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The effect of low-dose potassium supplementation on blood pressure in apparently healthy volunteers

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Epidemiological and clinical trials suggest an inverse relationship between dietary K intake and blood pressure (BP). Most trials however have been of short duration, the dose of K was high, and the results have been conflicting. The aim of the present study was to evaluate the effect on BP of a low-dose supplementation (24 mmol/d) for an extended period. A double-blind placebo-controlled trial was conducted on fifty-nine volunteers, randomly assigned to receive 24 mmol slow-release KCl/d (*n* 30) or a placebo (*n* 29). Measures of BP, anthropometric characteristics and urine analysis for electrolytes were recorded during a 1-week baseline period. Supplementation was for 6 weeks during which BP and changes in weight were assessed and a second 24 h urine collection made. The primary outcome was the change in mean arterial pressure (MAP); systolic BP (SBP) and diastolic BP (DBP) were secondary outcomes. After 6 weeks of supplementation MAP was reduced by 7·01 (95 % CI −9·12, −4·89; $P<0·001$) mmHg, SBP was reduced by 7·60 (95 % CI −10·46, −4·73; $P<0·001$) mmHg and DBP was reduced by 6·46 (95 % CI −8·74, −4·19; $P<0·001$) mmHg. The reduction in MAP was positively associated with baseline urinary Na:K ($P<0·034$). A low daily dietary supplement of K, equivalent to the content of five portions of fresh fruits and vegetables, induced a substantial reduction in MAP, similar in effect to single-drug therapy for hypertension.

Blood pressure: Potassium: Clinical trials: Diet

Hypertension is an increasingly common chronic condition of individuals living in the most industrialized countries (Carrettero & Oparil, 2000; Primatesta *et al.* 2001), and is associated with an increased risk of cardiovascular and cerebrovascular disease (Sesso *et al.* 2000; Psaty *et al.* 2001). The association between vascular diseases and blood pressure (BP) appears to be present even amongst non-hypertensive subjects with normal to high BP (Kannel, 1996). A small decrease in BP may lead to a significant decrease in the incidence and prevalence of hypertension in the population (Hypertension Prevention Trial Research Group, 1990), reducing considerably mortality and morbidity of high-BP-related diseases (Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, 1997; Sesso *et al.* 2000; Psaty *et al.* 2001). High BP is thus an important modifiable risk factor for vascular diseases.

The non-pharmacological management of BP is an important and widely accepted means of preventing and treating hypertension (Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, 1997). Amongst the factors influencing BP, much attention has been paid to differences in diet. Intra-population studies have shown that not only are vegetarian diets consistently found to be associated with low BP (Sacks & Kass, 1988) and to be effective in lowering BP in both normotensive and hypertensive individuals (Rouse *et al.* 1983) but that an increased intake of fruits and vegetables may have a significant hypotensive effect (Appel *et al.* 1997), focusing attention on nutrients derived largely from these foods.

Attention is currently focused on dietary Na, and particularly on Na:K as factors influencing BP (Dyer *et al.* 1994). Although Na restriction is widely recommended as a non-pharmacological means of preventing and treating hypertension (Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, 1997) the epidemiological and clinical studies that have advocated this approach are intensely debated (Freedman & Petitti, 2001). The decrease in Na consumption necessary to exert a small decrease in BP (100 mmol/d; Dyer *et al.* 1994) is acknowledged to be difficult to achieve and to sustain (Sinaiko *et al.* 1993), and might even represent a risk for some in the population (Graudal *et al.* 1998). Moreover Na restriction might be beneficial only for a fraction of the population defined as salt-sensitive (Morris *et al.* 1999). A strong interconnection between the intake of the two electrolytes and BP level is suggested by observational

Abbreviations: BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure.

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studies, since urinary Na:K seems to be more related to BP levels than the urinary excretion of the two minerals alone (Dyer *et al.* 1994).

