Effect of Low Sodium Diet or Potassium Supplementation on Adolescent Blood Pressure

Alan R. Sinaiko, Orlando Gomez-Marin, and Ronald J. Prineas

The roots of essential hypertension extend back into the first two decades of life, suggesting that effective intervention during those years may lead to a reduction in the incidence of adult hypertension. Decreasing the dietary sodium/potassium ratio offers a potentially effective approach to blood pressure reduction. This study tested the feasibility of 3-year sodium reduction or potassium supplementation in adolescents and the effect of these interventions on the rate of rise of blood pressure during adolescence. After 19,452 5th to 8th grade students were screened, 210 from the upper 15 percentiles of blood pressure distribution (105 boys, 105 girls) were randomly assigned to one of three groups: low sodium diet (70 mmol sodium intake per day), potassium chloride supplementation (normal diet plus 1 mmol/kg potassium chloride per day), or placebo (normal diet plus placebo capsule). Capsules for the potassium chloride and placebo groups were administered in a double blind protocol. Blood pressure was measured every 3 months for 3 years. The effect of the intervention was determined by comparing the rate of rise (slope) of blood pressure among the groups using a random-coefficient growth curve model. The boys groups and the girls placebo group had similar positive blood pressure slopes that were significantly different from zero. The girls low sodium group had a slightly negative slope (significantly lower than the slope of the girls placebo group), and the girls potassium group had a slightly positive slope. Both of these slopes were not significantly different from zero and were significantly lower than the slopes of the respective boys groups. These results show that dietary sodium and potassium changes within the first two decades of life can reduce blood pressure in girls. Differences in blood pressure response between boys and girls suggest different sensitivities to supplemental potassium or dietary sodium change. The feasibility of long-term dietary sodium reduction in the United States, particularly in boys, is limited.

KEY WORDS • blood pressure • adolescents • intervention studies • sodium • potassium • hypertension, essential

Evidence from genetic1 and epidemiological2 studies has shown that the roots of essential hypertension extend back into the first decades of life. Although the prevalence of overt hypertension is very low during childhood and adolescence,3 blood pressure at this age follows a tracking pattern4,5 that continues into the third and fourth decades.6 This suggests that blood pressure early in life may be an indicator of the risk for adult essential hypertension and that the early introduction of intervention strategies may lead to a reduction in the high incidence of elevated blood pressure.

Modification of sodium or potassium intake (i.e., decreasing the dietary sodium/potassium ratio) offers a potentially effective, nonpharmacological approach to blood pressure reduction.7 The existing support for sodium reduction among adults is substantial. The international epidemiological study INTERSALT, conducted in 52 centers worldwide, has shown a significant effect of the intervention on adolescent blood pressure 15 in normotensive children. Reductions in sodium intake have not been effective in lowering blood pressure in normotensive children and adolescents,8-10 with one exception.11 Support for increasing dietary potassium to reduce blood pressure also comes mainly from adults. Epidemiological studies have reported an inverse relation between potassium intake and both blood pressure8,12 and stroke,13 and short-term clinical trials have shown that supplements of oral potassium significantly lower systolic blood pressure.14 Experience with sodium and potassium intervention in children and adolescents has been limited and is handicapped by the short-term nature of the studies. Potassium supplementation for 4 weeks did not reduce blood pressure15 in normotensive children. Reductions in sodium intake have not been effective in lowering blood pressure in normotensive children and adolescents,16,17 with one exception.18

The present study was designed to assess the feasibility of maintaining long-term sodium reduction or potassium supplementation among adolescents and to determine the effect of these interventions on blood pressure...
during normal adolescent development. Because the average yearly increase in blood pressure during adolescence is small, it was anticipated that repeated measures of blood pressure would be needed to demonstrate potential significant differences between the intervention groups.

Methods

Recruitment of Participants

This study was approved by the Committee on the Use of Human Subjects in Research. Informed consent was obtained from all participants and their parents or guardians.

A detailed description of the design of this study has previously been published.\textsuperscript{19} Participants were recruited after 5th to 8th grade students in the St. Paul and Minneapolis public schools were screened. The blood pressure of 19,452 students (93.4\% of all those eligible) was measured twice on the right arm and with the student in the seated position by trained personnel using a standard clinical sphygmomanometer and following a standardized protocol.\textsuperscript{20} All children whose systolic blood pressure (mean of two measurements) equaled or exceeded the 70th percentile of the age-specific distribution developed from this screening had their blood pressure measured on a second occasion (rescreening) under identical circumstances. All black, Hispanic, and white children whose blood pressure at the rescreening was above 109 mm Hg for boys and 108 mm Hg for girls were invited to participate in the study (approximately the upper 15\% of all children screened, i.e., 3,223 students).

