Management of Hypertension in High School Students by Using New Salt Titrator Tape

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SUMMARY In a blood pressure screening program involving 6589 high school students, 180 male (4.7%) and 17 female (0.6%) students were identified as borderline hypertensive. The 174 hypertensive male adolescents studied further showed pathophysiological features such as a significantly higher frequency of obesity, higher 24-hour urinary sodium excretion, higher hematocrit value, higher sodium and lower potassium concentration in red blood cells, and higher ouabain-sensitive sodium efflux compared with the control group (231 male students; p < 0.05). When used alone, the ordinary 10-week period of counseling about a low salt diet failed to significantly reduce the blood pressure of hypertensive students. However, when education and counseling efforts were combined with self-monitoring of salt (chloride) excretion in overnight urine samples using a new salt titrator tape developed in our laboratory, 24-hour urinary sodium excretion, weight, and blood pressure decreased significantly over 10 weeks (mean reduction: 52 mEq/day for 24-hour urinary sodium excretion, 1.7 kg for weight, 12/7 mm Hg for blood pressure). These results indicate that blood pressure of borderline hypertensive adolescents could be effectively reduced with this nonpharmacological method of dietary education. Such systematic management might be of importance for the prevention of essential hypertension. (Hypertension 8: 1164–1171, 1986)

KEY WORDS • sodium intake • borderline hypertension • adolescents

A undisputed goal of antihypertensive therapy is to prevent the associated cardiac, cerebral, and renal complications. However, the etiological mechanisms underlying essential hypertension remain unsolved. A complex interplay of genetic and environmental factors appears to be involved. Therefore, various treatment programs have been applied, but no definitive hypertension management program has been established.

Juveniles with borderline hypertension or high normal blood pressure (BP) have a twofold to fourfold greater risk of fixed hypertension developing during adulthood compared with normotensive adolescents. Nonpharmacological management of hypertension may be effective in adolescent borderline hypertension because this population has less arteriosclerosis. We believe it more appropriate to investigate the pathophysiology and treatment of hypertension in its early stage, in adolescents with less arteriosclerotic involvement, than in its fixed stage, in adults with marked arteriosclerotic involvement.

Among juveniles, high school students are particularly appropriate candidates for hypertension screening and prophylactic education programs. The present investigation was performed to examine the pathophysiology of adolescent borderline hypertension and the effectiveness of our program of education and management of hypertension through diet control (salt restriction) using a new salt titrator tape.

Materials and Methods

Subjects and Procedures

From 1981 to 1983, a total of 6589 students (3837 male, 2752 female; age, 15–18 years) from six high schools in Yokohama City and Kawasaki City, Japan, were examined. Resting, seated BP was measured twice with a mercurial standard sphygmomanometer. The subject’s height and weight also were measured. Diastolic BP (DBP) was taken as the fourth (DBP4) and fifth (DBP5) Korotkoff phase, and systolic BP (SBP) was taken as the first Korotkoff phase. After 2
weeks, resting BP (SBP and DBP5) was remeasured. Male students with SBP higher than 140 mm Hg on two occasions measured 2 weeks apart were considered borderline hypertensive (BHT) and chosen for further study. Male students with SBP of 130 mm Hg or lower and with no history of cardiac or renal diseases were randomly selected as controls (C).

Both groups of students completed questionnaires on their medical and family histories of hypertension. The answers were checked and confirmed by nurses. After receiving instructions from the nurses, each student collected a 24-hour urine sample using a proportional sampling device (Memorette, Sumitomo Bake-lite, Tokyo, Japan) that is designed to collect 1/50th of each urination volume. The principles and accuracy of the method have been reported.9,10

Urinary Na and K excretion were measured with a flame photometer (Model 775; Hitachi, Tokyo, Japan). The 24-hour creatinine excretion was measured with an autoanalyzer using Jaffe’s reaction. Total urinary nitrogen was measured by the Kjehldahl-Nessler method.

