Effect of Modest Salt Reduction on Blood Pressure, Urinary Albumin, and Pulse Wave Velocity in White, Black, and Asian Mild Hypertensives

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Abstract—A reduction in salt intake lowers blood pressure. However, most previous trials were in whites with few in blacks and Asians. Salt reduction may also reduce other cardiovascular risk factors (eg, urinary albumin excretion, arterial stiffness). However, few well-controlled trials have studied these effects. We carried out a randomized double-blind crossover trial of salt restriction with slow sodium or placebo, each for 6 weeks, in 71 whites, 69 blacks, and 29 Asians with untreated mildly raised blood pressure. From slow sodium to placebo, urinary sodium was reduced from 165±58 (±SD) to 110±49 mmol/24 hours (9.7 to 6.5 g/d salt). With this reduction in salt intake, there was a significant decrease in blood pressure from 146±13/91±8 to 141±12/88±9 mm Hg ($P<0.001$), urinary albumin from 10.2 (IQR: 6.8 to 18.9) to 9.1 (6.6 to 14.0) mg/24 hours ($P<0.001$), albumin/creatinine ratio from 0.81 (0.47 to 1.43) to 0.66 (0.44 to 1.22) mg/mmol ($P<0.001$), and carotid-femoral pulse wave velocity from 11.5±2.3 to 11.1±1.9 m/s ($P<0.01$). Subgroup analysis showed that the reductions in blood pressure and urinary albumin/creatinine ratio were significant in all groups, and the decrease in pulse wave velocity was significant in blacks only. These results demonstrate that a modest reduction in salt intake, approximately the amount of the current public health recommendations, causes significant falls in blood pressure in all 3 ethnic groups. Furthermore, it reduces urinary albumin and improves large artery compliance. Although both could be attributable to the falls in blood pressure, they may carry additional benefits on reducing cardiovascular disease above that obtained from the blood pressure falls alone. **(*Hypertension*. 2009;54:482-488.)**

Key Words: salt reduction ■ blood pressure ■ ethnic group ■ urinary albumin ■ pulse wave velocity

There is much evidence from epidemiological, migration, intervention, treatment, genetic, and animal studies that dietary salt (sodium chloride) plays an important role in regulating blood pressure (BP), and our current high salt intake is largely responsible for the rise in BP with age.[1] Many randomized trials have demonstrated that a modest reduction in salt intake lowers BP.[2] However, most previous trials were carried out in white individuals. There were only very limited number of trials in blacks[3,4] and even fewer in Asians.

Increasing evidence suggests that a lower salt intake may have other beneficial effects (eg, reducing urinary albumin excretion,[5,6] decreasing arterial stiffness as measured by pulse wave velocity[7]). The evidence for these other effects is mainly from epidemiological and animal studies. Few well-controlled trials have studied whether a modest reduction in salt intake has such effects in humans.

The average salt intake, as measured by 24-hour urinary sodium, was 8.6 g/d (equivalent to 3.4 g sodium) for adults in the UK according a recent survey in 2008.[8] However, at the time when our study protocol was developed, it was 9.5 g/d,[9] which is very similar to the current salt intake in most countries in the world (ie, ≈9 to 12 g/d). The UK and U.S. recommendations are to reduce salt intake to <6 g/d[10,11] and the World Health Organization's recommendation is <5 g/d.[12] We carried out a randomized double-blind placebo-controlled trial to determine the effects of a modest reduction in salt intake, as recommended, on BP in 3 ethnic groups (whites, blacks, and Asians) with untreated mildly raised BP. At the same time, our study aimed to determine the effects of a modest reduction in salt intake on 24-hour urinary albumin excretion and pulse wave velocity.

Methods

Participants

Individuals, aged 30 to 75 years, with sitting systolic BP 140 to 170 mm Hg or diastolic 90 to 105 mm Hg, and with no previous treatment for raised BP, were eligible for the study. Exclusion criteria were any secondary cause of hypertension, impaired renal function with plasma creatinine >150 μmol/L, previous stroke, ischemic heart disease, heart failure, diabetes mellitus, malignancy,

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or liver disease. Women who were pregnant or breast feeding or on oral contraceptive pills were also excluded.