The children and their parents were seen at four separate clinic visits before randomization into three study groups. The goals of these visits were to introduce participants to the study, to test compliance with planned study activities (e.g., 24-hour urine collections), and to collect baseline data. At the third clinic visit, each child was given a 2-week trial of twice-daily potassium chloride (KCl) capsules (8 mmol KCl per capsule). At the fourth clinic visit, participants who had successfully followed the assigned series of tasks and had taken 75\% or more of the capsules were randomly assigned to one of the following three study groups.

Low sodium diet group. Participants in this group and their parents met with trained nutritionists seven times during the first 3 months of the study for instruction on the gradual reduction of dietary sodium to 1,600 mg (70 mmol/day per each family member). For the duration of the study, these nutritionists conducted reinforcement sessions during the regular three-monthly clinic visits and made telephone calls between visits to all participants and their parents. To monitor dietary sodium intake and compliance, electrolyte excretion was measured yearly in 24-hour urine collections.

Potassium chloride capsule group. Participants in this group remained on their normal diets. They received potassium supplementation of 1 mmol/kg body wt per 24 hours (maximum of 80 mmol per 24 hours) administered in capsules (Micro-K, 8 mmol or 600 mg KCl per capsule, kindly supplied by Wyeth-Ayerst) containing film-coated microencapsulated KCl crystals. The daily potassium was divided into two equal doses administered morning and evening with meals. At each three-monthly clinic visit, the KCl intake was adjusted according to changes in body weight. Compliance in the KCl group was monitored by 24-hour urine electrolyte excretion and by capsule counts.

Placebo capsule group. Participants in this group received capsules identical in shape and color to the KCl capsules (also supplied by Wyeth-Ayerst) and were treated in an identical fashion to the potassium supplementation group.

All capsules were administered double blind.

Longitudinal Evaluation

Participants were seen every 3 months within a 2-week window on either side of a predetermined appointment date, based on the date of randomization into the study. Immediately after arriving for the clinic appointment and before any other clinic activities, participants were placed in a quiet room for a uniform rest period, after which a random-zero sphygmomanometer was used to measure blood pressure on the right arm with participants in a seated position. The averages of two measures of systolic and fifth-phase diastolic blood pressure were used for analysis. At each 12-month visit, a routine urinalysis and 24-hour urine collection were obtained. All participants had an opportunity to complete at least 3 study years.

Statistical Analysis

Analyses were performed using the \textit{BMDP}\textsuperscript{21} and \textit{SAS}\textsuperscript{22} statistical packages. Independent or matched pairs \textit{t} tests, as appropriate, were used for comparison of means between two groups. Analysis of variance and analysis of covariance were used when more than two groups were compared. Whenever pairwise comparisons were performed, nominal alpha levels were adjusted using Bonferroni's technique. All analyses were performed using unadjusted blood pressures and were repeated using blood pressures adjusted for body mass index and/or initial (baseline) blood pressure levels, as suggested by Laird and Wang.\textsuperscript{23}

For analysis and comparison of the blood pressure slopes, a random-coefficient growth curve model approach was used.\textsuperscript{24} Major advantages of this approach are that 1) the timing of the blood pressure measurements over the course of the study does not need to be uniform for all individuals and 2) the pattern of the blood pressure measurements does not need to be the same for all individuals.\textsuperscript{25}

An appropriate regression model was fitted to blood pressure data from each participant, resulting in a vector of estimated coefficients. The distributional assumptions of the vectors of coefficients were assessed with adjustment for the multivariate situation. Because all assumptions were satisfied, the estimated coefficients for individuals were combined to obtain an average growth curve for each of the various groups in the study.

All data are mean±SEM. A value of \textit{p}≤0.05 was considered to be statistically significant.

Results

Participants

Of the 3,223 5th to 8th grade students eligible for participation in the study according to the blood pressure criteria, 643, 401, and 329, respectively, attended...
the first, second, and third clinic visits, and 210 successfully completed the prerandomization requirements and were entered into the study. A comparison between the 210 participants and the nonparticipating 3,013 eligible children did not yield any significant differences in blood pressure or anthropometric measurements. The three randomized groups were evenly divided between boys and girls. The white:black ratio of 7.4:1 was the same in each intervention group. There were no significant differences between intervention groups in age, Tanner score, body size, or blood pressure level at randomization (Table 1).