Epidemiological studies have indicated that populations or individuals accustomed to a high K intake have lower BP levels (Langford, 1983; Intersalt Cooperative Research Group, 1988) and have a very low occurrence of hypertension and related vascular diseases when compared with populations or individuals having a low K intake (Frisancho *et al.* 1984). A transmigrational study has also shown that BP was increased in individuals moving from an area of high K intake to an area of low K intake (Ward *et al.* 1980). However a considerable number of randomised controlled trials on K supplementation have produced inconclusive or conflicting results (Whelton *et al.* 1997).

Some clinical studies have also indicated that the K-induced hypotensive effect increases with time (Cappuccio & MacGregor, 1991), becoming more pronounced after about 6 weeks of supplementation (Siani *et al.* 1987). In many of the studies reviewed by Whelton *et al.* (1997) their duration was short, the number of subjects (predominantly hypertensive) was small and the supplement of K was high, ranging from 60 to 200 mmol/d, an amount that is unlikely to be achieved by dietary means alone in most of the population. Despite the diversity of experimental designs that had been employed, nevertheless it seemed that the response to K supplementation was not directly related to dose level.

The aim of the present study was to isolate and evaluate the effect on BP of a modest increase in dietary K. A randomised placebo-controlled double-blind trial was therefore conducted on apparently healthy volunteers over an extended period of time (six weeks) using a dose level of K (24 mmol/d) approximating the content of five portions of fruits and vegetables.

Subjects and methods

Subjects

Seventy-one subjects aged between 25 to 65 years were recruited from amongst the academic and postgraduate research staff of King's College London. Of these subjects, fifty-nine completed the study.

At the first visit, characteristics influencing BP (Beevers *et al.* 2001*a*,*b*; O'Brien *et al.* 2001*a*) such as age, gender and ethnic origin were recorded. Participants were interviewed during the first appointment about their general health conditions and regarding the known lifestyle factors that may be involved in the determination of BP (Beevers *et al.* 2001*a*,*b*; O'Brien *et al.* 2001*a*), such as smoking habit, alcohol consumption (units per week), use of medications and physical activity. Physical activity was assessed by questioning the subjects, and based on hours of physical activity per week, was scored from 1 to 4 representing ≤ 1, between 1 to 2, between 2 to 4, and ≥ 4 h per week respectively.

In order to obtain strongly motivated subjects the volunteers were not attracted either with economic incentive or reimbursement for their participation. Written informed consent was obtained from each participant before taking part in the study, which was approved by the King's College London Research Ethics Committee for Research Involving Human Subjects.

Exclusion criteria

The main exclusion criteria were diseases or conditions that might involve collateral effects from K supplementation or interfere with its metabolism (Medline plus, 2002). These were: insulin-dependent diabetes mellitus; non-insulin-dependent diabetes mellitus; diabetes insipidus; cardiovascular diseases (including events of cardiac arrhythmia and peripheral arterial disease) or previous cardiovascular events; any kind of renal diseases; metabolic acidosis; current peptic ulcers; dysphagia; general digestive problems; gastric surgery; pregnancy and lactation. Other exclusion criteria were the use of anti-hypertensive drugs, and the use of drugs known to interfere with K metabolism.

In order to avoid confounding, the subjects who during the study period changed either their usual diet or other general lifestyle factors known to influence BP were excluded from the study. Subjects taking other medications for which K supplementation was not contraindicated, or mineral and vitamin supplements, were allowed to participate in the study with the provision that they continued to use these products.

Design of the trial

The study took the form of a randomised double-blind placebo-controlled trial with the aim of testing the effect of K supplementation on BP. At the first visit the seventy-one subjects meeting the inclusion criteria were randomly assigned to receive either a K supplement (n 36) or a placebo (n 35) using a computer-generated randomisation code (Statistical Package for the IBM Personal Computer Version 2.1, 1983; EPISTAT Inc., Richardson, TX, USA). Patients were not stratified in any manner before being randomly assigned in a 1:1 ratio.

