Threshold Effect of Urinary Sodium Excretion on the Prevalence of Hypertension.

Orawan Anupraiwan, MD, Somnuek Domrongkitchaiporn, MD, Sukit Yamwong, MD, Supachai Tanomsup, MD, and Piyamitr Sritara, MD

Division of Cardiology, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, 10400

Abstract

Background: Prior studies in different populations showed a significant correlation between 24-hour urinary sodium excretion and blood pressure. However, the relationship between urinary sodium excretion and blood pressure might deviate in different populations. We, therefore, conducted this study to determine the relationship between 24-hour urinary sodium excretion and blood pressure, and the prevalence of hypertension in a Thai population cohort.

Methods: Between May and July 2008, 415 participants from the Electricity Generating Authority of Thailand (EGAT) were enrolled in this study. The studied population consisted mainly of the urban middle-class Thai population, aged 52 ± 4 years old, 64% males. All participants answered questionnaires, underwent basic physical examination, and provided a 24-hour urine sample for the determination of sodium excretion. Correlation between urinary sodium excretion and blood pressure was analyzed.

Results: The prevalence of hypertension was 24.6%. The mean systolic blood pressure was 137 ± 16 mmHg in the hypertensive group and 116 ± 11 mmHg in the normotensive group. The 24-hour urinary sodium excretion was significantly higher in the hypertensive group compared to the normotensive group (median = 179 interquartile range 107 versus 155 interquartile range 82 mmol/day; P = 0.03). The 24-hour urinary sodium excretion was positively correlated with systolic blood pressure (r=0.03; p=0.01) and diastolic blood pressure (r=0.02; p=0.02). After classifying 24-hour urinary sodium excretion into 5 quintiles (<114, 114-145, 146-174, 175-230, and > 230 mmol/day), the prevalence of hypertension (systolic blood pressure ≥ 140 mmHg) were 21%, 19%, 20%, 32%, and 34%, respectively. The prevalence of hypertension was increased significantly when urinary sodium excretion was greater than 175 mmol/day, indicating a threshold effect for urinary sodium excretion on the prevalence of hypertension. Age (OR=1.100, 95% CI=1.041–1.613) and 24-hour urinary sodium excretion more than 175 mmol (OR=2.028, 95% CI=1.262–3.259) were independent risk factors for hypertension.

Conclusions: There was a significant correlation between blood pressure and 24-hour urinary sodium excretion with both systolic and diastolic blood pressure. Both age and levels of 24-hour urinary sodium excretion more than 175 mmol were an independent risk factor for hypertension. A threshold level of urinary sodium excretion for hypertension was found in this population group.

Keywords: 24-hour urinary sodium excretion, Hypertension

Introduction

Blood pressure is a prominent predictor of stroke and cardiovascular diseases. Previous epidemiological studies and clinical research have demonstrated a relationship between sodium intake and blood pressure (1-6). High dietary salt intake has been associated with high blood pressure, or a higher prevalence of hypertension, resulting in a higher prevalence of stroke and cardiovascular diseases (7).
Randomized control trials have demonstrated the effect of reduced dietary salt intake on blood pressure. The blood pressure-lowering effect is dependent on the degree of dietary salt intake reduction (8,9), without a threshold effect (10,11). Salt consumption of less than 5 g/day (<2 g/day of sodium) has been recommended for blood pressure reduction (12). However, the relationship between salt intake and blood pressure varies between different populations (13-15). Different recommended amounts of salt intake may be needed in different populations. The recommendation has been implemented in various populations without studies to evaluate its effectiveness. In order to study the relationship between salt intake and the prevalence of hypertension, salt intake should be estimated accurately. Salt intake can be estimated by measuring urinary sodium excretion by 24-hour urine collection (16,17). Twenty-four hour urine collection can capture 85-90% of the dietary sodium consumption. This method is more accurate than dietary recall, which is commonly affected by subjective reporting of dietary intake (18).

We, therefore, conducted this study to determine the relationship between 24-hour urinary sodium excretion and the prevalence of hypertension in a Thai population cohort.