Participants were recruited from the Blood Pressure Unit outpatient clinic and from general practices in South London. The classification of ethnic groups was based on participants' self-identified ethnicity, and further assessed by research nurses according to skin color and participants' and their parents' country of origin. A total of 187 individuals were recruited into the study. There were 77 whites, 75 blacks, and 35 Asians. Among the 75 blacks, 44 (59%) were black Africans, 30 (40%) were black Caribbeans, and 1 (1%) was of mixed ethnic origin (1 parent was black Caribbean and the other was white). Among the 35 Asians, 33 (94%) were of South Asian origin (ie, originating from the Indian subcontinent), 1 (3%) was Chinese, and 1 (3%) was of mixed ethnic origin (South Asian and white). The study was approved by the Wandsworth Local Research Ethics Committee. Written consent was obtained from all participants.

Study Design

The study was designed as a randomized double-blind crossover trial. All measurements were taken at baseline while on individuals' usual diet. After baseline measurements, participants were given detailed advice by specially trained nurses on how to reduce their salt intake, with an aim of achieving an intake of ≈5 g/d (85 mmol/d). They were advised not to add salt at the table or during cooking, and avoid foods that contained large amount of salt. Nurses went through with participants on what foods they usually ate and identified items with high salt content, and advised them to use low salt alternatives. In appropriate cases, the spouse or whoever cooked in the household was also seen. Advice was reinforced at each visit for the whole duration of the study. Salt-free bread was provided for those who had no easy access to it.

After 2 weeks on the reduced-salt diet, participants entered the randomized, double-blind, crossover trial of slow sodium versus placebo, but remained on the reduced salt diet. Randomization was stratified according to ethnic group using computer-generated random number, carried out by an independent company-Healthspan Group Ltd, who supplied slow sodium and slow sodium matching placebo tablets but had no involvement in the conduct of the trial. Participants were allocated in random order to take 9 slow sodium tablets (10 mmol sodium per tablet) or 9 placebo tablets daily for 6 weeks. They then crossed over to take the opposite tablets for 6 further weeks. All participants and research staff were unaware of the treatment allocation.

Measurements

The following measurements were performed at the end of each 6-week period. BP was measured by a validated automatic digital BP monitor (Omron HEM-705CP) in sitting position after 5 to 10 minute rest and in the same arm throughout the study. Three readings were taken at 1- to 2-minute intervals, and the mean of last 2 readings was used. Twenty-four–hour ambulatory blood pressure monitoring (ABPM) was performed using SpaceLabs 90207 devices.

Blood samples were taken for measurements of routine biochemistry, plasma renin activity and aldosterone. Two consecutive 24-hour urines were collected for measurements of urinary sodium, potassium, creatinine, calcium, and albumin. Participants were carefully instructed on how to accurately collect 24-hour urine by research nurses. The mean of 2 urinary measurements was used in the analysis. Urinary albumin was measured by laser immunonephelometry which had within-assay imprecision of 1.4 to 3.5% and between-assay imprecision of 1.3 to 1.7%. Urine samples with measured concentrations <2.1 mg/L were reanalyzed using a high sensitivity ELISA,[13] which had within-assay and between-assay imprecision of 3.7 to 5.4% and 4.1 to 6.3%, respectively.

Carotid-femoral pulse wave velocity was measured noninvasively using an automatic device Complior as previously described and validated.[14,15] Briefly, 2 pressure waveforms were recorded simultaneously with pressure-sensitive transducers which were placed on the skin at 2 sites, the common carotid artery and the femoral artery. The pressure waveforms were digitized, and calculation of the time delay between the 2 pressure upstrokes was initiated automatically. Measurement was repeated over 10 cardiac cycles and the mean was used.

Statistical Analysis

By means of sample size calculation, we estimated that 70 participants in each ethnic group (allowing 5% drop-out rate) were needed to detect a change of 4 mm Hg in systolic BP between slow sodium and placebo, with a power of 90% and $\alpha=0.05$, given a standard deviation of 10. This calculation was based on a very conservative estimate of a difference of 4 mm Hg in systolic BP between the 2 treatment periods.

