Effect of Dietary Potassium on Blood Pressure, Renal Function, Muscle Sympathetic Nerve Activity, and Forearm Vascular Resistance and Flow in Normotensive and Borderline Hypertensive Humans

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Christine A. Sinkey, RN, and Ruth A. Coleman, MT

We evaluated the effect of a low potassium diet on blood pressure in normotensive (NT) and in borderline hypertensive subjects (BHT). There were 11 BHT men (age, 24.6±1.2 years) and 10 NT men (age, 23.5±1.0 years). Subjects were studied while on both low potassium, high sodium (30 meq/day, 400 meq/day) diets and high potassium, high sodium (100 meq/day, 400 meq/day) diets, each taken for 6 days. During the low potassium diet, daytime ambulatory systolic blood pressure increased in both NT (123±5 mm Hg, low potassium, vs. 116±4 mm Hg, high potassium, p<0.01) and BHT groups (134±3, low potassium, vs. 124±3, high potassium, p<0.001). Mean blood pressure was not different in NT during the two diets but was significantly higher during the low potassium diet in BHT subjects (97±2 mm Hg low potassium, vs. 92±1 mm Hg, high potassium, p<0.05) without change in heart rate in BHT subjects during the two diets. Low potassium diet increased the postural rise in diastolic blood pressure when subjects changed from the supine position to quiet standing (standing diastolic blood pressure for NT: low potassium, 79±2 mm Hg vs. high potassium, 72±2 mm Hg; for BHT: low potassium, 89±2 mm Hg vs. high potassium diet, 83±2 mm Hg, p<0.01). The effects of low potassium diet on blood pressure were not related to marked changes in renal hemodynamics, in plasma renin activity, in aldosterone, or in norepinephrine, nor to increases in forearm vascular resistance or in muscle sympathetic nerve activity. In fact, muscle sympathetic nerve activity decreased in the BHT group during low potassium compared with high potassium diets (p<0.001) and did not change in the NT group. Sympathetic nerve activity was also higher in BHT compared with the NT group during high potassium and low potassium diets, p<0.001. In the NT group, the low potassium diet was associated with lower hematocrit levels, weight gain, and increased 24 hour urinary calcium levels. After the low potassium diet, serum potassium fell in both groups, and serum phosphorus fell significantly in the BHT group. In BHT and NT groups after 5 days of low potassium diet, a water load was associated with enhanced natriuresis compared with the high potassium diet (NT: 390±30 μeq/min, low potassium, vs. 280±28 μeq/min, high potassium, p<0.05; BHT: 364±29 μeq/min, low potassium, vs. 326±24 μeq/min, high potassium, p<0.05). We conclude that a low potassium diet is associated with elevation in blood pressure and disturbances in several electrolytes in BHT and NT subjects. The elevation in blood pressure during a low potassium diet appears to be mediated in part by volume expansion. (Circulation 1990;81:173–184)
The relation of diet to blood pressure has been under scrutiny for many years. The major investigative efforts have been devoted to the relation of dietary sodium intake or sodium chloride intake to blood pressure. Our earlier studies have suggested that a high sodium chloride dietary intake in borderline hypertensive subjects results in augmented forearm vascular resistance or enhanced renovascular resistance in response to upright posture. In these studies, potassium intake was relatively high, calculated to be 100 meq/day.

Retrospective epidemiologic studies have suggested that there may be an inverse relation between the prevalence of hypertension and potassium intake or a direct relation between hypertension and the urinary sodium to potassium ratio. Not all clinical studies have confirmed this inverse relation. A major problem with most epidemiologic studies, and indeed many of the relatively few clinical studies that have been performed, is the difficulty in finding populations who have an extremely low sodium diet that is not also high in potassium content or to devise such a diet.

Animal studies, particularly in Dahl salt-sensitive rats, have suggested that there is a protective effect of increased potassium intake with regard to hypertension. More recently, Tobian et al. have suggested that an increased potassium intake is protective against strokes in stroke prone salt-sensitive hypertensive rats. In addition, Tobian and colleagues have suggested that an increased potassium intake reduces the severity of the renal lesions noted in the salt-loaded Dahl salt-sensitive rats.

Recently, relatively small controlled studies have evaluated the effect of potassium intake on blood pressure in patients with mild or moderate, essential hypertension and in normotensive subjects. Results from these studies have been inconsistent. For example, Limura et al. showed a small but significant decrease in arterial pressure in a randomized crossover study with very high potassium daily intake. MacGregor et al. found that increasing potassium daily intake by 60 meq resulted in a variable blood pressure response. Richards et al. noted little change in blood pressures when potassium intake was increased from 60 to 200 meq. Krishna et al. reported that 9 days of low potassium diet (10 mmol/day) plus usual sodium intake (120–200 mmol/day) increased blood pressure in normotensive men.