The study consisted of a baseline period of 1 week during which BP and body weight were measured at the beginning and end, and a 24 h urine sample was collected in order to estimate electrolyte intake. During a 6-week intervention phase BP and body weight were measured at 3-week intervals, and a second 24 h urine sample was collected during the final week. KCl was administered as one slow-release tablet containing 8 mmol KCl (Slow-K Tablets 600 mg; kindly supplied by Alliance Pharmaceuticals Ltd, Avonbridge House, Chippenham, Wilts., UK) three times daily with meals. The placebo contained sorbitol and fructose.

The patients and the investigator were unaware of the type of supplement being given, other than that it was a nutrient. The placebo and KCl pills were provided in identical containers. The adherence of the volunteers to the treatment was assessed at each visit by questioning, and by counting the pills returned. Compliance was calculated as a percentage of prescribed dosage actually consumed.

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Blood pressure, heart rate and body mass index

Each BP measurement was performed following current recommendations (Beevers *et al.* 2001*a*,*b*; O'Brien *et al.* 2001*a*). BP was assessed at the same time of day (within 30 min) for every appointment in order to avoid the influence of circadian variations in BP (Beevers *et al.* 2001*a*,*b*; O'Brien *et al.* 2001*a*), at approximately the same heart rate, and by the same observer using the same instruments throughout the study for each measurement. The subjects were instructed not to smoke, eat or drink during the 30 min before each appointment. They were also given verbal and written notice to avoid exercising 30 min before the appointment, to come to the appointment with an empty bladder and to maintain strictly their usual habits on the day of the appointment (coffee, tea, meals consumed at the same time of the day). BP measurements were performed after the subjects had rested quietly for at least 5 min in the seated position. Two different cuffs (350 mm and 420 mm) were used depending on the arm circumference. At each visit at least three readings for systolic BP (SBP) and diastolic BP (DBP) and heart rate were taken at 2 min intervals in the left arm using a semi-automated device employing the oscillometric method (Omron M5-I; Omron Healthcare Europe B.V., Hoofddorp, The Netherlands). The first readings of each assessment were ignored in order to avoid results affected by the defence reaction (Beevers *et al.* 2001*a*,*b*; O'Brien *et al.* 2001*a*) and the last two readings were averaged and recorded. This value was confirmed after a 2 min interval with a Hawksley random zero sphygmomanometer (Hawksley and Sons, Lancing, Sussex, UK) according to current guidelines produced by the British Hypertension Society (O'Brien *et al.* 2001*b*), since automatic devices may be unsuitable for some individuals for which there is no obvious reason (O'Brien *et al.* 2001*a*). SBP was measured as the point of appearance of the Korotkoff sounds (Phase I) and DBP was measured as the point of complete disappearance of the Korotkoff sounds (Phase V) according to the guidelines given by the British Hypertension Society (Beevers *et al.* 2001*a*,*b*; O'Brien *et al.* 2001*a*). All values for BP shown in the tables were obtained from the semi-automated device alone.

Subjects with either SBP$\geq$140 mmHg or DBP level $\geq$ 90 mmHg were considered to be hypertensive.

Mean arterial pressure (MAP) was computed as MAP = (2 DBP+SBP)/3 (Wilson *et al.* 1999; Vander *et al.* 2000).

Urine collection and laboratory analysis

Subjects were given instructions on providing the 24 h urine collection for analysis of Na, K and chloride. Urinary volumes were measured and a sample refrigerated for a few days before analysis. Urinary K and Na were analysed by flame photometry (Corning 410 Flame Photometer; Corning Science Products, Corning Limited, Halstead, Essex, UK) and chloride content was assessed by potentiometric titration (926 Chloride Analyzer; Corning Medical and Scientific). For K and Na analyses the linear regression of the standards and the interpolation of the data were performed using a Hewlett Packard 97 SO Calculator (Hewlett HP Packard, 1000 N.E. Circle Blvd, Corvallis, OR, USA). Na only was measured in the final sample.