**Methods**

The study was conducted between May and July 2008 among employees of the Electricity Generating Authority of Thailand (EGAT). All subjects completed a self-administered questionnaire, underwent a physical examination, and provided fasting blood samples, a spot urine sample, and a 24-hour urine specimen collection. The inclusion criteria were 1) having serum creatinine less than 1.5 mg/dl, 2) not taking diuretics or NSAIDs within 2 weeks before the study. Subjects who failed to complete the self-administered questionnaire or failed to provide a complete 24-hour urine collection were excluded from this study. All of the questionnaires were checked by trained staff to verify the data. A trained nurse measured height and body weight without shoes and took blood pressure by using a calibrated automatic blood pressure monitor (UA-767 Plus model). The device measured blood pressure by an oscillometric technique with ± 3 mmHg or ± 2% accuracy, pressure range of 20-280 mmHg, and validated according to the British Hypertension Society (BHS) protocol (19). The blood pressure cuff sizes were 22-32 cm. Blood pressure was measured after subjects rested for at least 5 minutes in a sitting position and each reading was made twice, and then averaged. Subjects were classified as hypertensive if their blood pressure were ≥ 140/90 mmHg, or they were currently taking prescribed blood pressure lowering therapy (12).

The blood samples were taken to determine serum creatinine and a spot urine examination was obtained from all of the participants. The 24-hour urine collection was obtained to determine urinary sodium and creatinine excretions. All subjects were carefully instructed on a proper technique for a 24-hour urine collection. The urine specimens were delivered to the staff on the following day. An interview was done with every subject to assure a complete collection of the urine specimen before acceptance. Incomplete collected specimens were discarded and additional urine collections were requested from subjects until the satisfied specimens were obtained. Any urine specimen with 24-hour creatinine excretion less than 20 mg/kg/day in males or 15 mg/kg/day in females was considered an incomplete collection and was excluded from the study.

Biochemical analyses of all blood and urine samples were done in the Central laboratory of Ramathibodi hospital. A standardized procedure for shipment to preserve specimens was deployed. All samples were stored deeply frozen and were analyzed by automated biochemical analytic methods.

The protocol of this study was reviewed and approved by the Ramathibodi Ethics Committee, No. 05-51-19. A written informed consent was obtained from all subjects.

**Statistical analysis**

Blood pressure of individual participants was the mean of the two recorded readings. Body mass index (BMI) was calculated as weight divided by height squared (kg/m²). The 24 hour urine sodium excretion was measured repeatedly to calculate total urine clearance per day.

To adjust the relationship between 24-hour urinary sodium excretion and hypertension, the Mann-Whitney U test was used for analysis. The correlation coefficient and
linear regression analysis was used for adjusting the relationship between blood pressure and 24-hour urinary sodium excretion. After classifying 24-hour urinary sodium excretion into 5 quintiles (<114, 114-145, 146-174, 175-230, and >230 mmol/day), the relationship between systolic blood pressure and the 5 quintiles of 24-hour urinary sodium excretion was analyzed by the one-way ANOVA. The relationship between the prevalence of hypertension and each quintile of urine sodium excretion was determined by a Pearson Chi-square test. A multivariate regression analysis was used for adjusting the relationship between hypertension and 24-hour urinary sodium excretion, controlled for age, sex, and BMI. The Statistical Package for the social Sciences software (SPSS. Version 16.0, SPSS Inc., Chicago, IL, USA) was used for analysis.

**Results**

Two thirds of the EGAT employees were surveyed and of these 1,561 EGAT participants were re-surveyed between May and July 2008 and attended the examination. The 24-hour urine specimens were collected from 440 volunteers, 425 participants completed the inclusion criteria, and 10 participants failed because of the exclusion criteria (Figure 1). Therefore, data were available on 415 subjects aged between 44 and 64 years old (51.6 ± 4.1 years), of whom 265 (64%) were male. Figure 1 shows the enrollment for the study population.

The baseline characteristics of participants are shown in Table 1. In the hypertensive group, mean age, BMI, waist circumference, and blood pressure, both systolic and diastolic blood pressure, were more than the normotensive group.

**Table 1.** Baseline characteristics compared between the hypertensive and normotensive group.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Hypertensive (n = 105)</th>
<th>Normotensive (n = 310)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.7</td>
<td>4.4</td>
<td>51.2</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.0</td>
<td>20.6</td>
<td>24.4</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>89.8</td>
<td>8.4</td>
<td>84.6</td>
</tr>
<tr>
<td>Blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>137.1</td>
<td>15.7</td>
<td>116.0</td>
</tr>
<tr>
<td>Diastolic</td>
<td>87.9</td>
<td>10.9</td>
<td>75.3</td>
</tr>
</tbody>
</table>

SD = standard deviation, BMI = body mass index

**Table 2.** The multiple logistic regression analysis of the effect of 24-hour urinary sodium excretion (>175 mmol) on hypertension adjusted for age, sex, and BMI.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>1.265</td>
<td>(0.774 – 2.066)</td>
<td>0.348</td>
</tr>
<tr>
<td>BMI</td>
<td>1.023</td>
<td>(0.988 – 1.059)</td>
<td>0.195</td>
</tr>
<tr>
<td>Age</td>
<td>1.100</td>
<td>(1.041 – 1.613)</td>
<td>0.001</td>
</tr>
<tr>
<td>24-hour urinary sodium excretion &gt; 175 mmol</td>
<td>2.028</td>
<td>(1.262 – 3.259)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