Paired Student *t* test was used to compare the difference between slow sodium and placebo for normally distributed variables, and Wilcoxon signed ranks test was used for variables that were not normally distributed (ie, plasma renin activity, 24-hour urinary albumin, urinary albumin/creatinine ratio). A 2-tailed probability value of <0.05 was regarded as statistically significant. All statistical analyses were performed using SPSS.

Among the 187 individuals who entered the study, 2 blacks withdrew before randomization, leaving 185 participants who entered the randomized crossover trial. In total, 169 participants completed the trial and 16 (6 whites, 4 blacks, and 6 Asians) withdrew. The results reported here are based on the 169 participants who completed the study.

Results

Results in All Participants

The mean age was 50±11 (SD) years. There were 71 whites, 69 blacks, and 29 Asians. At baseline (ie, on participants' usual diet) the mean 24-hour urinary sodium was 131±50 mmol which is equivalent to 7.7 g salt. The average BP was 147±13/91±8 mm Hg. Other baseline characteristics, ABPM, and biochemistry data are summarized in Table 1.

During the randomized crossover phase, the mean 24-hour urinary sodium was 165±58 mmol (9.7 g salt) on slow sodium and 110±49 mmol (6.5 g salt) on placebo. There was, therefore, a reduction of 55 mmol (3.2 g salt) from slow sodium to placebo. With this reduction in salt intake, BP fell from 146±13/91±8 mm Hg on slow sodium to 141±12/88±9 mm Hg on placebo (ie, an average fall of 4.8 mm Hg [$P<0.001$] in systolic and 2.2 mm Hg [$P<0.001$] in diastolic BP). Pulse pressure also fell significantly. Additionally there were significant falls in mean 24-hour, daytime, and nighttime BP (Table 2).

The median 24-hour urinary albumin was 10.2 mg (interquartile range, IQR: 6.8 to 18.9) on slow sodium, and 9.1 mg (6.6 to 14.0) on placebo. There was, therefore, an 11% reduction ($P<0.001$) from slow sodium to placebo. Furthermore, there was a significant reduction in urinary albumin/creatinine ratio (Table 2).

From slow sodium to placebo, there was a significant decrease in pulse wave velocity (Table 2). Both 24-hour urinary calcium and calcium/creatinine ratio were reduced significantly (Table 2). There was also a small but significant reduction in body weight, an increase in plasma renin activity and aldosterone, and a small but significant increase in plasma creatinine (Table 2).

Results by Ethnic Group

From slow sodium to placebo, salt intake as calculated from 24-hour urinary sodium was reduced by 3.5 g/d in whites, 2.7 g/d in blacks, and 4.0 g/d in Asians. With these reductions in

Table 1. Baseline Characteristics of the Participants

Variable	All Participants	Baseline Characteristics by Ethnic Group		
		Whites	Blacks	Asians
Age, y	50 (11)	52 (12)	50 (9)	47 (10)
Sex, male/female	113/56	56/15	34/35	23/6
BMI, kg/m^2	29 (5)	28 (5)	31 (5)	27 (5)
Office BP				
SBP, mm Hg	147 (13)	146 (12)	149 (13)	142 (13)
DBP, mm Hg	91 (8)	90 (8)	90 (8)	92 (10)
Ambulatory BP, mm Hg				
24-hour SBP	139 (10)	137 (9)	142 (10)	137 (9)
24-hour DBP	86 (8)	85 (7)	86 (9)	87 (8)
Day SBP	146 (10)	145 (9)	147 (10)	145 (10)
Day DBP	91 (9)	91 (8)	91 (9)	94 (9)
Night SBP	131 (11)	128 (10)	136 (11)	129 (10)
Night DBP	79 (9)	78 (8)	81 (10)	80 (8)
Urinary measurements				
Volume, mL/24 hours	1738 (736)	1925 (908)	1600 (542)	1609 (568)
Sodium, mmol/24 hours	131 (50)	127 (51)	132 (46)	138 (57)
Potassium, mmol/24 hours	77 (26)	87 (22)	71 (29)	71 (20)
Creatinine, mmol/24 hours	14.8 (4.4)	15.0 (4.1)	15.0 (4.2)	13.8 (5.6)
Plasma measurements				
Sodium, mmol/L	140 (1.9)	139 (1.9)	140 (1.8)	139 (1.6)
Potassium, mmol/L	4.4 (0.3)	4.4 (0.3)	4.4 (0.4)	4.5 (0.3)
Creatinine, μmol/L	83 (15)	81 (13)	86 (17)	81 (14)
Renin activity, ng/mL/h*	0.3 (0.1 to 0.6)	0.5 (0.3 to 0.9)	0.1 (0.1 to 0.2)	0.3 (0.1 to 0.5)
Aldosterone, pmol/L	387 (175)	456 (179)	315 (145)	392 (167)