Because of the potential interaction between potassium and other ions, potassium and many hormones of interest in hypertension, and because of earlier studies with sodium that showed a slight decrease in serum potassium levels after sodium loading, we evaluated the effect of a low potassium diet on blood pressure, including possible mechanisms for alteration in blood pressure. The present study tested the hypothesis that a low potassium and high sodium chloride diet would augment the abnormalities previously noted in blood pressure and the renal circua...
K=39.1 mg). Diets were calculated to be eucaloric for each subject and were adjusted to the individual’s projected activity level. Both diets contained about 3,000 calories/day with a calcium content of 320 mg/1,000 calories. Calories were distributed as 15% protein, 40% fat, and 45% carbohydrate. The protein sources were about 87% animal protein and 13% vegetable protein. The fat composition had a polyunsaturated to saturated fat ratio of approximately 0.6. The carbohydrate sources were 34% granulated sugar, 10% corn starch, and 56% other, including bread, cookies, fruit, and soda pop. The diets provided about 12 g dietary fiber. Random samples of diets were ashed and were analyzed for sodium, potassium, and calcium content. The high potassium diets (n=6) contained 368±6 meq Na/day, 92±5 meq K/day, and 1,162±44 mg Ca/day. The low potassium diets (n=10) contained 371±10 meq Na/day; 29±3 meq K/day, 1,112±37 mg Ca/day.

Subjects continued their normal daily activities and were asked to refrain from strenuous physical exercise such as running. They reported to the Clinical Research Center at least once per day to receive meals for the day, to be weighed, to deliver urine specimens, and to have blood pressures and heart rate measured. Subjects were instructed not to ingest anything other than the diet and distilled water supplied by the Clinical Research Center. Experimental diets were eaten by the subjects for 6 days. A 24-hour urine collection for sodium, potassium, chloride, calcium, phosphorus, magnesium, and creatinine levels was obtained daily to ensure that subjects were in comparable sodium and potassium balance by day 5 before beginning experimental procedures for renal function on day 6 and to assess any alterations of calcium, phosphorus, and magnesium levels produced by diet.

During day 5, daytime (8:00 AM to 10:00 PM) ambulatory blood pressures were taken with a Del Mar Avionics Pressuremeter II (Del Mar, Irvine, California).22 On the evening of day 5, all subjects were admitted to the Clinical Research Center where they slept overnight. On the morning of day 6, subjects remained supine while a catheter was inserted into a peripheral vein, and subjects underwent studies of renal function and renal circulation during supine and upright postures.2

Studies of Renal Function and Circulation

On day 6, the subjects took only liquids after midnight and received 1,000 ml water orally at 7:00 AM followed by 200 ml/30 min water orally during the renal studies. After an hour equilibrium, which began between 7:30 and 7:45 AM, standard renal function tests with inulin and p-aminohippurate (PAH) as measures of glomerular filtration rate and renal plasma flow, respectively, were performed as previously reported.2,23,24 Urine collections were obtained by spontaneous voiding. At least two sequential 10-minute urine collections were obtained at the end of a 1-hour equilibrium period to ensure that urine flow was stable (+15%) before beginning the clearance periods.

When urine flow was stable, subjects underwent three 30-minute clearance periods. The first two periods were obtained while the subjects were supine, and the third was obtained during quiet standing. Urine was collected every 30 minutes, and at the midpoint of each period, a blood sample was obtained. Urine and blood were analyzed for inulin, PAH, creatinine, sodium, potassium, and osmolality at each period. The following were calculated for each period: clearance of inulin for determination of glomerular filtration rate, clearance of PAH for the estimation of renal plasma flow, fractional excretion of sodium and potassium, osmolar clearance, and free water clearance.2 Blood pressures were taken with a standard mercury sphygmomanometer every 5–10 minutes throughout the clearance periods, and a renal vascular resistance index was calculated by averaging the mean blood pressures (diastolic blood pressure plus one-third pulse pressure) for the period divided by PAH clearance.

To assess humoral factors potentially related to vascular resistance and particularly related to sodium and potassium clearances, forearm venous blood was obtained for measurements of plasma renin activity, and aldosterone and norepinephrine levels during the second supine period and at the midpoint of the standing period. Hematocrit levels were also measured during the supine and standing periods.

Microneurography

The microneurographic method for direct intraneural recordings from human peripheral nerves was developed by Vallbo et al25 and Wallin and Sundlof26 and performed at the University of Iowa in recent years.27 Sympathetic nerve recordings were obtained with sterile insulated tungsten microelectrodes 0.2-mm diameter in the shaft, tapering to an uninsulated tip of 1–5 μm inserted into a fascicle of a peroneal nerve. A reference electrode was inserted subcutaneously about 2 cm from the recording electrode. The electrodes were connected to a differential preamplifier with a gain of 1,000 and an amplifier with a variable gain of 30–80.

The path of the peroneal nerve as it courses around the fibular head was determined by using cutaneous stimulation. Cutaneous stimulation at 50 to 90 V, 0.2 msec, and 1 Hz overlying a nerve evoked involuntary muscle contractions.