An estimate of customary Na intake was made by averaging the Na content of the two urine collections. All the electrolyte data presented in Table 1 were derived from the first urine collection only.

Table 1. Baseline characteristics of the participants in the study*
(Mean values and standard errors of the mean)

Type of treatment...	Potassium chloride (*n* 30)		Placebo (*n* 29)	
	Mean	SEM	Mean	SEM
Age (years)	44·5	2·1	41·7	2·2
Women (%)	53		35	
European (%)	83		83	
Middle-Eastern (%)	7		7	
South Asian (%)	3		7	
East Asian (%)	7		3	
BMI (kg/m^2)	26·06	0·64	24·90	0·82
Physical activity (classes)†	2·10	0·19	2·14	0·18
Alcohol consumption (units/week)	8·6	1·5	10·3	1·5
Smokers (%)	23		28	
Hypertensives (%)	20		7	
Heart rate (pulses/min)	66·6	1·4	67·7	2·0
MAP (mmHg)	89·9	2·1	85·6	1·9
SBP (mmHg)	118·2	2·6	115·7	2·4
DBP (mmHg)	75·5	2·1	70·5	1·8
Urinary Na (mmol/d)	175·4	13·0	155·1	9·1
Urinary Cl (mmol/d)	170·6	13·0	148·7	8·9
Urinary K (mmol/d)	84·0	4·5	84·0	5·2
Urinary Na:K	2·13	0·13	2·01	0·17

MAP, mean arterial pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.
* There were no significant differences at baseline between the two groups (two-sample *t* test or chi-squared test).
† Physical activity was assessed by questioning the subjects, and based on hours of physical activity per week and was scored from 1 to 4 representing $\leq$1, between 1 to 2, between 2 to 4, and $\geq$4 h of physical activity per week respectively.

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Outcomes

The mean difference in MAP change between the K-supplemented and the placebo group was chosen as the primary outcome, while mean changes in DBP and SBP were chosen as secondary outcomes. This choice was made in order to evaluate the overall change in BP since the MAP summarizes both SBP and DBP with a single value. Moreover SBP and DBP may change within each individual with different patterns and sign, making it difficult to determine the direction and importance of changes in BP.

Statistical analysis

Our trial was designed to test the alternative hypothesis that the change in BP would differ between the K-supplemented group and the placebo group.

The baseline BP used for the statistical analysis was the average of the measurements taken during the first-week period.

For interval level variables (for example, BP), differences between groups were tested using the two-sample *t* test while differences within each group were tested with the paired *t* test. For ordinal level variables (for example, compliance) these tests were performed using the Mann–Whitney test and the Wilcoxon signed rank test for comparisons between and within the two groups respectively. The chi-squared test was used to assess the significance of differences between the groups for nominal level variables (for example, gender).

Correlations between the different variables and both BP and changes in BP were initially tested using a stepwise regression analysis. Thereafter a regression analysis was performed based on the variables present in the final stepwise model. Variables that were found to be correlated with baseline BP were included as covariates in a repeated measurement ANOVA (SPSS 10.0 for Windows; SPSS Inc. Headquarters, 233 S. Wacker Drive, Chicago, IL, USA).

Data are presented as mean values and standard errors of the mean and 95 % CI. A P value of $\leq 0{\cdot}05$ was considered to be statistically significant. All calculations except the repeated measurement ANOVA were performed with the Minitab statistical package (Minitab release 13.1; Minitab Inc., 3081 Enterprise Drive, State College, PA, USA).

Results

Subject details

Seventy-one subjects were enrolled in the study, of whom fifty-nine completed. Three subjects in both groups quit the study during the baseline period. In the active group three volunteers were excluded because of changes in lifestyle, while in the placebo group, two retired for personal reasons, and one was excluded because of change in medication.