All values are expressed as mean (SD) unless marked with *, where values are median (IQR). SBP indicates systolic BP; DBP, diastolic BP; BMI, body mass index.

salt intake, there were significant falls in BP in all 3 ethnic groups (Figure). BP fell by 4.6/2.2, 4.8/2.2, and 5.4/2.2 mm Hg in whites, blacks, and Asians, respectively. Pulse pressure also fell significantly in all groups. Daytime BP showed a significant fall in all groups, and nighttime BP fell significantly in whites and blacks but not in Asians (Table 3).

With salt reduction, 24-hour urinary albumin was reduced by 9% in whites ($P<0.05$), 14% in blacks ($P=0.057$), and 14% in Asians ($P<0.05$). There was a significant decrease in urinary albumin/creatinine ratio in all 3 groups (Table 3). From slow sodium to placebo, pulse wave velocity was decreased significantly in blacks but not in whites and Asians (Table 3). There were significant reductions in both 24-hour urinary calcium and calcium/creatinine ratio in all 3 groups. Plasma renin activity and aldosterone showed significant increases in whites, but in blacks and Asians there was no significant change in either parameter (Table 3).

Discussion

Key Findings

First, our study is the largest double-blind trial of modest salt reduction which also involves a large number of black and Asian participants. The study demonstrates that a modest reduction in salt intake, as currently recommended,[10,11] causes significant and important falls in BP in all 3 ethnic groups of individuals with mildly raised BP. The results in Asian participants (94% were of South Asian origin) are of particular interest, as this is the first longer-term modest salt reduction trial in this group and demonstrates a clear benefit of salt reduction. Second, our study, for the first time, provides evidence from a well-controlled randomized trial that a longer-term modest reduction in salt intake reduces urinary albumin excretion in white, black, and Asian hypertensive individuals. Although the decrease in albumin excretion could be, at least in part, attributable to the reductions in BP, it is likely to have additional benefits on reducing both renal and cardiovascular disease above that which would be obtained from the BP falls alone. Third, our study shows that, in blacks, a modest reduction in salt intake reduces carotid-femoral pulse wave velocity, suggesting an improvement in large elastic artery compliance. Although this decrease in pulse wave velocity could be attributable to the falls in BP, it may also carry an additional benefit on reducing cardiovascular risk. Fourth, our study confirms the findings from other trials that a decrease in salt intake reduces 24-hour urinary calcium and calcium/creatinine ratio.[16] Importantly, our study demonstrates these effects in all 3 ethnic groups of hypertensive individuals. These results, in conjunction