After the nerve was mapped, the electrodes were inserted. The recording electrode was advanced toward the nerve with the electrode delivering 3–4 V. When the electrode entered a nerve fascicle to muscle, the stimulation elicited involuntary muscle twitching in the distal extremity. The stimulation was then terminated, and the electrode was left in position.

The electrode was switched to a recording mode to detect spontaneous sympathetic nerve action potentials, and 6 minutes of muscle sympathetic nerve activity were recorded for each subject. The search
for a satisfactory recording site was limited to 1 hour but usually required only 10–30 minutes. Once a satisfactory site was obtained, the electrode was left in that position for the remainder of the experiment.

**Forearm Blood Flow and Lower Body Negative Pressure**

Forearm blood flow was measured with a mercury-in-Silastic strain gauge plethysmographic technique. Forearm vascular resistance, expressed in arbitrary units, was calculated by dividing mean blood pressure (mm Hg) by blood flow (ml/min per 100 ml forearm volume). The vasoconstrictor response of the forearm circulation to unloading of low- and high-pressure baroreceptors was assessed by graded lower body negative pressure as previously reported. To accomplish this, the lower extremities and lower abdomen below the waist were placed in a specially constructed chamber to which graded negative pressures were applied at -10, -20, and -40 mm Hg.

**Chemical Measurements**

The following were measured with standard methods in our laboratory. Inulin was measured by the Anthrone method of White and Sampson, and PAH was measured by the method of Smith et al. A Beckman DU-20 spectrophotometer (Arlington Heights, Illinois) was used for inulin and PAH measurements. Plasma renin activity was measured by radioimmunoassay of angiotensin I. Creatinine and phosphorus levels were measured by the autoanalyzer method on a Technicon AutoAnalyzer II (Technicon Instrument, Tarrytown, New York). Sodium and potassium levels were measured by ion-selective electrodes (Beckman E2A Na/K electrode system, Arlington Heights, Illinois). Chloride levels were measured by chloride meter (Buchler-Cotlove, Buchler Instruments, Fort Lee, New Jersey). Osmolalities were measured by the freezing point depression method (Micro-Osmette, Precision Systems, Sudbury, Massachusetts). Total calcium levels were measured by the o-cresolphthalein method read at 575 nm (Sigma Diagnostics, St. Louis, Missouri). Magnesium levels were measured by Calmagite color complex method read at 520 nm (Sigma Diagnostics). Serum aldosterone levels were measured by radioimmunoassay (BioScience, Van Nuys, California).

Plasma catecholamine levels were measured by an enzymatic assay in the Cardiovascular Center Laboratory (Cat-A-Kit, Upjohn, Kalamazoo, Michigan).

**Statistical Analysis**

Data from the first two supine control periods were averaged. Between group comparisons were performed by unpaired t test after analysis of the data by the CLINFO Statistical Pac (Wilk-Shapiro Test) for normal distribution. Comparisons within the same group were performed by paired t tests. Repeated measures analysis of variance was used where appropriate, including analysis of muscle sympathetic nerve activity and forearm blood flow and resistance. Significance was considered at p less than 0.05. Data are mean±SEM.

**Results**

The values for outpatient screening blood pressure obtained during the ad libitum diets were as follows. For NT subjects, blood pressure was 108±2/72±2 mm Hg, and for BHT subjects, blood pressure was 121±3/85±2 mm Hg (NT vs. BHT, systolic and diastolic blood pressures, p<0.001). The blood pressure for the highest screening pressures obtained for NT subjects was 114±3/76±2, and for BHT subjects, blood pressure was 133±3/94±2 (NT vs. BHT, systolic and diastolic blood pressures, p<0.001).

During the daytime on day 5 of both diets, ambulatory blood pressures were obtained in seven NT and eight BHT subjects (Table 1). As anticipated, BHT subjects had significantly higher mean blood pressures on both diets compared with NT subjects (p<0.01, on both diets). Ambulatory systolic blood pressure was increased significantly in both NT and BHT subjects after the low potassium diet. As shown in Table 1, BHT subjects showed a greater frequency of diastolic blood pressure of 90 mm Hg or more compared with NT subjects after both diets, significantly so after the high potassium diet (p<0.01). However, the frequency of these elevations was not significantly affected by diet. Mean blood pressure was significantly increased by the low potassium diet compared to the high potassium diet in the BHT group, p<0.05. In seven of eight BHT subjects, mean blood pressure rose with the low potassium diet. This trend was not observed in the seven NT subjects. Heart rate, obtained simultaneously with the ambu-
latory blood pressure determinations, did not change in either the NT or BHT group during the low potassium diet (Table 1).

**Balance Data**

Both groups of NT and BHT subjects achieved comparable balance during each diet by the time renal function and other studies were performed as indicated by their 24-hour urine sodium and potassium excretion on day 5 (Table 2). BHT subjects excreted slightly more potassium on the high potassium diet than did the NT subjects on a similar diet ($p<0.05$).