On the day students brought in their urine samples, resting BP was measured twice. A venous blood sample also was taken. Red blood cell (RBC) count, hemoglobin concentration, and hematocrit value were measured with an automatic counter (Model S; Coulter Electronics, Hialeah, FL, USA). Serum was analyzed to determine Na, K, creatinine, total cholesterol, and high density lipoprotein cholesterol (K-Agar method).11

The Na and K concentrations in RBCs were measured with a flame photometer after the RBCs were washed by an ultrasonic wave—hemolysis washing method12 to remove any trapped electrolyte-rich plasma. Ouabain-sensitive Na efflux from the RBC membrane was determined by modifying the method of Cumberbatch and Morgan.13 In our method, Na concentrations in RBCs were measured after a 2-hour incubation in the presence or absence of 10^{-4} M ouabain. The difference between each value represents ouabain-sensitive Na efflux from RBC membrane (nmol/L of RBC/hr). The details and accuracy of the method have been reported.14

Precision of Salt Titrator Tape

The salt titrator tape (chloride titrator tape) developed in our laboratory is a 5 × 80-mm plastic strip with six 5 × 5-mm patches impregnated with AgNO₃ and 2,7-dichlorofluorescein. The amount of the reagents in each patch is adjusted to react with the Cl equivalent of 6, 8, 10, 12, 14, and 16 g/L of urinary NaCl. In the presence of Cl, AgNO₃ is converted to AgCl, and the tape color changes from red to yellow within 60 seconds (Figure 1).

To assess the precision of the salt titrator tape, overnight urine samples were collected from 61 subjects. The Cl content (x) was measured with a chloride meter, and the Cl content of samples (y) was measured by the subject using the salt titrator tape. Further, for each of these urine samples, Na content was determined with a flame photometer and the value was compared with the estimates determined with the salt titrator tape.

The following preliminary experiments were performed to confirm that 24-hour urinary salt excretion can be assumed from values obtained in an overnight urine sample. The aforementioned urine collection method was used to obtain 103 samples of 24-hour urine collections. The Na concentration was determined with a flame photometer, and 24-hour urinary salt excretion was measured. The concentration of Cl was determined with the salt titrator tape for the first urination of each subject (mean collection time, 7 ± 2 hours) on the morning of the test day, and salt excretion in the overnight urine sample was determined by self-measurement.

Student Education and Monitoring Program

To assess the effectiveness of our hypertension management program using the salt titrator tape, the following investigations were performed from 1981 to 1984.

In 1981, 50 BHT students were selected for a 10-week educational program focusing on low dietary salt intake. In this group, 24-hour urine samples were collected for Na, K, and creatinine analyses according to the aforementioned urine sampling method. On the day students brought their urine samples to the hospital, resting BP (SBP, DBP5) was measured twice and nurses discussed the medical importance of hypertension and salt restriction. After 5 weeks, resting BP was measured again and the nurses provided each subject with individual dietary counseling. After 10 weeks, resting BP was measured twice and 24-hour urine samples were collected again for Na, K, and creatinine analyses.

During 1982 to 1983, another 100 BHT students (the 50 students in the 1981 BHT group were not included) from the study population were selected for a 10-week hypertension education and dietary counseling program that included self-monitoring of urinary Cl excretion with the new salt titrator tape. In this expanded program, the students were instructed to use the salt titrator tape, which was handed out for once-a-week testing of overnight urine samples at home. In our education program, students were encouraged to keep NaCl excretion in overnight (7 ± 2 hours) urine samples under 1 to 2 g.15

In 1984, another 42 male BHT students were selected for the long-term (6 months) hypertension management program with the salt titrator tape. After 6 months, 24-hour urine samples for Na, K, and creatinine analyses were collected and BP and body weight were measured.

Statistical Analyses

All data are expressed as mean ± SD, and the differences between groups were analyzed using unpaired t test and F tests. A paired t test was used for intergroup comparisons. The level for significance was a probability of less than 5% (p < 0.05).
Salt-Tape

Dichlorofluorescein

Red → Yellow

AgNO₃ → AgCl

80 mm

5 mm

8 k/L

14 k/L

16 k/L

Over 16 k/L

12 k/L

10 k/L

8 k/L

6 k/L

5 mm

no change : under 5 k/L

Example

FIGURE 1. Measurement of urinary chloride concentration with salt titrator tape. Sixty seconds after the salt titrator tape is dipped in urine, the chloride concentration is read directly from the strip according to the red-to-yellow color change. For example, as shown on the strip to the right, the 6 and 8 g/L patches are completely yellow, while the 10 g/L patch show spots of yellow. This result indicates that the NaCl concentration is between 6 and 10 g/L (i.e., approximately 9 g/L).

