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ORIGINAL ARTICLE

Urinary calcium excretion, sodium intake and blood pressure in a multi-ethnic population: results of the Wandsworth Heart and Stroke Study

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Background: **Hypertension is associated with increased urinary calcium excretion (UCa). A high sodium intake increases both UCa and blood pressure (BP). However, it is not clear whether these effects are modified by gender or ethnic origin.**
Objectives: **To examine the relationships between BP, urinary sodium (UNa), gender and ethnic origin with both daily and fasting UCa in a population-based study.**
Design and Methods: **Out of 1577 individuals taking part in a cross-sectional survey, 743 were considered for the present analysis (407 women, 336 men) as they were all untreated, had provided a complete 24-h urine collection, and had all measurements of anthropometry, BP, UNa and UCa. They were 277 whites, 227 of black African origin and 239 South Asians. Comparisons were also carried out in the 690 participants who also provided 3-h fasting urine collections.**
Results: **After adjustment for confounders including age, and gender, 24-h UCa was significantly and independently associated with ethnic origin, BP and UNa. Mean 24-h UCa was 4.62 (s.e. 0.11) mmol/d in whites, 3.33 (0.12) in South Asians and 3.16 (0.13) in blacks ($P < 0.001$). A 100 mmol higher UNa predicted a 1.04 mmol higher daily UCa ($P < 0.001$), and a 20 mm Hg higher systolic BP predicted a 0.28 mmol higher UCa. The slopes were not significantly different by ethnic group. The ethnic differences in UCa were present when fasting UCa was used instead (1.64 [0.05] μmol/min in whites, 1.08 [0.06] in South Asians and 1.13 [0.06] in blacks; $P < 0.001$).**
Conclusions: **These results indicate that BP, salt intake and ethnic origin are independent predictors of UCa in an unselected population. These relationships are unlikely to be the result of differences in Ca intake or intestinal Ca absorption as they are seen also after an overnight fast, suggesting that they may reflect differences in renal tubular handling. The estimated effects of either BP or sodium intake on UCa, sustained over many years, may be associated with significant effects on bone calcium content.**
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Keywords: urinary calcium; dietary sodium; blood pressure; ethnic origin

Introduction

Higher urinary calcium excretion (UCa) and ensuing secondary increase in parathyroid activity has been reported in essential hypertension.[1] Higher UCa has also been detected in children in the upper end of the blood pressure (BP) distribution[2] as well as in normotensive offsprings of hypertensive parents.[3] Moreover, a positive association between UCa and BP has been found in some population-based studies[4–6] and raised parathyroid hormone (PTH) activity has been described in young people in the upper BP distribution.[7] Although an increase in dietary sodium intake increases BP[8] and UCa,[9] the higher UCa of patients with essential hypertension appears to be independent of urinary sodium excretion (UNa)[1] and of intestinal calcium absorption.[10,11]

There has been little work investigating the effects of sodium and calcium intake upon the association between BP and UCa in population-based studies. Furthermore, there has been no comprehensive investigation of the effects of gender or ethnic origin upon these relationships. This is despite the fact that some studies suggest that 24-h UCa may be lower in females than males[12] and lower in black[13] and South Asians[14] than in whites.

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The aim of this study was therefore to investigate the independent associations of UCa with both UNa and BP in a population of middle-aged men and women of three different ethnic groups. For the first time in such an epidemiological study, measurements were made of both fasting timed and 24-h UCa. It has been suggested that after an overnight fast, the contribution of intestinal calcium absorption to UCa is minimised.[15,16] Thus the fasting UCa measurements were used to determine whether associations were independent of intestinal calcium absorption.