Baseline characteristics are shown in Table 1. There were no significant differences between the two groups with regard to age, BMI, urinary electrolyte excretion, Na:K, BP levels, heart rate, degree of physical activity and smoking habit. The number of subjects being of non-European ethnic origin and the number of hypertensives was small and so did not justify a separate statistical analysis for these subgroups. The K group contained more females than did the placebo group (53 % compared with 35 %) but the difference was not statistically significant and was not likely to have influenced the results of the present study since no significant correlation was found between mean changes in BP and gender as shown by the stepwise regression analysis.

Therefore the effect on BP of K supplementation could be evaluated by comparing the mean changes in BP level in the two entire intervention groups.

Compliance and side effects

The overall compliance to the treatment was very satisfactory, being 89 (SEM 2·5) % for the K group and 83 (SEM 3·1) % for the controls. The difference was not statistically significant. One individual receiving K claimed that he experienced an increase in appetite, although neither his weight nor his physical activity changed during the study. Two subjects in the placebo group reported side effects; one experienced occasional nausea associated with the consumption of the pills, while another subject reported transitory polyuria during the first week of treatment. Both volunteered to remain in the study, and their unexpected symptoms rapidly disappeared.

Blood pressure

Amongst the baseline characteristics all measures of BP (MAP, SBP and DBP) were positively related only to BMI (P=0·001, P=0·002, P=0·001 respectively) and age (P=0·001, P=0·001, P=0·005 respectively).

During treatment BP values changed significantly in both groups (Table 2). In the K group, at the end of the 6-week intervention period MAP, SBP and DBP had decreased significantly when compared with the baseline values. This decrease occurred gradually. A significant decrease in MAP was found at the end of the first 3-week intervention period, driven mainly by a significant decrease in DBP while in the same period SBP was not significantly reduced. In contrast, during the second 3-week period SBP decreased significantly contributing to a further fall in MAP.

At the end of the study, in the placebo group MAP had increased significantly due in great part to a significant change in DBP noted, again, after the first 3 weeks of treatment.

Comparisons between the mean changes in BP measurements of the two experimental groups demonstrate that the group treated with K experienced a marked and significant decrease in SBP and DBP, and thus in MAP (as shown in Table 3) when compared with the group given the placebo. The fall in BP occurred continuously during the length of the study, following a pattern similar to that described above for the changes in BP measurements from baseline values, but being more accentuated by the concomitant negative changes of BP values in the active group and positive changes in BP in the placebo group. A comparison of changes in MAP in the two groups is better appreciated in

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Table 2. Change from baseline in blood pressure at different periods of the study within the potassium and placebo groups‡
(Mean values and standard errors of the mean)

	Blood pressure (mmHg)						Mean difference in blood pressure (mmHg)					
	Week 0		Week 3		Week 6		Week 3−week 0		Week 6−week 3		Week 6−week 0	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Potassium (*n* 30)												
MAP	89·88	2·13	87·67	2·20	84·97	2·06	−2·21*	0·72	−2·70**	0·91	−4·91***	0·80
95 % CI							−3·69, 0·73		−4·57, −0·84		−6·54, −3·30	
SBP	118·15	2·62	117·17	2·71	111·93	2·52	−0·98	1·20	−5·23***	1·03	−6·22***	1·07
95 % CI							−3·43, 1·47		−7·33, −3·14		−8·40, −4·04	
DBP	75·48	2·07	72·95	2·08	71·47	1·90	−2·53†	0·73	−1·48	0·98	−4·02***	0·87
95 % CI							−4·03, −1·04		−3·50, 0·51		−5·80, −2·23	
Placebo (*n* 29)												
MAP	85·60	1·92	86·74	1·93	87·70	1·94	1·13	0·60	0·96	0·60	2·09*	0·70
95 % CI							−0·09, 2·36		−0·24, 2·16		0·68, 3·51	
SBP	115·74	2·41	116·04	2·32	117·12	2·37	0·30	0·84	1·08	0·73	1·38	0·95
95 % CI							−1·41, 2·01		−0·41, 2·57		−0·57, 3·33	
DBP	70·53	1·83	72·12	1·85	72·98	1·82	1·59††	0·66	0·86	0·65	2·45†	0·73
95 % CI							0·22, 2·94		−0·46, 2·19		0·96, 3·94	