RESULTS

Hypertension Screening of High School Students

In the first BP measurement, the mean SBP was 121 ± 13 mm Hg for the 3837 male students and 111 ± 12 mm Hg for the 2752 female students. The mean DBP was 66 ± 11 mmHg for male students and 64 ± 10 mm Hg for female students. On the first reading, the SBP of 345 male (9.0%) and 47 female (1.7%) students was higher than 140 mm Hg. The SBP of 180 male (4.7%) and 17 female (0.6%) students measured on two occasions 2 weeks apart was higher than 140 mm Hg. This group was defined as BHT. The BHT group, composed of 174 male students (6 male students with secondary hypertension were excluded), was enrolled for further study. The C group (231 male students) was randomly selected from students with SBP consistently lower than 130 mm Hg (Figure 2).

The mean BP for the two groups is shown in Table 1. The mean body weight for the 3837 male students was 59.8 ± 8.7 kg, with 77 kg marking the upper 95th percentile limit. The mean body weight among BHT students was 68.1 ± 15 kg. Fifty-two male students (30%) were found to be obese, weighing more than 77 kg. The mean Quetelet body mass index (body weight/height²) for the BHT group was significantly higher than that for the C group (p < 0.001). Thus, obesity was more common in the young BHT subjects (Figure 3).

The results of 24-hour electrolyte excretion and levels of serum electrolytes and cholesterol are given in Table 1. The RBC count, hemoglobin concentration, and hematocrit value were all significantly higher in BHT students. Similarly, Na concentration in RBCs and ouabain-sensitive Na efflux from RBCs were significantly higher in the BHT group. Mean K concentration in RBCs was lower in the BHT group than in the C group (see Table 1).

Of 405 students questioned on their family histories, 48% of the BHT group had family histories of hypertension while only 28% of the C group (excluding 65 respondents with uncertain family histories) had histories of hypertension. According to chi-square test, this difference was significant (see Table 1).

Precision of Salt Titrator Tape

The correlation coefficient between chloride meter (x) and salt titrator tape (y) was 0.96. The mean devi...
TABLE 1. Pathophysiological Findings in Borderline Hypertensive Group and Control Group

<table>
<thead>
<tr>
<th>Variable</th>
<th>BHT group (SBP &gt; 140 mm Hg)</th>
<th>Controls (SBP &lt; 130 mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>150.3 ± 9.8*</td>
<td>117.7 ± 12.2</td>
</tr>
<tr>
<td>Diastolic phase 4</td>
<td>81.1 ± 7.5*</td>
<td>72.8 ± 8.6</td>
</tr>
<tr>
<td>Diastolic phase 5</td>
<td>71.3 ± 10.6*</td>
<td>63.8 ± 9.9</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.1 ± 15.0*</td>
<td>59.3 ± 7.8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170.6 ± 5.8</td>
<td>168.9 ± 6.2</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.4 ± 4.6*</td>
<td>20.7 ± 2.3</td>
</tr>
<tr>
<td>24-hour urine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume (ml/day)</td>
<td>1044 ± 478†</td>
<td>914 ± 360</td>
</tr>
<tr>
<td>Creatinine (g/day)</td>
<td>1.64 ± 0.51*</td>
<td>1.37 ± 0.40</td>
</tr>
<tr>
<td>Total nitrogen (g/day)</td>
<td>12.1 ± 4.0*</td>
<td>9.9 ± 3.4</td>
</tr>
<tr>
<td>Na (mmol/day)</td>
<td>211 ± 94t</td>
<td>187 ± 80</td>
</tr>
<tr>
<td>K (mmol/day)</td>
<td>42.1 ± 16.6</td>
<td>39.5 ± 23.6</td>
</tr>
<tr>
<td>Serum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>174 ± 32*</td>
<td>154 ± 36</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>50.6 ± 10.8</td>
<td>52.3 ± 12.2</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.64 ± 0.36*</td>
<td>0.40 ± 0.32</td>
</tr>
<tr>
<td>Na (mmol/L)</td>
<td>143.2 ± 1.8†</td>
<td>142.5 ± 1.4</td>
</tr>
<tr>
<td>K (mmol/L)</td>
<td>4.3 ± 0.4*</td>
<td>4.6 ± 0.3</td>
</tr>
<tr>
<td>RBC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Count (×10⁶/mm³)</td>
<td>534 ± 33*</td>
<td>504 ± 38</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>15.6 ± 0.85*</td>
<td>14.2 ± 1.21</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>46.2 ± 2.44*</td>
<td>43.0 ± 3.32</td>
</tr>
<tr>
<td>Electrolyte concentration in RBCs (mmol/L RBC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na</td>
<td>9.70 ± 1.33*</td>
<td>8.90 ± 1.66</td>
</tr>
<tr>
<td>K</td>
<td>94.8 ± 3.62†</td>
<td>96.4 ± 3.47</td>
</tr>
<tr>
<td>Ouabain-sensitive Na efflux of RBC (mmol/L RBC/hr)</td>
<td>2.55 ± 0.31*</td>
<td>2.32 ± 0.33</td>
</tr>
<tr>
<td>Family history of hypertension (%)</td>
<td>48.0* (n = 160)</td>
<td>28.0 (n = 180)</td>
</tr>
</tbody>
</table>

