary sodium or potassium alone.

The China Health and Nutrition Survey [22] investigated the association of urinary Na/K and urinary sodium or potassium alone on the incidence of hypertension in China. This open-cohort study used data from 16,869 adults aged 20-60 years at enrollment beginning in 1989 and followed through 2009. The average dietary Na/K ratio was 2.8 in 2009. This study demonstrated a significant linear association between dietary Na/K and incidence of hypertension ($p<0.05$). Individuals in the highest quintile of dietary Na/K (≥ 4.9) had a significantly higher risk (HR of 2.14) for hypertension compared to lowest quintile of Na/K (< 1.8). Further, the dietary Na/K had a stronger association with the incidence of hypertension than dietary sodium (HR of 1.84 in the highest quintile) or potassium (HR of 0.66 in the highest quintile) alone.

Collectively, these studies provide evidence that the dietary Na/K would be a stronger predictor of changes in BP compared to dietary sodium or potassium alone. Based on the evidence discussed above, a Na/K ratio ≤ 1.0 may be beneficial for achieving optimal BP. The adequate intake level for sodium and potassium is currently set at 2,300 mg/d (100 mmol/d) and 4,700 mg/d (121 mmol/d) respectively, for adults in the United States and Canada [23], whereas the WHO guideline is $< 2,000$ mg/d (< 87 mmol/d) sodium and $\geq 3,500$ mg/d (≥ 90mmol/d) potassium for adults [24]. These estimates correspond to a molar Na/K ratio of < 0.8 based on US recommendations and < 1.0 based on WHO recommendations. However, according to NHANES 2014 data [9], the median dietary Na/K (estimated from urinary Na/K) in the US is about 3.2 and only one tenth of Americans have a dietary Na/K less than the recommended ratio of < 1.0. Therefore, practical and sustained efforts to lower dietary sodium to potassium ratio by modestly decreasing dietary sodium intake and increasing potassium intake would have a major impact on BP control and prevention and treatment of hypertension.

Future studies are needed to determine the optimal dietary sodium-to potassium-ratio for BP management. Randomized clinical studies in normotensive and hypertensive adults should evaluate the effects of a range of sodium-to-potassium ratios, at practical and physiological intake levels, on systolic and diastolic BP, incidence of hypertension and cardiovascular disease. Such trials would help determine optimal and practical dietary approaches to prevent and treat hypertension.

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