MAP, mean arterial pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.
Mean values were significantly different from zero: **P*=0·005, ***P*=0·006, ****P*=0·001, †*P*=0·002, ††*P*=0·024.
‡ Estimate for differences between the two groups was assessed by the paired *t* test. For details of subjects and procedures, see Table 1 and p. 54.

Fig. 1. Using repeated measurement ANOVA, in all cases (MAP, SBP, DBP) a significant difference was found in the time profile between the two groups (*P*=0·001). This was further confirmed by the repeated measurement ANOVA on changes in BP where the groups were found to differ significantly (*P*=0·001). The models included BMI and age as covariates. Regression analysis revealed that the changes in MAP and DBP induced by K supplementation were positively related to baseline urinary Na:K (*P*=0·034 and *P*=0·021 respectively), while the change in DBP was positively related to the baseline SBP (*P*=0·016) and negatively related to baseline DBP (*P*=0·001). The mean values for Na in the second urine sample were 166·3 (SEM 12·0) and 151·4 (SEM 11·6) mmol/d for the K and placebo group respectively. The difference in Na intake between the first and second measurements, as indicated by urinary Na excretion, was not statistically significant within and between groups and was not related to changes in BP.

Body mass index, heart rate and customary salt consumption

In neither of the groups did BMI or heart rate change significantly during the course of the investigation nor was there a significant difference between the two groups (Tables 4 and 5). An average value of the first and second analysis for Na was used to provide an approximate value for the customary salt intake of the entire cohort, which amounted to 9·42 g/d.

Table 3. Comparisons of mean changes in blood pressure levels between the potassium and the placebo group during the different periods of the study†
(Mean values and standard errors of the mean)

		Type of treatment					
		Potassium (*n* 30)		Placebo (*n* 29)		Potassium−placebo difference	
Period	Blood pressure (mmHg)	Mean	SEM	Mean	SEM	Mean	95 % CI
Week 0 to 3	MAP	−2·21	0·72	1·13	0·60	−3·34	−5·22, −1·47*
	SBP	−0·98	1·20	0·30	0·83	−1·28	−4·21, 1·65
	DBP	−2·53	0·73	1·58	0·66	−4·11	−6·09, −2·13*
Week 3 to 6	MAP	−2·70	0·91	0·96	0·59	−3·66	−5·84, −1·49*
	SBP	−5·23	1·00	1·08	0·73	−6·32	−8·84, −3·79*
	DBP	−1·48	0·97	0·87	0·65	−2·35	−4·70, 0·00**
Week 0 to 6	MAP	−4·91	0·79	2·09	0·69	−7·01	−9·12, −4·89*
	SBP	−6·22	1·10	1·38	0·95	−7·60	−10·46, −4·73*
	DBP	−4·02	0·87	2·45	0·73	−6·46	−8·74, −4·19*

MAP, mean arterial pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.
Significantly different from zero: **P*=0·001, ***P*=0·050.
† Estimates for differences between the two groups (potassium−placebo) were assessed by the two-sample *t* test. For details of subjects and procedures, see Table 1 and p. 54.