Compliance

Compliance with capsule-taking, measured as percentage of expected capsule use, was very high and slightly better, on average, over the entire 3 years of the study in the placebo than in the KC1 group (91 ±0.9%, range, 85.2–96.9%; 84.2±0.9%, range, 77.2–93%, respectively). There were no significant differences between boys and girls. The white: black ratio of 7:4:1 was the same in each intervention group. There were no significant differences between intervention groups in age, Tanner score, body size, or blood pressure level at randomization (Table 1).

Compliance with the low sodium diet was less successful. Neither the boys nor girls low sodium groups achieved the study goal of 70 mmol/day urinary sodium excretion. As noted in Table 2, mean 24-hour urinary sodium excretion in the boys low sodium group did not decrease at any point during the study. In contrast, a significant reduction from baseline in urinary sodium excretion was noted in the girls low sodium group, although the differences between the low sodium group and the other two girls groups were not statistically significant at every collection.

Compliance also was evaluated by calculation of 24-hour urinary sodium/potassium ratios (Table 2). For the boys, the ratio decreased significantly from baseline only in the potassium supplementation group, and it was significantly lower than that for the low sodium (p=0.0026) and placebo (p=0.0001) groups throughout the study. Among the girls, the sodium/potassium ratio decreased significantly from baseline in both the low sodium and potassium supplementation groups. The ratio was significantly lower in the potassium group than in the low sodium (p=0.005) and placebo (p=0.001) groups throughout the study.

Blood Pressure

Systolic blood pressure was significantly higher in boys than girls at all clinic visits. The low sodium boys group tended to have higher systolic blood pressure than the other two boys groups throughout the study, but there were no significant differences in systolic blood pressure among the three girls groups. Diastolic blood pressure was significantly higher in girls than boys for the first 2 years of the study. It tended to remain higher during the final year, but these differences were not statistically significant, and there were no significant differences between the boys or the girls groups.

The effect of the sodium and potassium interventions was evaluated by comparing the group average rate of increase (i.e., slope) of systolic blood pressure over the 3 years of observation (Table 3 and Figure 1). Each of the three boys groups had a positive slope that was significantly different from zero (low sodium, p<0.0001; potassium, p<0.0001; placebo, p<0.0001), but there were no significant differences in slope among the three groups.

The sodium and potassium interventions had a substantially different effect on systolic blood pressure in

**TABLE 1. Characteristics at Randomization (i.e., Baseline) of the Three Intervention Groups**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low sodium (n=70)</th>
<th>Potassium chloride (n=71)</th>
<th>Placebo (n=69)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys</td>
<td>35</td>
<td>36</td>
<td>34</td>
</tr>
<tr>
<td>Girls</td>
<td>35</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Age (years)</td>
<td>13.2±0.1</td>
<td>13.3±0.1</td>
<td>13.4±0.1</td>
</tr>
<tr>
<td>Tanner score</td>
<td>3.6±0.2</td>
<td>3.6±0.2</td>
<td>3.6±0.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.3±1.2</td>
<td>161.1±1.1</td>
<td>160.5±1.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.3±1.9</td>
<td>58.6±1.8</td>
<td>57.6±1.6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.5±0.5</td>
<td>22.3±0.5</td>
<td>22.2±0.5</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td>113.6±1.0</td>
<td>114.2±0.9</td>
<td>113.7±1.0</td>
</tr>
<tr>
<td>Systolic</td>
<td>63.4±1.5</td>
<td>66.6±1.3</td>
<td>65.3±1.4</td>
</tr>
</tbody>
</table>

BMI, body mass index. Values are mean±SEM.

**TABLE 2. Urinary 24-Hour Sodium and Potassium Excretion and Sodium/Potassium Ratio in Boys and Girls**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Months in study</th>
<th>n</th>
<th>Low sodium</th>
<th>Potassium chloride</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Na</td>
<td>K</td>
<td>Na/K</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Na</td>
<td>K</td>
<td>Na/K</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Na</td>
<td>K</td>
<td>Na/K</td>
</tr>
<tr>
<td>Boys</td>
<td>Baseline</td>
<td>35</td>
<td>142±11</td>
<td>59±3</td>
<td>2.5±0.2</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>31</td>
<td>158±14</td>
<td>65±5</td>
<td>2.8±0.3</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>21</td>
<td>143±13</td>
<td>58±6</td>
<td>2.9±0.4</td>
</tr>
<tr>
<td></td>
<td>36</td>
<td>15</td>
<td>162±21</td>
<td>64±10</td>
<td>2.9±0.4</td>
</tr>
<tr>
<td>Girls</td>
<td>Baseline</td>
<td>35</td>
<td>133±8</td>
<td>55±4</td>
<td>3.8±1.0</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>32</td>
<td>112±10</td>
<td>52±3</td>
<td>2.2±0.2</td>
</tr>
<tr>
<td></td>
<td>36</td>
<td>29</td>
<td>102±7</td>
<td>45±3</td>
<td>2.5±0.2</td>
</tr>
</tbody>
</table>