Urine calcium increased significantly in the NT group after receiving the low potassium diet ($p<0.01$) and increased, though nonsignificantly, in the BHT group (Table 2). On day 5 of both diets, urine calcium levels tended to be higher in the BHT than in the NT group, though not significantly different. The 24-hour urine phosphorus levels were not different between subject groups. The change in dietary potassium did not influence urinary phosphorus levels, tubular reabsorption of phosphate, or urinary magnesium levels. Urine chloride excretion was the same with both diets.

BHT subjects were slightly heavier than NT subjects at the start (day 0) of both diets. Both NT and BHT subjects lost weight during the high potassium diet (Table 2). NT subjects, however, gained weight (0.3±0.4 kg) on the low potassium diet, and BHT subjects lost less weight (−0.2 kg) on the low potassium diet compared with weight lost (−0.5 kg) on the high potassium diet.

Serum sodium levels were unchanged by diet (Table 3). Serum potassium levels fell significantly ($p<0.01$) in NT and BHT subjects on the low potassium diet. During the low potassium diet, serum phosphorus levels fell in both groups, reaching significance in the BHT group ($p<0.01$). Serum magnesium and calcium levels remained the same in both groups on both diets.

**Blood Pressure and Renal Hemodynamic Responses to Standing**

On day 6 of both diets, the effect of diet and orthostatic stress on renal function was studied (Table 4). Supine systolic pressures were higher in BHT subjects during low potassium diet ($p<0.05$). Upright systolic pressure fell in response to quiet standing in both groups, but the magnitude of the fall was not affected by diet.

Supine and standing diastolic blood pressures were higher in BHT subjects during low potassium diet ($p<0.05$ and $p<0.01$) (Table 4). In NT subjects after the high potassium diet, standing diastolic pressures decreased by 5 mm Hg but did not fall when the same individuals received the low potassium diet ($p=0.07$). BHT subjects receiving the high potassium diet had increased diastolic blood pressure by 2 mm Hg with standing, and after the low potassium diet, this rise increased to 6 mm Hg ($p=0.05$). The postural change in diastolic blood pressure with each diet was significantly different between the BHT and NT groups ($p<0.05$). Mean blood pressures were higher in BHT subjects during the low potassium compared with the high potassium diet. During the low potassium diet,

### Table 2. Urinary Electrolyte Levels and Weights in Normotensive and Borderline Hypertensive Subjects

<table>
<thead>
<tr>
<th></th>
<th>Normotensive (n=10)</th>
<th>Borderline hypertensive (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High K diet</td>
<td>Low K diet</td>
</tr>
<tr>
<td>24-Hr urine day 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na (meq)</td>
<td>343±20</td>
<td>302±21</td>
</tr>
<tr>
<td>K (meq)</td>
<td>62±4</td>
<td>27±2‡</td>
</tr>
<tr>
<td>Ca (mg)</td>
<td>232±33</td>
<td>326±37†</td>
</tr>
<tr>
<td>Cl (meq)</td>
<td>338±18</td>
<td>358±32</td>
</tr>
<tr>
<td>Weight (kg) Day 0</td>
<td>78.1±2.2</td>
<td>78.9±2.4</td>
</tr>
<tr>
<td>Weight (kg) Day 6</td>
<td>77.8±2.0</td>
<td>79.2±2.4</td>
</tr>
<tr>
<td>Change</td>
<td>−0.4±0.5</td>
<td>0.3±0.4</td>
</tr>
</tbody>
</table>

Values are mean±SEM. 1 meq Na=23 mg Na, 1 meq K=39.1 mg K, 1 meq Cl=35.5 mg Cl.

### Table 3. Serum Electrolyte Levels in Normotensive and Borderline Hypertensive Subjects

<table>
<thead>
<tr>
<th>Day 6, morning</th>
<th>Normotensive (n=10)</th>
<th>Borderline hypertensive (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High K diet</td>
<td>Low K diet</td>
</tr>
<tr>
<td>Serum Na (meq/l)</td>
<td>139±1</td>
<td>140±1</td>
</tr>
<tr>
<td>Serum K (meq/l)</td>
<td>3.8±0.04</td>
<td>3.5±0.06*</td>
</tr>
<tr>
<td>Serum P (mg/dl)</td>
<td>3.4±0.2</td>
<td>3.1±0.1</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

$p<0.01$ for High K vs. Low K diets, within-group comparisons.
heart rate was slightly higher in the BHT than in the NT group (Table 4).

Resting supine renal plasma flow (PAH clearance) was not altered by diet in either group (Table 4). Renal plasma flow fell with standing in both groups on both diets (p<0.01), but the fall was not significantly different after either diet for either group. During the low potassium diet, supine renal vascular resistance index was higher in the BHT group compared with that during the high potassium diet. Renal vascular resistance rose modestly after standing in NT and BHT groups on both diets, but the change in renal vascular resistance with standing was not significantly affected by diet, nor were there differences between groups. Glomerular filtration rate (inulin clearance) was not affected by diet except in the BHT group during standing. In BHT subjects, the lower inulin clearance during standing while on the high potassium diet was due to one subject whose glomerular filtration rate dropped to 45 ml/min.