Values are means ± SD. BHT = borderline hypertensive; SBP = Systolic blood pressure; HDL = high density lipoprotein; RBC = red blood cell. *p < 0.001, †p < 0.05, ‡p < 0.01, compared with control group values.

The correlation coefficient between flame photometer (x) and salt titrator tape (y) was 0.87, and the mean deviation (x̄−ȳ) was 1.00 ± 1.49 g/L. Thus, the salt titrator tape is useful in estimating the urinary NaCl concentration. The correlation coefficient between overnight urinary NaCl excretion determined using the salt titrator tape (x) and 24-hour urinary sodium excretion with a flame photometer (y) was 0.72 (Figure 4).

**Student Education and Monitoring Program**

From the 1981 hypertension education and dietary counseling program, data for 41 of 50 BHT students were obtained 10 weeks after the inception of the program. Nine students dropped out or were unable to collect urine samples adequately. During the education program without the self-monitoring using the salt titrator tape, 24-hour urinary Na excretion and SBP (average of 2 readings) decreased slightly (Table 2). The SBP dropped below 140 mm Hg in 26% of the BHT students (p<0.05).

From the 1982 to 1983 program featuring once-a-week self-monitoring of urinary salt excretion, data for 88 of 100 BHT students were obtained (see Table 2). After 10 weeks, mean urinary Na excretion and SBP decreased significantly (p<0.001). The SBP fell below 140 mm Hg in 63% of the BHT students. The mean reduction for SBP and for 24-hour urinary Na excretion was 12 ± 5 mm Hg and 52 ± 22 mEq/day, respectively. Compared with the effect on SBP reduction by dietary counseling alone, the effect by dietary counseling plus home monitoring using the salt titrator tape was significantly greater. The correlation coefficient between the changes in SBP and urinary Na excretion was 0.38 (p<0.05). Similarly, the mean reduction of body weight was 1.7 ± 0.4 kg, and the...
correlation coefficient between the changes in SBP and weight was 0.26 ($p < 0.1$). Creatinine and K excretion were not affected by the program.

The results of the 6-month hypertension management program in 1984 are shown in Table 3. Over 50% (23 male students) of the 42 BHT students complied with the long-term counseling program, which included self-monitoring with the salt titrator tape. In these 23 students, changes in SBP (15 mm Hg), urinary Na excretion (66 mEq/day), and weight (2.9 kg) were significant.