CI = confidence interval, BMI = body mass index
The prevalence of hypertension was 24.6% (non-age adjusted). The mean systolic blood pressure in the hypertensive group was 137 mmHg (standard deviation 16 mmHg) and in the normotensive group was 116 (standard deviation 11 mmHg). The 24-hour urinary sodium excretion was significantly higher in the hypertensive group compared to the normotensive group (Median = 179 interquartile range 107 versus 155 interquartile range 82 mmol/day (p = 0.03).

The 24-hour urinary sodium excretion were positively correlated with systolic blood pressure (r = 0.03; p = 0.01) and diastolic blood pressure (r = 0.02; p = 0.02) (Figure 2). Figure 3 shows a significant positive correlation between systolic blood pressure and 24-hr urinary sodium excretion after being classified into 5 quintiles (<114, 114-145, 146-174, 175-230, and > 230 mmol/day), (p = 0.03), and the prevalence of hypertension were 21%, 19%, 20%, 32%, and 34%, respectively. There was a significant increase in
the prevalence of hypertension when urinary sodium excretion was greater than 175 mmol/day \( (p = 0.005) \), indicating a threshold effect of urinary sodium excretion on the incidence of hypertension.

Multiple logistic regression analysis using hypertension as the dependent variable (Table 2) showed that the risk factors that had a statistically significant association with hypertension \( (P \text{ value} < 0.05) \) were age \( \text{Odds ratio} = 1.100, \text{95\% confidence interval} = 1.041 – 1.613 \) and 24-hour urinary sodium excretion more than 175 mmol/day \( \text{Odds ratio} = 2.028, \text{95\% confidence interval} = 1.262 – 3.259 \). No evidence of an association with hypertension was demonstrated for BMI and gender.

After adjusting for the relationship between spot and 24-hour urinary sodium excretion by linear regression analysis (Figure 4), no correlation between these factors was observed \( (r = 0.021, P = 0.547) \). The spot urinary sodium excretion was slightly positively correlated with systolic blood pressure \( (r = 0.03, P = 0.045) \), however, there was no correlation between spot urinary sodium and diastolic blood pressure \( (r = 0.02, P = 0.103) \) (Figure 5).

Discussion

The EGAT employees are urban-middle class, well educated, and not representative of the overall Thai population; thus the prevalence of this study is unlikely to be generalized to the Thai nation as a whole. Nevertheless, it can be applied to subgroups of similar socioeconomic

Figure 3. Relationship between systolic blood pressure and 24-hour urinary sodium excretion.

Figure 4. Linear regression between spot and 24-hour urinary sodium excretion

Figure 5. Linear regression between blood pressure and spot urinary sodium excretion
status. The prevalence of hypertension in this population may be higher than that in the general population, because of the higher age-standardization compared to the 2008 National Health Examination, where the prevalence of HT was reported in all age groups to be 21.4%. Because our group had a higher age-standard and the selection bias of the 24-hour urine specimen collection from the volunteers who tended to be more concerned with their health, probably led to an overestimation of the prevalence of hypertension.

The level of systolic blood pressure was slightly different (4 mmHg) between the group that had a urinary sodium excretion less and more than 175 mmol/day (Figure 4). However there was a significant increase in the prevalence of hypertension in the group with a 24-hour urinary excretion more than 175 mmol, which may result from the major populations in the hypertensive group (60%) having good blood pressure control (blood pressure < 140/90 mmHg) from blood pressure lowering therapy.

Previous studies reported a method of estimating 24-hour urinary sodium excretion from a second morning urine void collection (20,21) and in another study a spot urine specimen collection was done anytime (22). The correlation between the estimated value and measured value for spot urine collection is high when urine accumulated is from 8.00 am to 12.00 am, and the correlation is low when using night urine (23). However, there was no correlation between spot urine specimen collected from the first morning voided urine and 24-hour urinary sodium excretion in our study.

The significant positive correlation between 24-hr urinary sodium excretion and the level of systolic and diastolic blood pressures from our study are also confirmed in previous studies (1-6,13-15); nonetheless, this is the first study to demonstrate this correlation in a selected Thai population. Furthermore, there was a significant increase in the prevalence of hypertension when urinary sodium excretion was greater than 175 mmol/day, indicating a threshold effect of urinary sodium excretion on the prevalence of hypertension, which has never been demonstrated in previous studies.