Subjects and methods

Population

Participants were selected from general practitioners' registers in the South-West London area, as part of the Wandsworth Heart and Stroke Study (WHSS) as described in detail elsewhere.[17] In brief, the study was a population-based cross-sectional survey of men and women between 40 and 59 years old of three different ethnic groups: northern European origin (whites); West African or Caribbean origin (blacks) and South Asian Indian origin (S Asians). The study was designed so that there were approximately 250 people in each gender and ethnic group stratum. In all 1577 participants were studied between 1994 and 1996.[17]

Protocol

The participants were asked to attend a screening unit at St George's Hospital between 08.00 am and 12.00 noon. They were requested to fast for the 12 h prior to the visit. All attendees were administered a questionnaire, which was used to determine age, ethnic origin, history of migration, socioeconomic and lifestyle characteristics.[17] Height and weight were measured and used to calculate body mass index (BMI) (weight/(height)^2). Supine BP was measured with standardised procedure using an automatic machine (Arteriosonde, Roche, Nutley, NJ, USA) as previously described.[17]

After the interview participants were asked to collect a 24-h urine sample within a few days. They were given written detailed instructions on how to collect a complete 24-h urine sample and given a 2.5-L plastic bottle to take with them. Complete urine collections were either returned by the participants or were collected at the participant's address. Time and volume of collections were immediately recorded, aliquots taken and stored at −20°C until assayed. A timed urine collection after an overnight fast was also obtained on the morning of the investigation after the participants had drunk one-to-two glasses of tap water in the morning. Volume (in ml) and duration (in min) of the collection were recorded and specimens were aliquoted and stored at −20°C until assayed. UNa and creatinine concentrations were measured using an automated analyser. UCa concentration was measured using a spectrophotometric method (see below).

Participants were excluded from the analysis if they were taking any form of antihypertensive medication or other medicines that might affect their UCa (ie, thiazide diuretics). Of these untreated people, 743 with a complete set of the above measurements provided 24-h urine collections; 690 of these also provided a fasting timed urine collection. All subsequent results describing 24-h and fasting UCa are for these 743 and 690 subjects respectively. The exclusion of the treated participants did not substantially alter the distributions of UNa and UCa by gender and ethnic group or the outcome of the analyses presented.

UCa concentration was measured using the arsenazo III kit from Sigma Diagnostics (Sigma/Aldricht Co Ltd, Poole, Dorset, UK).[18] A 4-ml aliquot of urine was acidified to a pH of between 4 and 6 in order to dissolve any calcium that may have precipitated. After duplicate 10 μl samples of each urine sample had been distributed into separate tubes, 1-ml of the arsenazo III reagent was added to each. Tubes were mixed thoroughly and left at room temperature for 5 min, following which the absorbance at 600 nm was measured on a spectrophotometer (Beckman DU62). Seven calcium standards ranging from 0 to 15 mg/dL were prepared and used to calibrate each assay. Each assay also included duplicate measurements of three different quality control samples. The intra- and inter-assay coefficients of variation calculated from these were 2.5 and 4.8% respectively ($n = 117$).

Statistics

Statistical analysis was performed using the GLM procedure in SPSS version 8.0. The values of both 24-h and fasting UCa were not normally distributed (Kolmogorov–Smirnov tests: $z = 2.72$, $P < 0.001$ and $z = 3.26$, $P < 0.001$, respectively). A cubic root transformation normalised the frequency distributions of both 24-h ($z = 0.53$, $P = 0.94$) and fasting ($z = 0.65$, $P = 0.79$) UCa. Although, ideally, parametric tests should be applied to normally distributed data, we carried out the analyses with and without cubic root transformation of the data. Since the results of the two analyses were comparable, we report for simplicity the findings on non-transformed data. Means between two groups were compared using the two-tailed unpaired Student's *t*-test and between three groups using one-way analysis of variance (ANOVA) with subsequent pairwise comparisons using the Bonferroni adjustment. Multiple regression analysis was conducted using a general linear model with UCa as the dependent variable. Gender and ethnic group were represented as numerical values (female = 1; male = 2: white = 1; black = 2; S Asian = 3) and entered as fixed factors. Age, BMI, UNa and/or BP were entered as co-

variates and the programme estimated adjusted slopes and intercepts, with their respective standard errors, for the regression lines relating UCa with UNa or with BP. The programme also calculated and compared estimated adjusted means with respect to gender and ethnic origin. The estimated slopes of the regression lines were compared using analysis of co-variance (ANCOVA).

