Effects of Potassium Supplementation on Office, Home, and 24-h Blood Pressure in Patients With Essential Hypertension

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An increase in potassium (K) intake may lower blood pressure (BP), but inconsistent results have been obtained in clinical trials. We studied the effects of K supplementation in hypertensive patients with monitoring of home and ambulatory BP. Fifty-five patients with essential hypertension (26 men, 29 women, 36–77 years old) participated in this study. A 4-week K supplementation period and 4-week control period were assigned in a randomized crossover manner. During the K period, the subjects were given 64 mmol/day of K as slow-release KCl tablets. Office, home, and 24-h BP, as well as serum and urinary electrolytes, were measured at the end of each period. In the control period, office, home, and 24-h BP were 151 ± 2/88 ± 1 (mean ± SE), 138 ± 1/83 ± 1, and 137 ± 1/81 ± 1 mm Hg, respectively. Serum K increased from 4.15 ± 0.04 to 4.42 ± 0.05 mmol/L, and urinary K increased from 54 ± 2 to 96 ± 3 mmol/day with the K supplementation. Office, home, and 24-h BP were significantly lower in the K period than in the control period, although the differences were small (2.7 ± 1.1/1.4 ± 0.6, 3.6 ± 0.9/1.7 ± 0.5, 3.4 ± 1.0/1.2 ± 0.5 mm Hg, respectively). Changes in home and 24-h systolic BP with K supplementation were highly significant ($P < .001$), compared with office BP ($P < .05$). The change in 24-h systolic BP was correlated negatively with baseline BP and urinary Na/K ratio, and positively with baseline urinary K excretion. The changes in daytime and nighttime BP were comparable. These results indicate that increasing K intake lowers BP in hypertensive subjects, especially in those with higher BP and lower K intake. Our study supports the usefulness of K supplementation in the treatment of hypertension, although its antihypertensive effect may be small. Am J Hypertens 1998;11:1141–1146 © 1998 American Journal of Hypertension, Ltd.

KEY WORDS: **Essential hypertension, potassium, home blood pressure, ambulatory blood pressure.**

It has been suggested that deficiency of potassium (K) intake is associated with hypertension, and high dietary K intake may have a preventative effect. In epidemiologic studies, dietary intake of K has been shown to be inversely correlated with the level of blood pressure (BP) and the prevalence of hypertension.[1–3] Metaanalyses showed a significant reduction in BP with K supplementation,[4,5] although conflicting results have been reported concerning the effects of oral K supplementation in clinical studies.[6–10] Lifestyle modifications such as weight reduction and sodium (Na) restriction are widely recommended as basic methods in the therapy of hypertension. However, increasing dietary intake of K is not accepted as an important part of the nonpharmacologic treatment.[11,12]

Most earlier studies concerning K intake assessed only casual BP, which may be partially responsible for the inconsistent results. The effects of K supplementation on 24-h ambulatory BP have been examined in

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TABLE 1. CLINICAL CHARACTERISTICS OF THE STUDY SUBJECTS

Age (years)	36–77 (62.3 ± 1.2)
Gender (M/F)	26/29
Antihypertensive drug	38+, 17−
Body weight (kg)	63.1 ± 1.6
Body mass index (kg/m^2)	24.7 ± 0.4

only a few studies,[13,14] whereas those on home BP have not been investigated. Ambulatory BP monitoring and self-measurement of BP at home are useful methods for the diagnosis and treatment of hypertension.[15,16] As these methods provide multiple BP recordings and have good reproducibility, they seem particularly suitable to detect small changes in BP that may be produced by various nonpharmacologic approaches. We have shown that restriction of Na intake lowers BP throughout the day, whereas reduction of alcohol intake causes biphasic changes without altering average 24-h BP in hypertensive patients.[17,18]

In the present study, we assessed the effects of oral K supplements on office, home and 24-h BP of hypertensive patients in a randomized crossover manner. We also examined the relationships between the K-induced changes in BP and baseline levels of BP, Na intake, or K intake.