**Discussion**

**Pathophysiology of Juvenile Hypertension**

The risk factors for essential hypertension developing in adolescents have not been clearly defined. However, certain risk factors such as family history of hypertension, high BP, obesity, tachycardia, supranormal response to mental stress, decreased urinary kallikrein excretion, and elevated hematocrit values have been reported. Other recently reported risk factors include abnormal cellular membrane Na⁺, K⁺ transport in blood cells (RBCs, leukocytes, and lymphocytes), as seen in abnormal Na⁺-K⁺ cotransport, Na⁺,Li⁺ countertransport, and sodium permeability. Also, the increase in cellular Na concentration has been reported in essential hypertension and in normotensive persons with a family history of hypertension. Our previous studies have indicated increased Na and decreased K concentrations in RBCs in hypertensive and normotensive subjects with a family history of hypertension. Similar results were noted in juvenile borderline hypertensive subjects and normotensive adolescents with a family history of hypertension.

Despite the evidence of altered RBC ion membrane transport in hypertension, it is not known how closely
the RBC membrane approximates the cellular membrane of vascular smooth muscle. Cellular membrane ion transport is also altered in such disorders as blood diseases, 37 obesity, 38 hyperthyroidism, 39-41 renal failure, 32-34 and depression. 35 If the hypothesis of Blau
stein 36 and De Wardener and MacGregor 37 regarding the relationship between altered cellular membrane ion transport and hypertension is verified, measurements of RBC membrane ion transport and electrolyte concentration could become useful clinical tools for identifying those persons who will eventually acquire essential hypertension.

A number of studies 4, 7, 58 have reported the pathophysiolo
ogy of juvenile borderline hypertension, but many issues remain unsolved. Our present study confirms the previous reports 59-61 that obesity plays an important role in the pathophysiology of juvenile hypertension and that adolescent borderline hypertension is closely associated with excess intracellular Na relative to K.

Management of Hypertension in Adolescents

Many environmental factors such as excess Na intake, excess Na intake relative to K consumption, insufficient protein intake, 62 inadequate physical activity, 63 and obesity 58, 60, 61 seem to exacerbate hypertension. Among these factors, the relationship between Na intake and hypertension is the most interesting. Several investigators have reported a close correlation between Na intake and elevated blood pressure, 63-66 with some evidence of a lowering of BP by reducing salt intake. 64, 65 In contrast, others have failed to demonstrate such a relationship. 66-71

Dahl et al. 74, 75 examined the correlation between juvenile hypertension and excess salt intake using the salt-sensitive rat as an experimental model. These animals became hypertensive with salt loading at an early age. 74 Hypertension was sustained even after salt loading was discontinued. 76 Dahl et al. 77 suggested that excess Na intake in infancy plays an important role in the onset of hypertension.

The concept that essential hypertension could be prevented by reducing or eliminating environmental influences early in the course of juvenile hypertension is important in hypertension management. We have developed an effective program to reduce salt intake among adolescents. As our results indicated, hypertension education and dietary guidance alone have little impact on reducing salt intake or blood pressure, but they are quite effective when salt (CI) concentration in overnight urine samples is self-monitored using the salt titrator tape.

According to Luft et al., 7 the urinary Na excretion was highly correlated with urinary CI excretion: 24-hour urinary Na excretion was low when CI output in overnight urine was low, as determined by a CI titrator strip (Quntab Chloride Titrator; Ames, Elkhart, IN, USA). Thus, the measurement of overnight CI excretion is a useful means of assessing compliance with a low sodium diet. However, the test using the Quntab Chloride Titrator takes 20 minutes, and CI excretion must be calculated by conversion from a calibration table. Such calculations are inconvenient for patients' use at home. Moreover, this testing method uses toxic potassium chromate. In contrast, the new salt titrator tape is precise and suitable for at-home monitoring. Results are available in 1 minute, and CI concentration is read directly from the tape. Also, dichlororfluorescein is safe for patient kits.

Obesity and excessive salt intake seem to be major risk factors in juvenile hypertension, as sensible weight loss combined with salt restriction reduces BP. Our results indicate that dietary education and counseling augmented by self-monitoring at home using the salt titrator tape could be an effective means of restricting salt intake in juveniles with borderline hypertension. Such systematic management might be of importance for the prevention of essential hypertension.

Acknowledgments

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