Results

Characteristics of the population sample

Table 1 shows the characteristics of the population according to gender and ethnic origin. As expected from the study design, there were approximately equal numbers in each ethnic group. Black men were older than whites, who were older than the South Asians. Blacks were significantly heavier and had significantly higher BP than whites and South Asians.

Gender and ethnic group differences in UCa

The 24-h UCa of the whites was significantly higher than that of the blacks or S Asians in both sexes (Tables 1 and 2). The ethnic difference was also significant for the fasting UCa (Tables 1 and 2), suggesting that it was unlikely to be due to differences in intestinal calcium absorption between the three ethnic groups. Adjustment for age, BMI, gender, BP and UNa had little effect. Both the 24-h and fasting UCa remained significantly higher in the whites than in the blacks ($P < 0.001$ for both 24-h and fasting estimated adjusted means) and in the whites than in the S Asians ($P < 0.001$ for both) (Table 2). The effect was consistent in both men and women ($P = 0.36$ for interaction).

The mean 24-h UCa was significantly higher in men than in women (Table 3) in each ethnic group (Table 1). However, after adjustment for age, BMI, ethnic origin, BP and UNa the difference in the estimated adjusted mean 24-h UCa of men and women was no longer statistically significant ($P = 0.61$)

Table 1 Characteristics of untreated men and women by ethnic origin

	Whites	*Blacks*	*S Asians*	*P-value**
		Men		
n	120	92	124	
Age (years)	51 (6)	52 (6)	49 (6)	<0.001
BMI (kg/m^2)	25.2 (3.5)	26.6 (3.7)	24.3 (3.4)	<0.001
SBP (mm Hg)	124 (16)	133 (20)	127 (16)	0.001
DBP (mm Hg)	81 (9)	88 (11)	84 (9)	<0.001
Urinary variables				
UNa (mmol/24-h)	183 (69)	190 (74)	175 (74)	0.34
UCr (mmol/24-h)	14.2 (3.4)	18.3 (5.1)	12.7 (4.0)	<0.001
UCa (mmol/24-h)	4.76 (2.24)	3.53 (1.79)	3.68 (2.15)	<0.001
UVol (ml/24-h)	2945 (1226)	2268 (869)	2575 (1411)	<0.001
UCa (μmol/min)[a]	1.71 (1.17)	1.26 (0.90)	1.15 (0.94)	<0.001
Time (min)[a]	146 (52)	155 (50)	152 (53)	0.43
UVol (ml)[a]	271 (197)	181 (150)	255 (186)	0.002
		Women		
n	157	135	115	
Age (years)	50 (6)	50 (6)	49 (6)	0.19
BMI (kg/m^2)	25.7 (4.7)	29.0 (4.6)	26.7 (5.1)	<0.001
SBP (mm Hg)	121 (17)	130 (20)	126 (19)	<0.001
DBP (mm Hg)	77 (9)	83 (10)	79 (9)	<0.001
Urinary variables				
UNa (mmol/24-h)	141 (58)	156 (61)	141 (54)	0.048
UCr (mmol/24-h)	9.9 (2.6)	12.3 (2.8)	8.1 (2.4)	<0.001
UCa (mmol/24-h)	4.33 (2.22)	3.14 (1.86)	2.91 (1.51)	<0.001
UVol (ml/24-h)	2358 (984)	2387 (1191)	2367 (1087)	0.97
UCa (μmol/min)[b]	1.54 (1.00)	1.16 (1.00)	0.92 (0.71)	<0.001
Time (min)[b]	153 (48)	161 (58)	154 (67)	0.48
UVol (ml)[b]	313 (197)	297 (199)	299 (181)	0.75

Values shown are means (standard deviations). Mean values were compared by ANOVA. *P* for heterogeneity. SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; UNa, urinary sodium; UCr, urinary creatinine; UCa, urinary calcium; UVol, urinary volume. [a]Timed urine collections ($n = 110$, 85 and 114 respectively). [b]Timed urine collections ($n = 149$, 128 and 104, respectively).