MATERIALS AND METHODS

Subjects Sixty Japanese men and women with mild to moderate essential hypertension participated in this study. They were 36 to 77 years old, treated or untreated, and had office systolic BP (SBP) >140 mm Hg or diastolic BP (DBP) >90 mm Hg. Five patients were excluded from the study because of poor compliance (n = 2), poor ambulatory BP records (n = 2), or withdrawal due to gastrointestinal symptoms during K supplementation (n = 1). The remaining 55 subjects completed the study protocol with good records of ambulatory and home BP.

The clinical characteristics of the 55 patients are shown in Table 1. Among these subjects, 17 were untreated and 38 were treated with antihypertensive drugs. Thirteen patients were receiving monotherapy, and 25 patients were receiving combination therapy. Calcium antagonists were the most frequently prescribed drugs (n = 33), followed by β-blockers (n = 19), angiotensin-converting enzyme inhibitors (n = 10), α-blockers (n = 5), and diuretics (n = 3). Pharmacologic therapy was continued without any alterations throughout the study protocol.

Protocol The study protocol was approved by the Clinical Research Committee of our institute, and informed consent was given by each patient. A 4-week K supplementation period and 4-week control period were assigned in a randomized crossover design. During the K period, the subjects were given 64 mmol/day (2500 mg) of K as slow-release KCl tablets (two tablets four times daily). Placebo was not given during the control period because the placebo effect is usually negligible in the monitoring of ambulatory or home BP[15,16] and many patients were already taking antihypertensive drugs.

Office BP and 24-h ambulatory BP were measured at the end of the control and K supplementation periods. Home BP was measured throughout the study protocol. Fasting blood samples and 24-h urine samples were collected at the end of each period.

Measurements Office BP was measured twice in the sitting position by a physician with a mercury sphygmomanometer. Home BP was measured in the sitting position by the patients 3 times in the early morning and also in the late evening using semiautomatic devices employing the oscillometric method. Ambulatory BP was measured every 30 min for 25 to 26 h by the oscillometric method using TM-2421 (A&D Co. Ltd., Tokyo, Japan), the accuracy and performance of which have been demonstrated.[19] The accuracy of each recorder was also checked by simultaneous measurement with a mercury sphygmomanometer, and all recorders showed a difference of <10 mm Hg. The same recorder was used in each subject to avoid errors due to differences in equipment. Serum and urinary electrolyte levels were determined with an autoanalyzer TBA-80M (Toshiba, Tokyo, Japan).

Data Analysis Averages of the two measurements were used for analysis of office BP. For home BP, averages of the last 5 days' records in each period were employed. The first 60-min records of ambulatory BP were discarded for the analysis of 24-h BP because they may be substantially higher than the usual BP. We defined the daytime BP as that from 6:30 AM to 11:00 PM and the nighttime BP as that from 11:30 PM to 6:00 AM in this study.

Data are expressed as means and SEM. Student's paired or unpaired t test was used for comparison of two groups of data. Linear regression analysis was employed to assess correlations between two parameters. A $P < .05$ was considered statistically significant. Analyses were performed using StatView software (Abacus Concepts Inc., Berkeley, CA).

RESULTS

Serum concentration and urinary excretion of K increased and serum and urinary Na/K ratio decreased significantly with K supplementation (Table 2). Serum Na concentration and urinary Na excretion were comparable between the control and K supplementation periods. Urine volume, creatinine excretion, and both

TABLE 2. SERUM AND URINARY ELECTROLYTES IN THE CONTROL AND K SUPPLEMENTATION PERIODS

	Control period	K period
Serum		
Na (mmol/l)	141.3 ± 0.2	140.9 ± 0.2
K (mmol/l)	4.15 ± 0.04	4.42 ± 0.05*
Na/K ratio	34.2 ± 0.4	32.1 ± 0.4*
Urine		
Na (mmol/day)	190.1 ± 8.2	202.1 ± 7.5
K (mmol/day)	54.0 ± 2.1	95.6 ± 3.2*
Na/K ratio	3.73 ± 0.19	2.20 ± 0.09*

* $P < .001$ *between the two periods.*

serum and urinary levels of calcium and magnesium were also similar between the two periods.