All data are mean±SEM. Sodium and potassium excretions are shown in millimole per 24 hours.

*p<0.0001, compared with low sodium and placebo groups of same sex.

fp<0.0002, compared with potassium and placebo groups of same sex.

*fp<0.05, compared with placebo group of same sex.
TABLE 3. Mean Rate of Increase of Systolic and Diastolic Blood Pressure in Boys and Girls Intervention Groups

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>Intervention group</th>
<th>Slope</th>
<th>Z value</th>
<th>95% CI</th>
<th>Slope</th>
<th>Z value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low sodium</td>
<td>2.2±0.5*</td>
<td>4.55</td>
<td>1.3, 3.2</td>
<td>-0.5±0.4†</td>
<td>-1.19</td>
<td>-1.3, 0.3</td>
</tr>
<tr>
<td></td>
<td>Potassium chloride</td>
<td>1.9±0.4*</td>
<td>4.71</td>
<td>1.1, 2.7</td>
<td>0.5±0.4‡</td>
<td>1.39</td>
<td>-0.2, 1.4</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>1.6±0.4*</td>
<td>3.88</td>
<td>0.8, 2.5</td>
<td>1.4±0.4*</td>
<td>3.36</td>
<td>0.6, 2.2</td>
</tr>
<tr>
<td>DBP</td>
<td>Low sodium</td>
<td>1.8±0.8*</td>
<td>2.30</td>
<td>0.3, 3.4</td>
<td>0.1±0.5‡</td>
<td>0.29</td>
<td>-0.8, 1.1</td>
</tr>
<tr>
<td></td>
<td>Potassium chloride</td>
<td>1.6±0.7*</td>
<td>2.36</td>
<td>0.3, 3.0</td>
<td>0.9±0.5</td>
<td>1.83</td>
<td>-0.1, 1.9</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>3.2±0.7*</td>
<td>4.49</td>
<td>1.7, 4.6</td>
<td>1.8±0.5*</td>
<td>3.59</td>
<td>0.8, 2.8</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure. Data are mean±SEM. Rate of increase (slope) is shown as millimeters of mercury per year.

*P<0.01, compared with slope of boys group.
†P<0.01, compared with slope of girls placebo group.
‡P<0.01, compared with slope of boys group with same intervention.

the girls groups. The slope of the placebo group was positive and significantly different from zero (P<0.001). The slope of the potassium group was slightly positive and the slope of the low sodium group slightly negative, but neither was significantly different from zero. The slope of the low sodium group was significantly different from the placebo group (P<0.01).

The rate of increase in diastolic blood pressure followed a pattern similar to systolic blood pressure for both boys and girls (Table 3 and Figure 1). The slopes of the three boys groups were all significantly different from zero (low sodium, P<0.001; potassium, P<0.001; placebo, P<0.0001), and there was no significant difference among groups. The slope of the girls placebo group was positive and significantly different from zero (P<0.0001); the slopes of the low sodium and potassium girls also were positive but not significantly different from zero. A significant difference in the girls slopes was noted between the low sodium and placebo groups (P<0.01).

The effect of the sodium and potassium interventions was significantly different between the boys and girls. Although the slope for systolic blood pressure was not significantly different between the two placebo groups, the differences in slopes between the girls and boys low sodium groups and the girls and boys potassium groups were highly significant (P<0.0001 and P<0.01, respectively). Significant differences in slope between the boys and girls were observed for diastolic blood pressure only between the low sodium intervention groups (P<0.01).

Body mass index increased significantly in each of the six intervention groups, but there were no significant differences among the groups at any point during the study. Adjusting the blood pressure data for body mass index did not significantly affect any of the slopes or alter the results of slope analyses within or between sexes.