Table 2 Comparison of 24-h and fasting urinary calcium excretion between ethnic groups

	24-h urinary calcium (mmol/24-h)			*Fasting urinary calcium (μmol/min)*		
	n		*Adjusted*[a]	*n*		*Adjusted*[a]
Whites	277	4.51 (2.23)	4.62 (1.90)	259	1.61 (1.08)	1.64 (0.83)
Blacks	227	3.30 (1.84)	3.16 (1.92)	213	1.20 (0.96)	1.13 (0.85)
S Asians	239	3.31 (1.91)	3.33 (1.90)	218	1.04 (0.84)	1.08 (0.84)
P value*		<0.001	<0.001		<0.001	<0.001

Values are means (standard deviations). Means were compared using ANOVA or ANCOVA. [a]Adjusted for age, gender, BMI, BP and UNa. **P* for heterogeneity.

Table 3 Comparison of daily and fasting urinary calcium excretion by gender

	Daily urinary calcium (mmol/24-h)			*Fasting urinary calcium (μmol/min)*		
	n		*Adjusted*[a]	*n*		*Adjusted*[a]
Men	336	4.02 (2.16)	3.84 (1.98)	309	1.38 (1.04)	1.34 (0.84)
Women	407	3.54 (2.02)	3.69 (1.97)	381	1.24 (0.96)	1.28 (0.84)
P value		0.002	0.61		0.07	0.32

Values are means (standard deviations). Mean values were compared using the two-tailed unpaired Student's *t*-test. [a]Adjusted for age, ethnicity, BMI, BP and UNa.

(Table 3). No interaction with ethnicity was detected ($P = 0.15$).

Association of UCa with UNa after adjustment for BP

Table 4 and Figure 1a show the estimated adjusted regression lines relating 24-h UCa and UNa for each ethnic group after adjustment for age, BMI, gender and BP. There were consistent associations with UNa and no significant differences between whites, blacks or S Asians in the slopes of these regression lines ($P = 0.911$ by ANCOVA). However, the UCa of whites was higher than that of blacks or S Asians (intercepts in Figure 1a) and this was consistent with the differences reported in Table 2. The equation of the estimated regression line, adjusting for ethnic origin, is shown in Table 5. This suggests that a 100 mmol increase in 24-h UNa (ie, intake) would be associated with the loss of an additional 1.04 mmol of calcium in the urine per day. The association between the fasting UCa and UNa is

Table 4 Relationships of daily and fasting urinary calcium excretion with urinary sodium, systolic and diastolic BP in each ethnic group, adjusted for confounders

	Daily urinary calcium (mmol/24-h)			*Fasting urinary calcium (μmol/min)*		
	β	*s.e.(β)*	*P*	*β*	*s.e.(β)*	*P*
Whites		(n = 277)			(n = 259)	
U Na[a]	0.010	0.002	<0.001	0.009	0.001	<0.001
Systolic BP[b]	0.020	0.008	0.014	0.005	0.004	0.17
Diastolic BP[c]	0.032	0.015	0.28	0.009	0.007	0.20
Blacks		(*n* = 227)			(*n* = 213)	
U Na[a]	0.010	0.002	<0.001	0.009	0.001	<0.001
Systolic BP[b]	0.016	0.006	0.007	0.008	0.003	0.008
Diastolic BP[c]	0.019	0.011	0.089	0.007	0.005	0.20
S Asians		(*n* = 239)			(*n* = 218)	
U Na[a]	0.011	0.002	<0.001	0.008	0.001	<0.001
Systolic BP[b]	0.005	0.007	0.51	0.004	0.003	0.15
Diastolic BP[c]	0.013	0.013	0.31	0.003	0.006	0.53