Office, home, 24-h, and daytime and nighttime SBP were significantly lower in the K supplementation period than in the control period (Table 3). Changes in home SBP (−3.6 ± 0.9 mm Hg) and 24-h SBP (−3.4 ± 1.0 mm Hg) by K supplementation were highly significant ($P < .001$) compared with those in office SBP (−2.7 ± 1.1 mm Hg, $P < .05$), as shown in Figure 1. The changes in daytime SBP and nighttime SBP were similar. Office, home, and 24-h DBP also fell significantly with K supplementation (−1.4 ± 0.6 mm Hg, −1.6 ± 0.5 mm Hg, and −1.2 ± 0.5 mm Hg, respectively). However, the changes in daytime and nighttime DBP were not significant.

Changes in 24-h SBP by K supplementation correlated positively with levels of urinary K excretion in the control period (Figure 2). The changes in 24-h BP showed a tendency toward a negative correlation with the control levels of Na excretion ($P < .1$). There were negative correlations between the changes in 24-h SBP and urinary Na/K ratio or levels of 24-h SBP in the control period. Relations between the changes in office BP or home BP and urinary K or Na/K ratio were not statistically significant.

TABLE 3. OFFICE, HOME, AND AMBULATORY BP IN THE CONTROL AND K SUPPLEMENTATION PERIODS

	Control Period	K Period
Office		
SBP (mm Hg)	150.8 ± 1.7	147.9 ± 1.6*
DBP (mm Hg)	88.1 ± 1.3	86.8 ± 1.1*
Home		
SBP (mm Hg)	138.0 ± 1.3	134.3 ± 1.5†
DBP (mm Hg)	83.2 ± 0.8	81.6 ± 0.9‡
24-H		
SBP (mm Hg)	137.3 ± 1.3	133.9 ± 1.4†
DBP (mm Hg)	81.3 ± 1.0	80.1 ± 1.1*
Daytime		
SBP (mm Hg)	140.9 ± 1.3	138.0 ± 1.5‡
DBP (mm Hg)	83.8 ± 1.2	82.7 ± 1.2
Nighttime		
SBP (mm Hg)	129.0 ± 1.7	125.6 ± 1.5‡
DBP (mm Hg)	76.2 ± 0.9	74.9 ± 1.0

SBP: systolic blood pressure, DBP: diastolic blood pressure.

* $P < .05$, † $P < .001$, *and* ‡ $P < .01$ *between the two periods.*

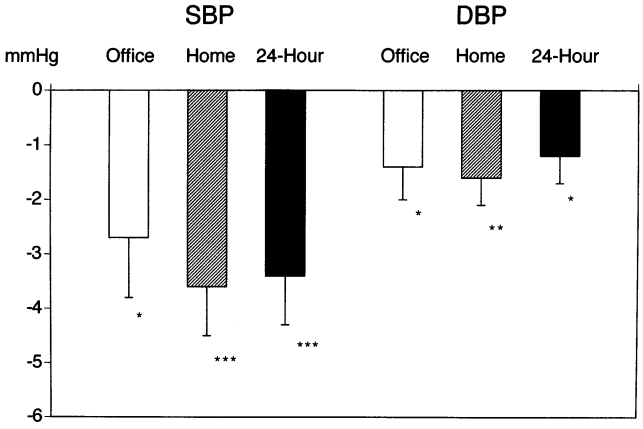

FIGURE 1. *Changes in office, home, and 24-h blood pressure by K supplementation. SBP: systolic blood pressure, DBP: diastolic blood pressure,* *$P < .05$, **$P < .01$, ***$P < .001$.

Table 4 shows the results of subgroup analyses for the changes in 24-h SBP by K supplementation. There were no significant differences in the changes in 24-h SBP between younger and older subjects, between men and women, or between treated and untreated patients. The order of K supplementation did not affect the changes in 24-h SBP. The changes in 24-h DBP, office BP, and home BP were also not influenced by these factors. The changes in 24-h SBP in patients taking calcium antagonists, β-blockers, angiotensin-converting enzyme inhibitors, α-blockers, and diuretics were −3.0 ± 1.2, −1.1 ± 1.6, −4.4 ± 2.1, −4.2 ± 3.1, and −2.0 ± 1.5 mm Hg, respectively. Effects of K supplementation on BP were not significantly different between these antihypertensive drugs.