Table 2. Changes in Variables From Slow Sodium to Placebo in All Participants

Variable	Slow Sodium	Placebo	Difference (95% CI)	*P* for Difference
Office BP and pulse rate				
SBP, mm Hg	146 (13)	141 (12)	−4.8 (−6.4 to −3.2)	<0.001
DBP, mm Hg	91 (8)	88 (9)	−2.2 (−3.1 to −1.4)	<0.001
Pulse pressure, mm Hg	55 (11)	53 (10)	−2.6 (−3.8 to −1.4)	<0.001
Pulse rate, beat/min	66 (11)	67 (10)	0.8 (−0.3 to 1.9)	0.172
Ambulatory BP, mm Hg				
24-hour SBP	141 (10)	137 (11)	−4.1 (−5.2 to −3.0)	<0.001
24-hour DBP	86 (9)	84 (9)	−1.9 (−2.6 to −1.1)	<0.001
Day SBP	147 (10)	143 (11)	−4.7 (−5.9 to −3.4)	<0.001
Day DBP	92 (9)	90 (9)	−2.2 (−3.1 to −1.3)	<0.001
Night SBP	133 (11)	130 (12)	−3.5 (−4.9 to −2.2)	<0.001
Night DBP	80 (9)	78 (10)	−1.7 (−2.7 to −0.7)	0.001
Urinary measurements				
Volume, mL/24 hours	1730 (697)	1736 (716)	6 (−68 to 80)	0.872
Sodium, mmol/24 hours	165 (58)	110 (49)	−55 (−64 to −46)	<0.001
Potassium, mmol/24 hours	73 (26)	71 (22)	−2 (−5 to 1)	0.274
Creatinine, mmol/24 hours	13.9 (4.4)	14.2 (4.3)	0.3 (−0.1 to 0.7)	0.144
Calcium, mmol/24 hours	4.3 (1.9)	3.9 (1.8)	−0.4 (−0.6 to −0.2)	<0.001
Calcium/creatinine ratio	0.33 (0.16)	0.29 (0.13)	−0.04 (−0.06 to −0.03)	<0.001
Albumin, mg/24-hours*	10.2 (6.8 to 18.9)	9.1 (6.6 to 14.0)		<0.001
Albumin/creatinine ratio, mg/mmol*	0.81 (0.47 to 1.43)	0.66 (0.44 to 1.22)		<0.001
Body weight, kg	85.5 (17.4)	85.2 (17.5)	−0.3 (−0.5 to −0.04)	0.021
Pulse wave velocity, m/s	11.5 (2.3)	11.1 (1.9)	−0.3 (−0.6 to −0.1)	0.004
Plasma measurements				
Sodium, mmol/L	139.5 (1.9)	139.5 (2.1)	−0.07 (−0.40 to 0.27)	0.701
Potassium, mmol/L	4.4 (0.3)	4.4 (0.3)	0.01 (−0.04 to 0.06)	0.632
Creatinine, μmol/L	82.3 (14.7)	83.8 (15.0)	1.5 (0.3 to 2.6)	0.013
Renin activity, ng/mL/h*	0.12 (0.10 to 0.51)	0.23 (0.10 to 0.68)		<0.001
Aldosterone, pmol/L	365 (175)	412 (187)	48 (26 to 70)	<0.001

All values are expressed as mean (SD) unless marked with *, where values are median (IQR).

with other evidence,[17] suggest that a lower salt intake, in the long-term, could play an important role in the prevention of osteoporosis.

Effect of Salt Reduction on BP

Blacks and Asians are the 2 main minority ethnic groups in the UK. Black individuals are more likely to develop high BP and the resulting stroke, heart failure, left ventricular hypertrophy, and kidney disease. People of South Asian origin have a greater risk of dying prematurely from coronary heart disease, and they also have a higher morbidity and mortality from end-stage renal disease and stroke compared with white population.[18] Despite being at a greater risk of cardiovascular disease, blacks and Asians are less studied with respect to the effects of salt reduction; in particular, there is no well-controlled longer-term salt reduction trial in people of South Asian origin. Our study is therefore important in filing this gap, and our results clearly show that a modest reduction in salt intake, as currently recommended, has a significant effect on BP in both black and Asian hypertensive individuals.

Previous studies that directly compared the BP-lowering effects of salt reduction between blacks and whites have shown that, for a similar reduction in salt intake, blacks had a greater fall in BP, and this was, at least in part, attributable to their less responsive renin–angiotensin system.[19] In our present study, it appeared that blacks had a similar fall in BP compared with whites; however, blacks achieved a smaller reduction in salt intake. Indeed, for a 1-g/d reduction in salt intake, the fall in BP was 1.8/0.8 mm Hg in blacks and 1.3/0.6 mm Hg in whites. This difference was not significant, but the results are consistent with findings from previous studies.[4,19]

One of the reasons for the lack of longer-term salt reduction trial in people of South Asian origin may be the difficulty in recruiting Asian individuals into the study. We made huge efforts on recruitment, however we only recruited 35 Asians (ie, approximately half the number planned). Additionally, Asian participants were more likely to withdraw from the study (ie, 6/35 [17.1%] Asians, 6/77 [7.8%] whites, and 6/75 [8.0%] blacks withdrew from our study).