The adjusted slopes (β) and s.e. (β) of the regression lines were estimated using a general linear model with urinary calcium as the dependent variable, gender entered as fixed factor and age, BMI, UNa and BP entered as covariates.
P values for slopes comparison by ANCOVA [a]0.911 for 24-h and 0.886 for fasting; [b]0.281 for 24-h and 0.783 for fasting; [c]0.570 for 24-h and 0.824 for fasting.

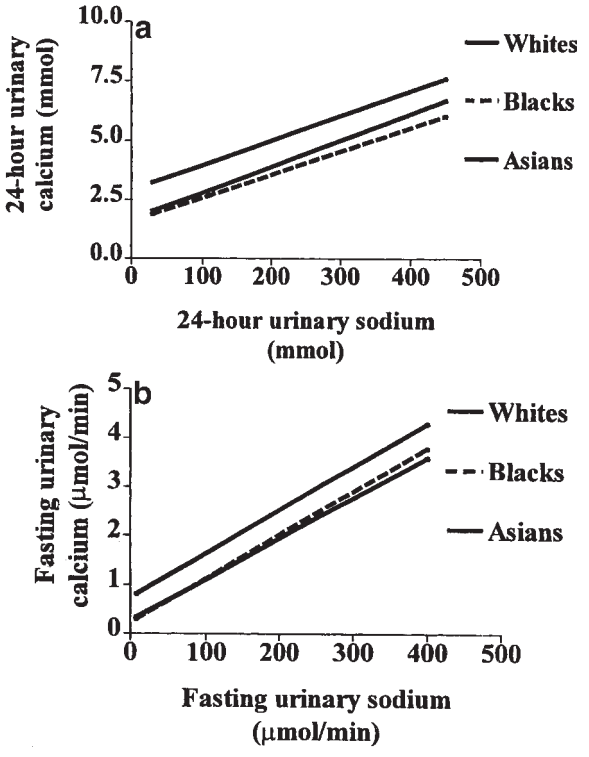

Figure 1 Relationship between (**a**) 24-h and (**b**) fasting UCa with UNa after adjustment for age, BMI, gender and BP in three ethnic groups. The lines represent the estimated regression lines for each ethnic group. Regression line equations were estimated using the general linear model with UCa as the dependent variable, gender as a fixed factor and age, BMI and BP as covariates. The number of subjects studied in (**a**) was 743 (277 whites; 227 blacks and 239 S Asians) and in (**b**) was 690 (259 whites; 213 blacks and 218 S Asians). There was no significant difference in the estimated slopes of the regression lines between the three ethnic groups in either (**a**) or (**b**) as assessed by ANCOVA (see Table 4). The equations defining the regression lines were: (**a**) for 24 h UCa whites 0.010 (UNa) + 2.779; blacks 0.010 (UNa) + 1.634; S Asians 0.011 (UNa) + 1.711; (**b**) for fasting UCa whites 0.009 (UNa) + 0.718; blacks 0.009 (UNa) + 0.274; S Asians 0.008 (UNa) + 0.291.

shown in Table 4 and Figure 1b. There were again no significant differences in the slopes of the estimated regression lines between whites, blacks and S. Asians ($P = 0.886$ by ANCOVA), although the fasting UCa of whites was higher than that of blacks and S Asians at every level of UNa (Figure 1b). After adjusting for age, BMI, gender, ethnic group and BP there was again a highly significant association between UCa and UNa with a slope very similar to that found in the 24-h measurements (Table 5).