DISCUSSION

In the present study, supplementation with 64 mmol/day of K for 4 weeks significantly lowered office, home, and 24-h ambulatory BP in hypertensive patients. The amount of supplemented K was equivalent to that of the average dietary K intake in the Japanese population, thus the total intake of K seemed to be doubled. Serum K concentration and urinary K excretion increased significantly, as expected. Our results provided additional support for the antihypertensive effects of high dietary K intake although the reduction in BP may be small.

Several clinical studies, including those in Japanese

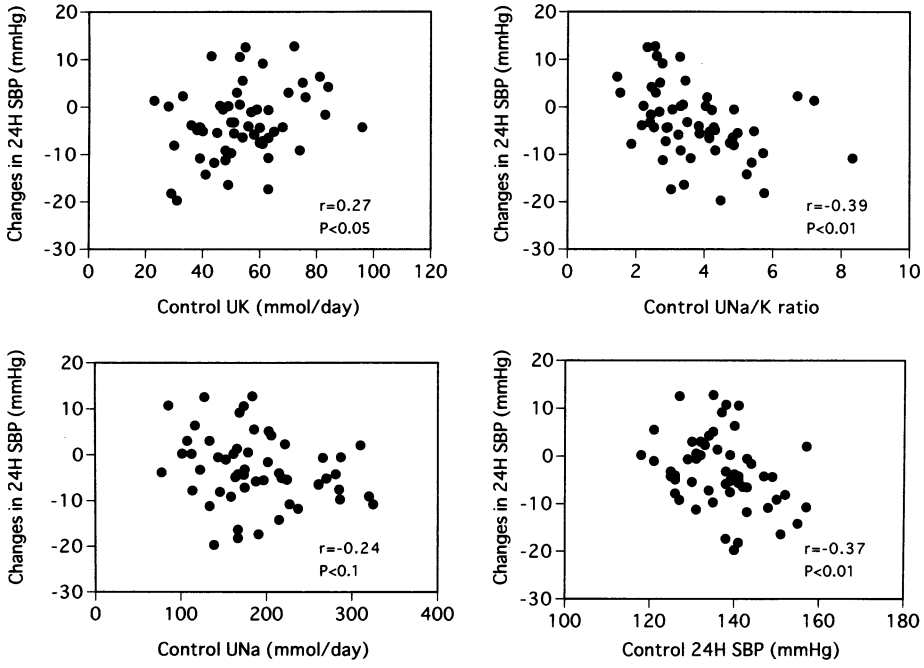

FIGURE 2. *Relationships between changes in 24-h SBP by K supplementation and levels of urinary K excretion, Na excretion, Na/K ratio, or 24-h SBP in the control period. UK: urinary K excretion, UNa: urinary Na excretion.*

subjects, showed the antihypertensive effects of K supplementation,[6–8] but other studies failed to confirm this beneficial action.[9,10] Among 33 randomized controlled trials, significant reductions in BP were seen in 11 studies.[5] However, metaanalyses demonstrated the BP-lowering effect of K supplementation.[4,5] In a recent metaanalysis by Whelton et al,[5] the average reduction in BP was 3.1/2.0 mm Hg after exclusion of an outlier, and tended to be greater in hypertensive patients (4.4/2.5 mm Hg) than in normotensive subjects (1.8/1.0 mm Hg). The median amount of K given was 75 mmol/day, and weighted net change in urinary K excretion was 53 mmol/day. Our results are consistent with this report although the magnitude of the depressor effect was slightly smaller.

Most earlier trials relied on measurement of casual BP, which might overestimate or underestimate the effect of K supplementation on BP because of several factors, such as poor reproducibility, observer bias, and placebo effect.[16–18,20] Monitoring of 24-h ambulatory BP and home BP is superior to measurement of casual BP to detect small changes in BP produced by nonpharmacologic intervention. The effects of K supplementation on ambulatory BP have been examined in few studies and those on home BP have not been studied. In the present study, office, home, and 24-h BP all fell after K supplementation. However, the changes in home and 24-h BP were more significant than the change in office BP.