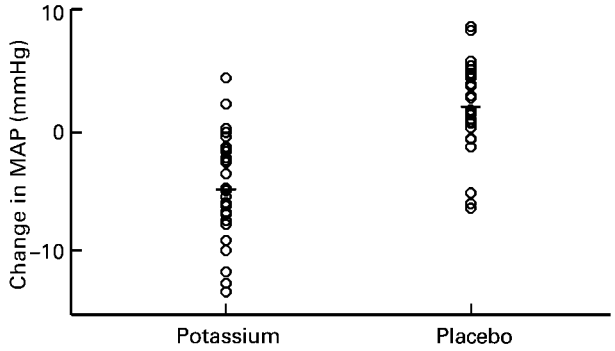

Fig. 1. Comparison of the changes in mean arterial pressure (MAP) between the potassium and the placebo group after 6 weeks of treatment. (—), Mean values. The mean change in MAP between the two groups was significantly different from 0 (P=0·001; two-sample t test).

Discussion

The effects of a modest K supplement on BP were studied in apparently healthy volunteers using a randomised double-blind placebo-controlled design.

Compliance in the active group was high, indicating that our subjects, on average, consumed 22 mmol KCl/d.

A small but significant rise in MAP was evident in all but six of the placebo group (see Fig. 1). This surprising observation can be attributed to a change in ambient temperature between the 1-week baseline period, when baseline measurements were recorded, and the ensuing 6-week intervention period. Between the two periods there was a notable drop in temperature of around 10°C. The influence of temperature on BP is well documented (Giaconi *et al.* 1989; Jansen *et al.* 2001). It is likely, therefore, that during the first week of the study the unusually high temperature had a hypotensive effect resulting from two different heat-induced mechanisms: a decrease in cardiac output arising from depletion of the plasma volume secondary to sweating; a decrease in peripheral resistance to blood flow due to vasodilation (Vander *et al.* 2000). However all subjects taking part in the study were subjected to the same environmental conditions; the influence of the change in temperature would thus apply equally to the active group.

MAP was significantly reduced following dietary K supplementation, the fall being progressive over the 6-week period of observation, with an early decrease in DBP in the first 3-week period followed by a decrease in SBP in the latter half of the study. It has previously been suggested that at least 6 weeks of supplementation might be needed to reveal a significant change in BP (Matlou *et al.* 1986; Kawano *et al.* 1998). In a trial lasting 15 weeks, it was noted that the greater rate of decrease in BP occurred between the third and sixth week of supplementation, while during the subsequent 9 weeks, the rate of decrease was extremely small (Siani *et al.* 1987). These observations have obvious implications, since most of the clinical trials on which meta-analyses have been based (Cappuccio & MacGregor, 1991; Whelton *et al.* 1997) have lasted less than 6 weeks.

The reduction in MAP reported in the present study (7·01 mmHg) was comparable to that achieved by

Table 4. Comparison of the body mass index of the participants in the study before and after the 6-week treatment period†

(Mean values and standard errors of the mean)

	BMI (kg/m^2)*						
	Week 0		Week 6		Week 6−week 0 difference		
Treatment	Mean	SEM	Mean	SEM	Mean	SEM	95% CI
Potassium (n 30)	26·06	0·64	26·09	0·65	0·03	0·07	−0·12, 0·18
Placebo (n 29)	24·90	0·82	25·02	0·86	0·12	0·75	−0·03, 0·28

* There were no significant differences between and within the two groups after the 6-week intervention period (two-sample t test and paired t test).
† For details of subjects and procedures, see Table 1 and p. 54.

Table 5. Change from baseline in heart rate (beats/min) at different periods of the study within the potassium and the placebo groups*

(Mean values and standard errors of the mean)

	Week 0		Week 3		Week 6		Week 3−week 0 difference		Week 6−week 3 difference		Week 6−week 0 difference	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Potassium (n 30)	66·57	1·41	66·07	1·54	66·77	1·35	−0·50	0·99	0·70	0·98	0·20	0·85
95% CI							−1·53, 1·93		−1·31, 2·70		−1·53, 1·93	
Placebo (n 29)	67·71	1·95	69·05	1·90	68·88	1·64	1·34	0·98	−0·17	0·72	1·17	1·18
95% CI							−0·72, 3·41		−1·64, 1·29		−1·24, 3·58	

* Estimates for differences between the two groups were assessed by the paired t test. There were no significant differences between the two groups. For details of subjects and procedures, see Table 1 and p. 54.