Association of UCa with BP after adjustment for UNa

The association between 24-h UCa and systolic BP in each ethnic group after adjusting for age, BMI, gender and 24-h UNa is shown in Table 4 and Figure 2a. There was no significant difference in the slopes between the three ethnic groups ($P = 0.281$ by ANCOVA). Thus the slope of the regression line for the association of 24-h UCa with systolic BP was estimated after adjustment for age, BMI, gender, UNa and ethnic origin (Table 5). The relationship was statistically significant and indicated that a 20 mm Hg increase in systolic BP would be associated with a 0.28 mmol per day increase in UCa. The association of fasting UCa with systolic BP in each ethnic group after adjusting for age, BMI, gender and fasting UNa is shown in Table 4 and Figure 2b. Again there was no significant difference in the estimated slopes of the regression lines of the three ethnic groups ($P = 0.783$ by ANCOVA). Thus the association between fasting UCa and systolic BP was also adjusted for ethnic origin, as well as the other confounding variables, and the slope is shown in Table 5. Again the relationship was statistically significant indicating that it was unlikely to be due to BP-related differences in intestinal calcium absorption. Regression line equations were also estimated for the relationship between UCa and diastolic BP after adjustment for age, BMI, gender and UNa. The estimated slopes did not differ significantly between the three different ethnic groups for either the 24-h ($P = 0.570$) or for the fasting ($P = 0.824$) UCa measurement. Thus the relationship was estimated after adjustment for ethnic group also (Table 5). The relationship between 24-h UCa and diastolic BP was statistically significant suggesting that an increase of 10 mm Hg in diastolic BP would be associated with an increase in UCa of 0.22 mmol per day. Fasting UCa also tended to be associated with diastolic BP after adjustment for the confounding variables ($P = 0.052$).

The relationships of both fasting and 24-h UCa with BP after adjustment for age, BMI, gender, ethnic group and UNa remained similar when using

Table 5 Relationships of daily and fasting urinary calcium excretion with urinary sodium, systolic and diastolic BP, adjusted for confounders

	Daily urinary calcium (mmol/24-h)			*Fasting urinary calcium (μmol/min)*		
	β	*s.e.(β)*	*P*	*β*	*s.e.(β)*	*P*
U Na	0.010	0.001	<0.001	0.009	0.001	<0.001
Systolic BP	0.014	0.004	<0.001	0.006	0.002	0.002
Diastolic BP	0.022	0.008	0.003	0.007	0.003	0.052

The adjusted slopes (β) and s.e.(β) of the regression lines were estimated using a general linear model with urinary calcium as the dependent variable, gender and ethnic group entered as fixed factors and age, BMI, UNa and BP entered as covariates.