TABLE 4. CHANGES IN 24-H SBP BY K SUPPLEMENTATION: SUBGROUP ANALYSIS

Factors	Changes in 24-h SBP (mm Hg)
Age (≥ 60 *v* < 60 years)	-3.3 ± 1.2 *v* -3.4 ± 1.4
Gender (men *v* women)	-2.8 ± 1.3 *v* -3.9 ± 1.3
Antihypertensive drug (+ *v* −)	-2.9 ± 1.1 *v* -4.5 ± 1.5
Order (control K *v* K control)	-2.8 ± 1.3 *v* -3.9 ± 1.2

Fotherby and Potter observed reductions in 24-h BP by 6/3 mm Hg and clinic BP by 10/6 mm Hg after 4-week K supplementation (60 mmol/day) in elderly hypertensive patients.[13] In their study, average baseline 24-h BP was 160/91 mm Hg and clinic BP was 187/96 mm Hg. The higher baseline BP may be related to the greater reduction in 24-h and clinic BP, compared with results from our study. Although all of our patients were still hypertensive, average 24-h BP and office BP were 137/81 and 151/88 mm Hg, respectively. We observed a negative relationship between the change in 24-h SBP and the baseline SBP level. Metaanalysis also showed that the reduction in BP by K supplementation was greater in hypertensive patients than in normotensive subjects.[4,5] Therefore, the antihypertensive action of dietary K appears to be enhanced with elevation of baseline BP.

Omvik and Myking failed to observe a reduction in 24-h BP by K supplementation with moderate Na restriction despite a significant decrease in casual BP in hypertensive patients.[14] However, K excretion increased only slightly in their study. The lack of antihypertensive effect on 24-h BP might be attributable to small amounts of supplemented K. Their results also

showed an overestimation of the treatment effect by casual BP measurement.

In the present study, the changes in 24-h SBP by K supplementation were correlated with urinary K excretion in the control period. This relationship suggests that the antihypertensive effect of K is greater in those with low habitual K intake than in individuals with already high K intake. This result is consistent with earlier studies that showed falls in BP by K supplementation in hypertensive patients with diuretic-induced hypokalemia[21] and increases in BP by dietary K restriction in patients with essential hypertension.[22]

It has been shown that the natriuretic action of K plays an important role in its antihypertensive effect.[22,23] The reduction in BP with K supplementation is obvious in Na-loaded hypertensive humans and animals,[8,23] but not in those on an Na-restricted diet.[9,23,24] In our study, urinary Na excretion was similar between the control and K supplementation periods. However, this simply means that dietary Na intake was comparable between the two periods. It is possible that natriuresis occurred in the early phase during K supplementation. The changes in 24-h SBP by K supplementation were marginally related to Na excretion in the control period, and the urinary Na/K ratio more closely correlated with the change in 24-h SBP, compared with urinary Na or K alone. The results of our and earlier studies suggested that K supplementation is particularly effective in hypertensive subjects eating a high-Na/low-K diet.

Age, gender, order of treatment, or use of antihypertensive drugs did not influence the effects of K supplementation on BP in the present study. Thiazide diuretics cause K depletion, and K supplementation appears to be effective in lowering BP in patients with diuretic-induced hypokalemia.[21] However, only three patients were given diuretics in our study. We also did not find significant differences in the effects of K supplementation between subjects taking five different classes of antihypertensive drugs.

In conclusion, the present study demonstrated that K supplementation lowers home BP and 24-h ambulatory BP, as well as office BP, in treated or untreated patients with essential hypertension. The antihypertensive effect was sustained throughout the day, and was greater in patients with high baseline BP, with low baseline K intakes, and with high urinary Na/K ratios. However, the average reduction in BP with the K supplementation was only 3–4/1–2 mm Hg. Furthermore, doubling K intake with diet only may be difficult to achieve for many hypertensive patients. Despite these limitations, our study supports the usefulness of high dietary K intake in the nonpharmacologic treatment of hypertension.

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