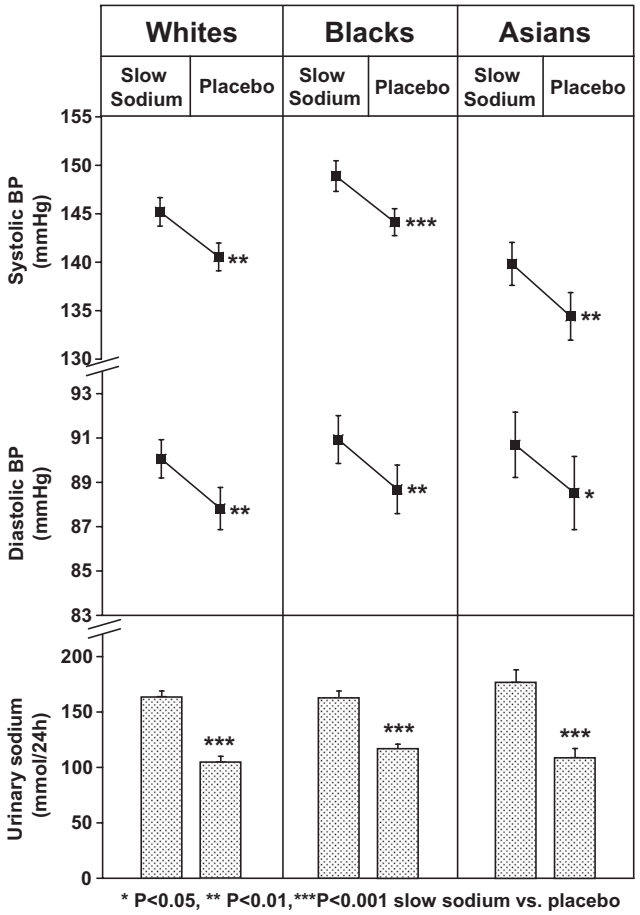

Figure. Blood pressure (BP) and urinary sodium excretion (mean±SEM) after 6 weeks on each phase of crossover trial in white (n=71), black (n=69), and Asian (n=29) hypertensive individuals.

Although only 29 Asians completed the trial, our study had sufficient power to detect a significant change in BP because of the fact that the change in BP between slow sodium and placebo observed in our study (systolic: 5.4 mm Hg) was greater than that anticipated in the initial sample size estimation. Indeed, we found a significant and important fall in both systolic and diastolic BP.

Effect of Salt Reduction on Urinary Albumin Excretion

Urinary albumin excretion has been shown to be an important and independent risk factor for the development and progression of renal disease and also for cardiovascular disease in individuals with diabetes, chronic kidney disease, hypertension, and the general population.[20,21] Importantly, the risk increases throughout the range of albumin excretion and there is no threshold. Several epidemiological studies have shown a direct association between salt intake and urinary albumin.[6,22] A randomized double-blind trial in 40 black hypertensive individuals demonstrated that a reduction in salt intake from ≈10 to 5 g/d reduced 24-hour urinary protein by 19% ($P<0.01$).[3] Other studies in patients with proteinuria or diabetes showed that the antiproteinuric effects of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker were abolished by increasing salt intake.[23] Recently Jones-Burton et al reviewed all available literature and concluded that "variations in dietary salt consumption directly influence albuminuria, with increasing salt intake associated with worsening albuminuria."[24] However, the majority of studies included in this review were of poor methodological quality (eg, study was not randomized, had a short duration, had concomitant antihypertensive drug treatments, or the study was conducted in patients with diabetes or kidney disease).

Our study is the first randomized trial looking at the effect of a longer-term modest reduction in salt intake on 24-hour urinary albumin in individuals with mildly raised BP and demonstrates a significant effect. Although the decrease in urinary albumin was small, from a population viewpoint, even a small reduction could be beneficial. The Framingham Offspring Study showed that, in a community-based sample of middle-aged nondiabetic and nonhypertensive individuals without microalbuminuria, urinary albumin excretion was directly related to both cardiovascular events and mortality.[21]