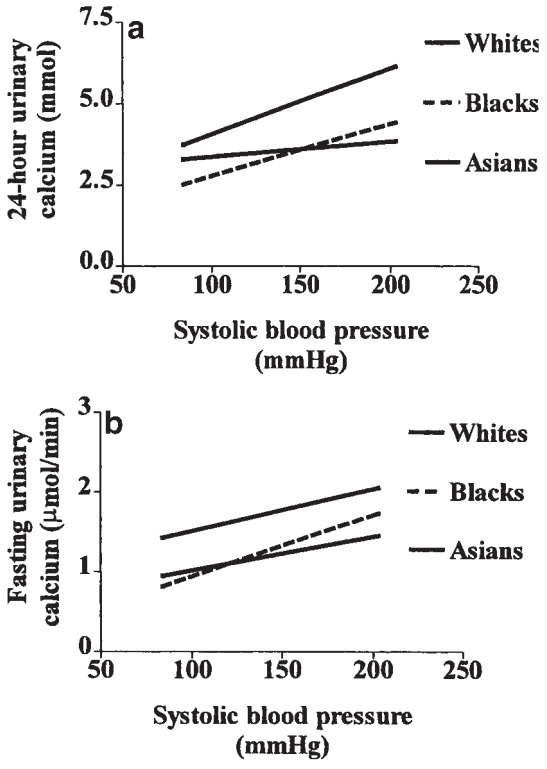

Figure 2 Relationship between (**a**) 24-h and (**b**) fasting UCa with systolic BP after adjustment for age, BMI, gender and UNa in three ethnic groups. The lines represent the estimated regression lines for each ethnic group. Regression line equations were estimated using the general linear model with UCa as the dependent variable, gender as fixed factor and age, BMI and UNa as covariates. The number of subjects studied in (**a**) was 743 (277 whites; 227 blacks and 239 S Asians) and in (**b**) was 690 (259 whites; 213 blacks and 218 S Asians). There was no significant difference in the estimated slopes of the regression lines between the three ethnic groups in either (**a**) or (**b**) as assessed by ANCOVA analysis (see Table 4). The equations defining the regression lines were: (**a**) for 24 h UCa whites 0.020 (SBP) + 1.987; blacks 0.016 (SBP) + 1.233; S Asians 0.005 (SBP) + 2.897; (**b**) for fasting UCa whites 0.005 (SBP) + 0.984; blacks 0.008 (SBP) + 0.232; S Asians 0.004 (SBP) + 0.566.

calcium and sodium-to-creatinine ratios (data not shown). This indicated that incomplete urine collections were unlikely to be a confounding factor in determining these associations.

Discussion

The results of this cross-sectional study of middle-aged men and women indicate that UCa is lower in blacks and S Asians than in whites. These ethnic differences were independent of age, BMI, gender, UNa, BP and indirect measurements of intestinal calcium absorption. In addition, multiple regression analyses suggested that there were positive relationships between UCa and both BP and UNa, even after adjustment for age, BMI, gender and ethnic group.

The study has some limitations. It is a cross-sectional study and, therefore, it does not determine cause-effect relationships and whether the hypercalciuria precedes the development of hypertension (or vice versa). However, the association between UCa and UNa is consistent with the direct effect of changes in sodium intake upon UCa, as found in intervention studies of manipulation of sodium intake.[9,19,20] Although we did not measure calcium or protein intake these dietary factors are unlikely to confound our results. A high calcium intake may lead to small increases in UCa,[21] yet the relationships were also present with fasting UCa. Moreover it would lower, rather than increase, BP.[22] A high protein intake is natriuretic and calciuretic[23] but it is associated with lower BP.[24–26] Finally, the epidemiological evidence suggests that whilst a higher calcium intake before the age of 25 years is associated with an increase in bone density in adolescent girls[27] and a higher bone mineral density in older women,[28] high calcium and animal protein intakes in adulthood do not prevent hip fractures.[29,30] Differences in diet by ethnic group could exist. However, they are unlikely to explain our findings as the relationships between UCa and both UNa and BP were not different by ethnic group. Finally, the exclusion of treated individuals rules out pharmacological interactions.

The effect of ethnic origin upon UCa is controversial. Although some studies show that blacks excrete less calcium in their urine than whites,[13,31] others have found no significant difference, even when dietary calcium intake was tightly controlled.[32] Only one study has been published which investigated the difference in UCa between whites and S Asians and found it lower in the S Asians.[14] The lower UCa of blacks and S Asians is attributed to secondary hyperparathyroidism resulting from the low serum 25-(OH)-D_3 in these two ethnic groups compared to whites.[14,33] Indeed, administration of 25-(OH)-D_3 in blacks increases UCa.[34] However, another study found no association between 25-(OH)-D_3 levels and UCa when comparing blacks with whites.[35] The present study found that the ethnic differences were still significant when fasting UCa was measured, suggesting that they were unlikely to be due to differences in intestinal calcium absorption and therefore unlikely to be related to vitamin D levels which mainly acts by increasing intestinal calcium absorption.

Nevertheless, the large differences in mean UCa between the three ethnic groups (with whites excreting approximately 1.0 mmol per day more calcium in their urine than blacks or S Asians) might help explain the higher bone density of blacks[36] and why osteoporosis[37,38] and bone fractures[39,40] are more common in whites than in blacks or S Asians. Despite these differences the association of UCa with both BP and UNa was independent of ethnic origin.