In the NT group, absolute and fractional sodium excretions were significantly higher, supine and standing, during the low potassium diet (Table 5). Absolute sodium excretion was also higher in the BHT group after the low potassium diet (Table 5).

The decrease in free water clearance with standing was greater in the BHT than in the NT group, reaching significance during the low potassium diet (p<0.05) (Table 5). There was no demonstrable dietary effect on free water clearance in either group. Potassium excretion on the low potassium diet was substantially less in both groups and did not change with standing in either group.

**Humoral Changes**

Plasma renin activity during supine and standing postures was not different between groups and was significantly lower after the low potassium diet in the BHT group in both positions and was significantly lower during standing in the NT group (Table 6).
Renin rose slightly with standing, but in the presence of a marked sodium chloride load, renin levels were generally suppressed even when standing. Serum aldosterone levels were not significantly different between groups nor significantly altered by diet. Plasma norepinephrine levels were not different between NT and BHT groups on either diet and rose significantly with standing in both groups during both diets. Supine and standing hematocrit levels were lower in NT subjects \((p<0.01, \&p<0.05, \&p<0.001, \text{for High K vs. Low K diets, within-group comparisons.})\) while receiving the low potassium diet. Hematocrit levels were slightly, though not significantly, lower during low potassium in BHT subjects.

**Muscle Sympathetic Nerve Activity**

Muscle sympathetic nerve activity was higher in the BHT than in the NT group during the high potassium and low potassium diets \((p<0.001, \text{each diet.})\). During the low diet, muscle sympathetic nerve activity fell in BHT \((p<0.001, \text{low potassium vs. high potassium diets})\) but was unchanged in NT subjects. The ratio of bursts per minute between the high potassium and low potassium diet was significantly less in NT \((1.1\pm0.1)\) than in BHT subjects \((1.9\pm0.3, p<0.05)\) (Table 7).

**Forearm Blood Flow**

Forearm blood flow and forearm vascular resistance were not different between the BHT and NT groups during either diet. The low potassium diet was accompanied by slightly greater forearm blood flows in both groups, but the diet effects were not significant (Table 7). Forearm vasoconstriction and forearm blood flow in response to graded lower body

### Table 5. Renal Function Data in Normotensive and Borderline Hypertensive Subjects

<table>
<thead>
<tr>
<th></th>
<th>Normotensive (n=10)</th>
<th>Borderline hypertensive (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High K diet</td>
<td>Low K diet</td>
</tr>
<tr>
<td></td>
<td>High K diet</td>
<td>Low K diet</td>
</tr>
<tr>
<td>Na excretion (µeq/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>280±28</td>
<td>390±30*</td>
</tr>
<tr>
<td>Standing</td>
<td>197±17</td>
<td>303±24†</td>
</tr>
<tr>
<td>Change</td>
<td>-83±16</td>
<td>-86±16</td>
</tr>
<tr>
<td>Fractional Na excretion (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>2.0±0.2</td>
<td>2.8±0.2*</td>
</tr>
<tr>
<td>Standing</td>
<td>1.5±0.1</td>
<td>2.2±0.2*</td>
</tr>
<tr>
<td>Change</td>
<td>-0.6±0.1</td>
<td>-0.6±0.1</td>
</tr>
<tr>
<td>Free water clearance (ml/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>10.3±0.5</td>
<td>10.1±0.9</td>
</tr>
<tr>
<td>Standing</td>
<td>6.8±1.0</td>
<td>7.1±1.1</td>
</tr>
<tr>
<td>Change</td>
<td>-3.5±0.8</td>
<td>-3.0±0.9</td>
</tr>
<tr>
<td>K excretion (µeq/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>77±10</td>
<td>43±4*</td>
</tr>
<tr>
<td>Standing</td>
<td>69±8</td>
<td>42±4†</td>
</tr>
<tr>
<td>Change</td>
<td>-8±4</td>
<td>-1±2</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

*\(p<0.05, \&p<0.01, \&p<0.001, \text{for High K vs. Low K diets, within-group comparisons.})*

### Table 6. Plasma Renin Activity, Serum Aldosterone, Plasma Norepinephrine, Hematocrit Levels in Normotensive and Borderline Hypertensive Subjects

<table>
<thead>
<tr>
<th></th>
<th>Normotensive (n=10)</th>
<th>Borderline hypertensive (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High K diet</td>
<td>Low K diet</td>
</tr>
<tr>
<td></td>
<td>High K diet</td>
<td>Low K diet</td>
</tr>
<tr>
<td>Plasma renin activity (ng/ml/hr)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>0.5±0.1</td>
<td>0.3±0.1</td>
</tr>
<tr>
<td>Standing</td>
<td>0.8±0.2</td>
<td>0.4±0.1*</td>
</tr>
<tr>
<td>Serum aldosterone (ng/dl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>3.6±0.5</td>
<td>2.9±0.3</td>
</tr>
<tr>
<td>Norepinephrine (pg/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>221±41</td>
<td>228±27</td>
</tr>
<tr>
<td>Standing</td>
<td>457±56</td>
<td>400±62</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supine</td>
<td>42.7±1.0</td>
<td>39.9±0.8*</td>
</tr>
<tr>
<td>Standing</td>
<td>43.2±0.9</td>
<td>42.4±0.9*</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

*\(p<0.05, \&p<0.01\text{ for High K vs. Low K diets, within-group comparisons.})*
negative pressure were not different between groups nor altered by diet (Figures 1 and 2).