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single-drug therapy for hypertension (Materson et al. 1993), and was substantial when compared with the mean fall calculated from thirty-three randomised trials (Whelton *et al.* 1997). MAP fell by 3·4 mmHg in the studies of at least 6 weeks duration, in which the supplement of KCl ranged from 60 to 120 mmol/d. The apparently greater efficacy of low-dose supplementation, also evident in two trials in which hypertensive patients received a daily supplement of 48 mmol KCl (Siani *et al.* 1987; Fotherby & Potter, 1997), may have an explanation in the nature of the anion ingested with K. It has been claimed that the pressor effect of Na is exerted only when Na is consumed as the chloride salt (Shore *et al.* 1988; Boegehold & Kotchen, 1991; Kotchen & Kotchen, 1997). A high intake of chloride may therefore antagonise the effect of K in high-dose supplementation.

When compared with the marginal benefits arising from a dietary salt restriction, the effects of a modest K supplement are encouraging. The results of the Intersalt Study (Intersalt Cooperative Research Group, 1988) predict that a decrease in Na intake of 100 mmol/d (5·8 g salt) would be associated with a decrease in BP of 3·14/0·14 mmHg, and a recent meta-analysis of randomized clinical trials (Graudal *et al.* 1998) found that a reduction in dietary Na of 100 mmol/d promoted a small but significant fall in BP of 0·8/0·2 and 3·6/1·6 mmHg in normotensive and hypertensive subjects respectively.

Na and K have contrary effects on BP but the relationship is more subtle. Evidence from epidemiological studies and clinical trials (Geleijnse *et al.* 1990; Dyer *et al.* 1994) has indicated that Na:K is positively correlated with BP, and that the nature of this association appears to be stronger than that for urinary K and Na alone. The recent Dietary Approaches to Stop Hypertension (DASH) salt study (Sacks *et al.* 2001) comprised two dietary groups; a typical American diet and the DASH diet proposed for the reduction of cardiovascular and cerebrovascular diseases in the US population, but adjusted to provide the same amount of Na. At baseline, the difference in BP between the groups was 5·9/2·9 mmHg, almost three times as great as the fall in BP induced by a reduction in Na intake of 50 mmol/d. It is noteworthy that the DASH diet provided twice as much K. When, however, the Na content of the diets was restricted by a further 50 mmol/d, the effect of K was attenuated, the difference between the dietary groups falling to 2·2/1·0 mmHg. Clearly K supplementation is most beneficial in subjects consuming a high-salt diet (Whelton *et al.* 1997; Kawano *et al.* 1998), as observed in our subjects, who had a mean salt intake of around 9·5 g/d. Conversely salt sensitivity, defined as an increase in MAP resulting from salt loading (Morris *et al.* 1999), is dose-dependently suppressed when dietary K is increased within the normal range of intake.

The recommended intake of K in the UK (Department of Health, 1991) is 90 mmol/d, some 20 mmol above the average consumption (Gregory *et al.* 1990). A general and chronic low-grade K deficiency, therefore, affects a large part of the population, the occurrence being particularly striking in the elderly (Bates *et al.* 1999) and amongst those belonging to the low social-economic classes (Smith & Brunner, 1997). As a means of reducing the incidence of cardiovascular and cerebrovascular disease, diet modification involving an increased consumption of fresh fruits and vegetables may be unrealistic because of their relatively high cost. Eight of our subjects (14 %), none of whom was aware of any abnormality in BP, were found to be hypertensive during the course of the study, a finding that highlights the importance of ensuring, among other things, an adequate intake of K. As an alternative or complementary strategy, diet supplementation with K or fortification of processed foods may offer an inexpensive and safe preventive measure to confront a major public health problem.

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