Effect of Salt Reduction on Large Elastic Artery Compliance

Pulse wave velocity is a measure of arterial distensibility, and an increased pulse wave velocity is an index of arterial stiffness. In a study of 2 Chinese populations, Avolio et al demonstrated that the age-associated increase in pulse wave velocity was blunted in the population with a lower salt intake.[7] Several other studies in white individuals with normal or raised BP showed that a reduction in salt intake reduced pulse wave velocity.[25,26] However, a recent randomized trial in 29 overweight and obese normotensive individuals showed no significant change in aortic pulse wave velocity when salt intake was reduced from 9.2 to 3.8 g/d for 2 weeks, in spite of a significant improvement in endothelial function as measured by brachial artery flow-mediated dilatation.[27] Our study showed that a modest reduction in salt intake for 6 weeks reduced pulse wave velocity overall, but subgroup analysis indicated that the effect was significant only in blacks despite the fact that blacks achieved a smaller reduction in salt intake and a similar fall in BP, compared with whites and Asians.

Pulse pressure is a surrogate marker for large artery stiffness.[28] In our study, there was a significant decrease in pulse pressure with salt reduction in all 3 ethnic groups, although the decrease in pulse wave velocity was significant in blacks only. These results suggest that salt reduction may improve arterial distensibility in all hypertensives.

Epidemiological studies have shown that aortic pulse wave velocity is a strong independent predictor of future cardiovascular events, even after accounting for the effect of concomitant change in BP.[29] Therefore the reduction in pulse wave velocity with a decrease in salt intake could have an additional benefit on reducing cardiovascular disease although the reduction in pulse wave velocity could be, at least partially, attributable to the falls in BP that occurred with salt reduction. Other researchers have suggested that the improvement in central arterial compliance may be an important mechanism for the falls in BP with salt reduction.[26]

Table 3. Changes in Variables From Slow Sodium to Placebo by Ethnic Group

	Whites		Blacks		Asians	
Variable	Slow Sodium	Placebo	Slow Sodium	Placebo	Slow Sodium	Placebo
Office BP and pulse rate						
SBP, mm Hg	145 (12)	141 (12)‡	149 (13)	144 (12)§	140 (12)	134 (13)‡
DBP, mm Hg	90 (7)	88 (8)‡	91 (9)	89 (9)‡	91 (8)	89 (9)†
Pulse pressure, mm Hg	55 (10)	53 (11)†	58 (11)	55 (10)†	49 (7)	46 (8)†
Pulse rate, beat/min	65 (11)	66 (10)†	68 (10)	67 (10)	67 (11)	69 (12)
Ambulatory BP, mm Hg						
24-hour SBP	138 (9)	134 (10)§	145 (9)	140 (10)§	137 (12)	135 (12)
24-hour DBP	85 (8)	83 (8)‡	88 (9)	86 (10)‡	87 (9)	85 (8)
Day SBP	146 (10)	141 (10)§	150 (10)	145 (11)§	144 (11)	140 (13)†
Day DBP	91 (9)	89 (9)†	93 (10)	90 (10)‡	93 (9)	90 (9)†
Night SBP	129 (10)	126 (11)§	138 (10)	134 (12)§	130 (12)	129 (13)
Night DBP	78 (8)	75 (8)†	83 (9)	81 (10)†	80 (8)	80 (10)
Urinary measurements						
Volume, mL/24 hours	1919 (792)	1950 (783)	1552 (567)	1537 (629)	1689 (630)	1686 (602)
Sodium, mmol/24 hours	163 (54)	104 (54)§	162 (59)	116 (44)§	176 (64)	108 (49)§
Potassium, mmol/24 hours	84 (24)	81 (20)	64 (28)	62 (18)	70 (21)	70 (22)
Creatinine, mmol/24 hours	13.7 (3.8)	14.0 (3.9)	14.3 (4.7)	14.9 (4.5)	13.4 (5.2)	12.9 (4.5)
Calcium, mmol/24 hours	4.8 (1.8)	4.5 (1.7)†	3.8 (2.0)	3.4 (1.8)†	4.2 (1.8)	3.7 (1.5)‡
Calcium/creatinine ratio	0.38 (0.17)	0.34 (0.14)‡	0.28 (0.14)	0.24 (0.11)§	0.34 (0.14)	0.30 (0.10)†
Albumin, mg/24 hours*	9.6 (6.2 to 16.1)	8.7 (6.5 to 13.1)†	11.3 (6.4 to 21.1)	9.7 (6.7 to 18.2)¶	9.5 (7.0 to 16.0)	8.2 (6.6 to 13.2)†
Albumin/creatinine ratio, mg/mmol*	0.72 (0.45 to 1.31)	0.62 (0.41 to 0.98)‡	0.89 (0.49 to 1.70)	0.68 (0.42 to 1.45)‡	0.86 (0.57 to 1.54)	0.75 (0.57 to 1.04)†
Body weight, kg	85.3 (16.8)	85.0 (17.0)	88.7 (17.7)	88.4 (17.8)	78.1 (16.6)	78.0 (16.6)
Pulse wave velocity, m/s	11.3 (2.6)	11.1 (1.9)	11.7 (2.0)	11.2 (1.8)‡	11.3 (2.2)	11.2 (2.2)
Plasma measurements						
Sodium, mmol/L	139.5 (1.7)	139.3 (2.1)	139.4 (2.0)	139.9 (2.3)‖	139.9 (2.4)	138.9 (1.6)†
Potassium, mmol/L	4.5 (0.3)	4.4 (0.3)	4.3 (0.4)	4.4 (0.4)	4.5 (0.3)	4.5 (0.3)
Creatinine, μmol/L	80.3 (13.6)	81.1 (12.4)	85.1 (15.7)	86.7 (16.7)	80.7 (14.5)	83.5 (16.1)
Renin activity, ng/mL/h*	0.35 (0.12 to 0.72)	0.55 (0.25 to 0.95)§	0.10 (0.10 to 0.11)	0.10 (0.10 to 0.17)	0.12 (0.10 to 0.62)	0.20 (0.11 to 0.63)
Aldosterone, pmol/L	414 (174)	486 (186)§	303 (142)	332 (161)	390 (206)	423 (172)