**Discussion**

Some investigators have suggested that increases in potassium attenuate the blood pressure effects of high sodium intake, and others have reported that low potassium will increase blood pressure in normal individuals. We wished to determine whether a decreased potassium intake, in the presence of a high level of sodium intake, would increase blood pressure in NT and BHT young men. We also wished to determine the mechanisms for the anticipated rise in blood pressure in studies of renal, humoral, and neurogenic factors. The major findings of our study are that a 6-day low potassium diet compared with a high potassium diet, coupled with a high sodium intake in both diets, produced elevations of ambulatory systolic blood pressure in both NT and BHT and resulted in an increase in mean ambulatory blood pressure in BHT subjects. In addition, the low potassium, high sodium diet increased diastolic blood pressure and enhanced the abnormal orthostatic hypertension during quiet standing observed in the BHT group receiving the high potassium, high sodium diet. Our data are of particular and unique interest because they show that this increase in mean pressure due to the low potassium diet is persistent during daytime activities in BHT subjects and show a persistent increase in systolic blood pressure induced by a low potassium diet even in NT subjects. Despite a decrease in serum potassium levels in both groups, the increases in blood pressure during the low potassium diet are associated with modestly increased renovascular resistance only in the BHT group, and no increases in forearm vascular resistance or directly measured muscle sympathetic nerve traffic were found. Plasma renin activity was suppressed and norepinephrine did not change during the low potassium diet. In the NT group, the low potassium diet compared with the high potassium diet was accompanied by an increase in body weight, lower hematocrit levels, and increased urinary calcium excretion. At the end of the low potassium diet period, NT and BHT subjects showed an increase in sodium excretion in response to a water load. These data suggest that increased plasma volume is a major factor in the elevation in blood pressure accompanying low potassium intake.

The levels of dietary potassium in the high potassium diet chosen in this study are not as high as those

### Table 7. Muscle Sympathetic Nerve Activity, Forearm Blood Flow and Forearm Vascular Resistance in Normotensive and Borderline Hypertensive Subjects

<table>
<thead>
<tr>
<th></th>
<th>Normotensive (n=9)</th>
<th>Borderline hypertensive (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High K diet</td>
<td>Low K diet</td>
</tr>
<tr>
<td>Muscle sympathetic nerve activity*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bursts/min</td>
<td>12.1±1.2</td>
<td>11.6±1.1</td>
</tr>
<tr>
<td>Bursts/min ratio</td>
<td>1.1±0.1</td>
<td>1.9±0.3</td>
</tr>
<tr>
<td>Forearm blood flow (ml/min/100 ml volume)</td>
<td>5.2±0.6</td>
<td>5.9±1.0</td>
</tr>
<tr>
<td>Mean blood pressure (mm Hg)</td>
<td>89.0±2.6</td>
<td>88.4±2.3</td>
</tr>
<tr>
<td>Forearm vascular resistance (MBP/FBF)</td>
<td>19.3±2.5</td>
<td>18.4±2.9</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

MBP, mean blood pressure; FBF, forearm blood flow.

*Data on muscle sympathetic nerve activity are for seven normotensive and eight borderline hypertensive subjects.

†p<0.001 for High K vs. Low K, within-group comparison (repeated-measures analysis of variance).

![Figure 1](image_url)  
**Figure 1.** Plot of response of forearm blood flow to lower body negative pressure (LBNP) in normotensive subjects (n=9) and borderline hypertensive subjects (n=9) during a high Na, 100 meq K/day diet and a high Na, 30 meq K/day diet. Measurements were made during a control period and during the application of graded LBNP at -10, -20, and -40 mm Hg. ©, 100 meq K diet (high K); ·, 30 meq K diet (low K).
levels previously used in other studies. They are, however, well within the range often achieved spontaneously by individuals living in the United States. Our previous studies of young white subjects with essential hypertension in our geographic area have shown that the average potassium intake determined by 24-hour urine potassium excretion is between 60 and 70 meq/24 hr. Other investigators, however, have reported that potassium intake in other geographic areas of the United States may be quite low, as low as 20–40 meq/24 hr. The levels we chose to study use a threefold difference in potassium intake, which is achievable with spontaneous dietary changes.