Quantitatively, we estimated that a 100 mmol increase in 24-h UNa (and therefore in sodium intake) per day would be associated with an additional 1.0 mmol per day renal calcium loss, in

keeping with other studies.[41,42] Moreover, it is comparable to the increase in UCa seen in intervention studies in which individuals' dietary sodium intake is altered.[19,20,41] As UNa reflects sodium intake when subjects are in balance,[43] these intervention studies suggest that differences in sodium intake are the likely cause of the association between UNa and UCa.

The mechanism determining the association between sodium intake and UCa is unclear. It may be a direct tubular effect, since sodium re-absorption provides the electrochemical driving force for paracellular calcium re-absorption in the renal proximal tubule and thick ascending limb of the loop of Henle.[44] The association between UNa and UCa may be mediated by extra-renal mechanisms that are activated by the increase in extracellular fluid volume that occurs when dietary sodium intake is raised. Increases in extracellular volume induced by a variety of different mechanisms cause increases in UCa[45] and one study has suggested that an increase in extracellular fluid volume may precede the increases in both UNa and UCa.[19]

We estimated that a 20 mm Hg higher systolic BP is associated with a 0.28 mmol higher daily UCa, which was independent of UNa. UCa is also increased in experimental models of hypertension[46] and in patients with primary aldosteronism.[47] At present, however, the mechanism responsible for this relationships remains unknown. Two main hypotheses have been presented.[48] The first postulates that there is a primary renal defect that results in both raised BP and an altered relationship between renal sodium and calcium handling.[49] Alternatively a primary defect in the kidney's ability to excrete sodium in hypertension would trigger compensatory mechanisms to restore sodium balance at the expense of a higher BP and increased renal calcium loss. MacGregor and Cappuccio[45] have argued that a reduction in venous compliance following sodium retention and volume expansion may cause a shift in blood distribution from the periphery to the centre of the body. Since increases in central blood volume have been reported to increase UCa,[50–54] the higher central blood volume of patients with hypertension may be the trigger for their hypercalciuria.

In the present study the relationship between UCa and BP was independent of UNa. It therefore seems likely that the mechanism responsible for the positive association between UCa and BP may be different from that by which sodium intake affects UCa.

Regardless of the mechanisms causing the associations of UCa with BP and UNa, the results suggest that differences in sodium intake and BP well within the range of values observed in Western populations, if sustained over time, may have important long-term consequences, as shown in animal models.[55–57] As hypercalciuria is an important risk factor for the development of kidney stones,[58,59] both a high sodium diet and a high BP may be associated with an increased risk of developing this disease. Furthermore, if the additional renal calcium loss associated with a high sodium intake and/or high BP is not adequately compensated by increases in intestinal calcium absorption, there may be a tendency to a reduced plasma ionized calcium, activation of compensatory hormonal mechanisms to restore plasma calcium with resulting increases in bone re-sorption.[45] Thus a high sodium intake and high BP may increase the risk of developing osteoporosis.[41,45] To support this view are the recent findings that the prevalence and incidence of kidney stones seem to be increased in people with hypertension,[60–63] that bone density is lower in elderly females at the higher end of the BP distribution than those at the lower end,[64] and that bone mineral density is associated with levels of salt intake in both young[65] and old[66] women.

From the values calculated in this study, the additional calcium lost in the urine if sodium intake was increased by 100 mmol per day for 10 years would be equivalent to approximately 10% of total body calcium. Similarly, our estimates suggest that over 10 years, a 20 mm Hg higher systolic BP would be associated with an additional renal loss of calcium equivalent to more than 1% of total body calcium. These effects on total body calcium may contribute to the risk of kidney stone disease and loss of bone. A reduction in salt intake may help prevent both.[67]

Acknowledgements

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