All values are expressed as mean (SD) unless marked with *, where values are median (IQR). †$P<0.05$, ‡$P<0.01$, §$P<0.001$, ‖$P=0.050$, ¶$P=0.057$ compared with slow-sodium period.

Effect of Salt Reduction on Urinary Calcium Excretion

Salt intake is one of the major dietary determinants of urinary calcium excretion.[30] Until recently, it was assumed that when salt intake was increased, the increase in calcium excretion was compensated for by an increase in intestinal calcium absorption. There is now evidence to suggest that, when salt intake is increased, there is a negative calcium balance with stimulation of mechanisms, not only to increase intestinal absorption of calcium but also to mobilize calcium from bone. A study in postmenopausal women showed that the loss of hip bone density over 2 years was related to 24-hour urinary sodium at entry to the study and was as strong as that relating to calcium intake.[17]

Evidence from animal, clinical, and epidemiological studies suggests that raised BP is associated with increased calcium loss and, thereby, increasing the risk of osteoporosis.[31] Our study showed that a modest reduction in salt intake not only lowered BP, but also reduced urinary calcium in individuals with raised BP. A lower salt intake, in the long-term, may be particularly beneficial to these people in terms of preventing osteoporosis.

Perspectives

Worldwide almost 1 billion individuals had high BP in 2000, and this was projected to increase to 1.56 billion by 2025.[32] Our study demonstrates that a modest reduction in salt intake, approximately the amount of the current public health recommendations, causes significant and clinically relevant falls in BP in all 3 ethnic groups of individuals with mildly raised BP. Furthermore, our study shows that a modest reduction in salt intake has other beneficial effects (ie, reducing urinary albumin excretion, improving large elastic artery compliance, and decreasing urinary calcium excretion). These results, in conjunction with other evidence,[17,21,33] suggest that a lower salt intake, in the long-term, could play an important role in

the prevention of cardiovascular disease, renal disease, and osteoporosis. Although our study was carried out in individuals with raised BP, it is likely that the general population would also benefit from a reduction in salt intake because there is a continuous relationship between salt intake, BP, albumin excretion, and cardiovascular risk.[21,34] This is reinforced by the findings from prospective studies in general populations and outcome trials in individuals with prehypertension (average BP: 127/85 mm Hg), which demonstrated that a lower salt intake was related to a lower risk of cardiovascular disease.[33,35] Our present study provides further support for the current recommendations to reduce salt intake to <6 g/d in adults.

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Disclosures

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