Short-term alterations in potassium level achieved by intravenous infusion, interarterial infusion, dialysis, or by changes in the composition of the perfusate of isolated vascular strips all alter vascular contractility. As potassium concentration is decreased below physiologic levels, vasoconstriction usually results, whereas when potassium concentrations are increased above physiologic levels, vasodilation results. The data on the effect of short-term changes in potassium in intact animals are consistent. In dogs pretreated with diuretics, infusion of a low potassium, low magnesium solution decreased serum potassium from 3.7 to 2.7 meq/l and serum magnesium from 1.9 to 1.3 meq/l and resulted in increased arterial pressure and peripheral resistance. Similarly, reduction in serum potassium levels results in vasoconstriction in various vascular beds, including the forelimb, the renal arteries, and the coronary arteries. Recently, endothelium-dependent relaxation of vessels from Dahl salt-sensitive rats was shown to be enhanced when rats were fed potassium supplement in their diet, although serum potassium levels were not significantly changed.

The epidemiologic studies in humans on the association between potassium intake and blood pressure are consistent with the short-term infusion data; however, when the serum potassium level has been measured, reduction in serum potassium levels in individuals on a low potassium diet is often minimal.

In our study, we lowered the serum potassium level by 0.2–0.3 meq/l to a serum potassium level of 3.5–3.6 meq/l with the low potassium diet in the NT and BHT groups. The changes we found in serum potassium levels were probably not sufficient to stimulate a uniform direct vascular response because renal vascular resistance was increased only in the BHT group, whereas supine and forearm vascular resistance did not change with the low potassium diet in either group.

Most studies in humans concerning the relation between potassium intake and blood pressure have been conducted with potassium supplementation. MacGregor et al supplemented patients with 64 meq KCl/day or placebo in addition to their regular diet and sodium intake of approximately 140–170 mmol. The high potassium program was associated with a decrease in the blood pressure from 154/99 to 148/95 mm Hg, whereas there were no changes in blood pressure with placebo, nor were there changes in plasma renin activity or aldosterone concentration. Potassium therapy did result in a significant natriuresis compared with placebo. Svetkey et al performed a similar study in which patients received a supplement of 120 meq/d of microencapsulated KCl. An antihypertensive response of approximately the same magnitude as in the study by MacGregor et al was noted; this was thought to be more marked in blacks than whites. On the other hand, Richards et al were unable to show any effect of potassium supplementation on blood pressure. It has been difficult to show effects of potassium supplementation on blood pressure or urinary sodium excretion in normotensive subjects except at very high sodium intakes.

The mechanism whereby the low potassium diet results in increases in blood pressure (or whereby potassium supplementation may result in a fall in blood pressure) has not been extensively studied in humans. Fujita and Ando have shown that potas-

![Figure 2](image-url)

**Figure 2.** Plot of response of forearm vascular resistance to lower body negative pressure (LBNP) in normotensive subjects (n=9) and borderline hypertensive subjects (n=9) during a high Na, 100 meq K/day diet and during a high Na, 30 meq K/day diet. Measurements were made during the control period and during graded application of LBNP as in Figure 1. Forearm vascular resistance is measured in units derived from mean blood pressure divided by forearm blood flow (ml/min per 100 ml forearm volume). ○, 100 meq K (high K) diet; ●, 30 meq K (low K) diet.
sium treatment results in an enhanced cumulative sodium excretion and a decrease in plasma volume as well as a decrease in total body sodium. Renin activity in their study increased slightly in the potassium-treated group, but peripheral resistance was not significantly changed by potassium treatment. Cardiac output was increased in their group of subjects not receiving potassium. Tabuchi et al37 studied a group of hypertensive patients during supplementation of potassium to 156 meq/day and noted that blood pressure was reduced when potassium intake was increased and when there was an increase in sodium excretion. A positive correlation was found between the pressor response to salt loading and the antihypertensive response to potassium supplementation. Urinary prostaglandin and plasma norepinephrine levels were increased by the addition of potassium.

In an extension of the earlier study, Fujita et al38 noted that potassium supplementation with 96 meq KCl/day suppressed the rise in blood pressure after salt loading in borderline hypertensive subjects. They noted that plasma renin activity and plasma aldosterone concentration during salt loading were relatively higher in patients receiving potassium supplementation compared with patients who were salt loaded and who did not receive potassium supplementation, and they attributed this to the slight natriuresis occurring with potassium supplements.

Bianchetti et al40 also studied potassium supplementation (100 mM K/day) in normotensive members from normotensive and hypertensive families as well as in 11 patients with borderline hypertension. In these individuals, after potassium supplementation, plasma renin activity, plasma angiotensin II levels, and plasma aldosterone levels all increased significantly. However, urinary sodium excretion was not increased significantly by potassium supplementation in any group, nor was creatinine clearance altered.