Discussion

This is the first reported multiyear study attempting sodium or potassium interventions in adolescents. Sodium restriction and potassium supplementation were chosen because of mounting evidence that sodium and potassium directly affect systemic blood pressure. Although the exact mechanism through which sodium influences blood pressure is not known, considerable epidemiological information, dating back to Dahl's early observations, strongly suggests that sodium intake...
and blood pressure level are intimately related. The most persuasive of these studies, INTERSALT, conducted in 10,000 people in 32 countries, found that a 3.4 mm Hg increase in systolic blood pressure could be expected over 10 years for each 100 mmol/day of dietary sodium.\(^8\) A review of 78 separate trials in adults showed that a 50 mmol decrease in sodium intake lowers systolic blood pressure by an average of 4 mm Hg in normotensive and 7 mm Hg in hypertensive individuals.\(^10\)

The effect of potassium supplementation on blood pressure has not been studied as extensively as sodium. Results from INTERSALT showed a strong inverse relation between urinary potassium excretion and blood pressure.\(^8\) A recent meta-analysis of 19 clinical trials with potassium (13 with hypertensive patients) confirmed the significant antihypertensive effect of potassium chloride.\(^14\)

The participants and parents in this study had intensive education and training sessions during the initial 3 months of intervention, were counseled by an experienced nutritionist/interventionist at each clinic visit, and were contacted by telephone at the midpoint between clinic visits. Nevertheless, neither the girls nor boys low sodium groups were successful in reaching the target level of 70 mmol of sodium per day. The girls group had a significant reduction in sodium intake and a lower sodium/potassium ratio than the other groups. The boys low sodium group did not reduce either sodium intake or the sodium/potassium ratio, and they had a substantially higher dropout rate. An explanation for this contrast in compliance is not apparent, but it probably is related to differences in motivation, lifestyle, and maturity between boys and girls at this age. Capsule counts at each clinic visit and measurement of potassium in 24-hour urine collections confirmed the compliance of both sexes with the capsule-taking. Because virtually all capsules were taken at home, it was easier for parents to be involved and monitor the intervention.

Of note was the significant difference in response to the sodium and potassium interventions between the boys and girls. The slopes of the boys low sodium and potassium groups showed significant yearly increases that were no different from the boys placebo group. In contrast, the slopes of the girls low sodium and potassium groups were not significantly different from zero and substantially lower than the slope of the girls placebo group, although only the low sodium slope was significantly lower. Moreover, there was a highly significant difference in slope between the girls low sodium and potassium groups and their respective boys groups. The validity of these differences between boys and girls is supported by the similarity of slopes between the boys and girls placebo groups.

Few studies examining the effect of sodium or potassium on blood pressure have been reported in children or adolescents. Significant correlations between urinary sodium and blood pressure have not been found in children under free-living dietary conditions.\(^27\)–\(^30\) Intervention studies with low sodium diets or potassium supplementation have been conducted for shorter periods than this study\(^5,17,18\) and did not result in a reduction in blood pressure. It is of interest that when a decrease in blood pressure was seen, the response occurred only\(^16,20,30\) or primarily\(^18\) in girls.

It is not readily apparent why the response was different between the boys and the girls in this study, except for the low sodium groups in which there was total noncompliance by the boys. The slightly lower slope of the girls placebo group compared with the boys placebo group is similar to the difference during adolescence documented in the Task Force report.\(^31\) It is unlikely that sexual maturity played a role, because the participants were matched for age and sexual maturity; however, laboratory evaluation of puberty-related hormones was not performed.

Epidemiological studies have shown that small reductions in blood pressure within a population can have a significant effect on hypertension-related adverse medical events.\(^7,32\) The data from this study show that dietary changes within the first two decades of life can reduce the rate of increase of blood pressure in girls. Although these interventions did not have a similar effect in boys, the dietary sodium reduction was not tested because of the lack of compliance with the intervention protocol. It is doubtful that long-term sodium reduction, particularly among boys, is feasible in the United States without societal change regarding availability and consumption of low salt foods. Nevertheless, the differences in blood pressure response found in this study suggest a different sensitivity to dietary sodium or potassium between boys and girls. Studies are needed to explore the mechanisms for this sex difference.

Acknowledgments

We thank the following members of the Data and Safety Monitoring Committee: Chairman, Dr. Robert Wallace, Dr. Alfred Fish, Dr. James Neaton, and Ching-Ping Hong.

References

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Hypertension. 1993;21:989-994
doi: 10.1161/01.HYP.21.6.989

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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