In one study in normal men with dietary potassium restriction (10 vs. 90 meq K, plus 35 meq Na), Krishna et al40 reported that cumulative sodium balance was positive during low potassium but negative during the high potassium diet. In addition, low potassium diet blunted the urinary sodium excretion of an isotonic saline infusion. Thus, dietary potassium restriction appears to blunt sodium excretion and is part of a continuum in which dietary potassium loading enhances sodium excretion. Recent work by Krishna et al40 showed a 5-mm Hg rise in blood pressure in normal subjects after 9 days of 10 mmol potassium diet, which is consistent with our study.19

We were not able to show a difference in urine sodium excretion in either of our groups receiving a low potassium diet when compared with a high potassium diet. Nevertheless, we have convincing evidence, taken in toto, to support the concept that a low potassium diet leads to volume expansion. First, we observed a slight difference in weight changes during the two diets. In the NT group, caloric intake remained the same, but mean weight decreased from the beginning to the end of the high potassium diet period, and mean weight increased during the low potassium diet. In the BHT group, mean weight decreased during both diets, although the weight loss tended to be less during the low potassium diet. Although caloric intake was calculated to be isocaloric, and subjects ate all their food and were not hungry, we speculate that caloric need was underestimated and accounted for the weight loss, especially during the high potassium diet in both groups. As an indirect marker of volume expansion, the plasma hematocrit level was significantly lower in NT and somewhat lower in BHT subjects while receiving the low potassium diet. In addition, the urinary sodium excretion response to a water load at the end of the diet periods was significantly increased during the low potassium diet in both groups during supine and standing clearance periods. These data are compatible with greater sodium retention during the low potassium diet and the excretion of sodium when the diet ends and a water load is given.

Plasma renin activity, particularly during the standing period, was lower after the low potassium diet, probably secondary to volume expansion. The absolute levels of renin, aldosterone, and norepinephrine are directionally consistent with those noted in earlier studies.38,39

Of interest was the increased calcium excretion found in NT subjects and to a lesser degree in BHT subjects receiving the low potassium diet. The mechanism responsible for the increased calcium excretion is not clear, and, also, the role of the calcium loss in the increase in blood pressure found in the low potassium groups is not clear from the results of the study. Total serum calcium levels did not change. Ionized calcium levels were not measured. However, we have no reason to anticipate that protein binding in these healthy individuals would be substantially different between diets. Thus, during the low potassium diet, we interpret the tendency toward increased weight, lower hematocrit levels, increased sodium excretion during a water load, lower plasma renin activity, and increased urinary calcium levels41,42 as compatible with volume expansion in both groups.

We also observed a decrease in serum phosphorus during dietary potassium restriction and previously reported that low dietary potassium decreases muscle phosphorus content and increases muscle sodium content.43 In an attempt to indirectly assess parathyroid hormone activity, urinary phosphate levels were measured, and the tubular reabsorption of phosphate was calculated. These were not different between the dietary periods.

Because chloride intake may be important in the blood pressure response to sodium, we measured urinary chlorides to evaluate chloride balance on day 4 of the balance periods.44,45 Urinary chloride did not significantly change because of the different diets.

Despite the increase in diastolic pressure noted with quiet standing in the NT and BHT groups after the low potassium diet compared with the high
potassium diet, little simultaneous change in renal function could be shown. Renal vascular resistance after standing was higher, as expected, in the NT and BHT groups, yet there was no difference in renal vascular resistance when the diet periods were paired except for in the BHT group in whom supine renal vascular resistance was increased, largely because of an increase in blood pressure. Absolute values for renal plasma flow and glomerular filtration rate were not significantly influenced by diet except for the glomerular filtration rate during standing in BHT, and this was due to one BHT subject whose glomerular filtration rate dropped markedly during the high potassium diet while standing. The decrease in free water clearance observed with quiet standing, which was greater in the BHT group, was not influenced by diet.

The lack of change in heart rate in BHT subjects observed during the ambulatory blood pressure monitoring, despite an increase in mean and systolic blood pressure, is unexplained. This could be a reflection of diet electrolyte-induced sympathetic or parasympathetic dysfunction. Plasma norepinephrine levels fell slightly, and muscle sympathetic nerve activity also fell slightly in the BHT subjects on the low potassium diet, suggesting an appropriate and slightly suppressed sympathetic activity probably in response to volume expansion. Although cardiac output was not measured, we must conclude that it was probably increased during the low potassium diet because heart rate was unchanged, systolic blood pressure was increased, and forearm vascular resistance was unchanged or slightly decreased.

In summary, this study shows an increase in daytime ambulatory systolic blood pressures in the NT and BHT subjects during low potassium diet as well as an increase in mean blood pressure during the ambulatory daytime monitoring in the BHT subjects. Low potassium diet also augments the rise in diastolic pressure during standing in both groups. The effects of the low potassium diet on blood pressure appear not to be related to marked renal hemodynamic changes, to changes in plasma renin activity, or aldosterone or plasma norepinephrine levels, nor to increases in forearm peripheral vascular resistance or muscle sympathetic nerve activity. In NT subjects, the low potassium diet increased urinary calcium excretion significantly and was associated with increased weight and lowered hematocrit levels. In both groups, a water load at the end of the low potassium diet produced an enhanced natriuresis compared with a water load at the end of the high potassium diet. Serum potassium levels fell in both groups, and serum phosphorus levels fell significantly in BHT subjects during the low potassium diet. Changes in dietary potassium are therefore associated with disturbances in the balance of several electrolytes. It appears that volume expansion mediates, in part, the elevation in blood pressure due to low potassium intake.

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References


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