Form prior studies (1-6,13-15) and our study it has been demonstrated that there is a variation in the prevalence of hypertension and 24-hour urinary sodium excretion among populations. The difference of a relationship between the level of 24-hour urinary sodium excretion and the prevalence of HT, may result from multifactorial factors such as a neurohormonal effect, dietary culture, commercial food processing, individualistic additive salt intake, and a genetic response to salt-sensitivity. For Thai population we have shown preliminary data of salt intake and blood pressure response and these data will be applied to a cohort study in the future.

Finally, we agree with the WHO recommendation in the restriction of salt consumption to reduce hypertension; however in the Thai population there is still no definite data as to the exact amount of salt restriction. We suggested the level of 175 mmol/day or 10 grams of dietary salt intake is the threshold effect on the prevalence of hypertension. The cutoff point for the Thai population in the restriction of salt consumption from our study may be higher than the WHO recommendation.

Conclusion

There was a significant correlation between blood pressure, both systolic and diastolic, and 24-hour urinary sodium excretion. Both age and the level of 24-hour urinary sodium excretion more than 175 mmol were independent risk factors for hypertension. A threshold level of urinary sodium excretion for hypertension was found in this population group.

Acknowledgement

The study was supported by Mahidol University Grant, No 230. The contribution of the EGAT staff for this study was highly appreciated.

Conflict of Interest

None

References


การศึกษาเพื่อหาปริมาณของโซเดียมในปัสสาวะที่เก็บภายใน 24 ชั่วโมง (24-hour urinary sodium excretion) ที่มีผลต่อความขุ่นของภาวะความดันโลหิตสูง (prevalence of hypertension)

อรวรรณ อนุประวัฒน, สมนึก คณภิญโญ, สุกิจ แย้มวงษ์, ศุภชัย ถนอมทรัพย์, ปปัญมิตร ศรีธรา

บทคัดย่อ:
วัตถุประสงค์: จากการศึกษาที่ผ่านมาพบว่าปริมาณของโซเดียมในปัสสาวะที่เก็บภายใน 24 ชั่วโมง (24-hour urinary sodium excretion) มีความสัมพันธ์กับระดับของความดันโลหิต อย่างไรก็ตามความสัมพันธ์ดังกล่าวมีความแตกต่างกันในแต่ละประชากร จึงเป็นที่มาของการศึกษานี้เพื่อหาความสัมพันธ์ระหว่าง 24-hour urinary sodium excretion, ความดันโลหิต, และความชุกของภาวะความดันโลหิตสูง (prevalence of hypertension) ในประชากรไทย

วิธีการศึกษา: ทำการศึกษาในพนักงานการไฟฟ้าฝ่ายผลิต 415 คน ระหว่าง พฤศจิกายน - กรกฎาคม 2551, อายุเฉลี่ย 52 ± 4 ปี, เพศชายเท่าๆกับ 64 หลังจากผู้เข้าร่วมการศึกษาตอบแบบสอบถามจะได้รับ การตรวจร่างกาย และเก็บปัสสาวะ 24 ชั่วโมงเพื่อหาความสัมพันธ์ระหว่างปริมาณของโซเดียมในปัสสาวะกับความดันโลหิต

ผลการศึกษา: พบว่ามีความขุ่นของภาวะความดันโลหิตสูงร้อยละ 24.6, ในกลุ่มที่มีภาวะความดันโลหิตสูงมี mean systolic blood pressure สูงกว่ากลุ่มที่ไม่มีภาวะความดันโลหิตสูง (137 ± 16 versus 116 ± 11 mmHg) และปริมาณของ 24-hour urinary sodium excretion นั้นมีระดับสูงกว่าในกลุ่มที่มีภาวะความดันโลหิตสูงเมื่อเทียบกับกลุ่มที่ไม่มีภาวะความดันโลหิตสูง (Median = 179 interquartile range 107 versus 155 interquartile range 82 mmol/day; P = 0.03) และพบความสัมพันธ์ระหว่างปริมาณของโซเดียมในปัสสาวะกับ systolic blood pressure (r = 0.03; P = 0.01) และ diastolic blood pressure (r = 0.02; P = 0.02) ที่สูงขึ้น, หลังจากแบ่ง 24-hour urinary sodium excretion ออกเป็น 5 กลุ่ม (<114, 114-145, 146-174, 175-230, and > 230 mmol/day) พบว่ามีความขุ่นของภาวะความดันโลหิตสูงร้อยละ 21, 19, 20, 32, และ 34 ตามลำดับและในกลุ่มที่มีปริมาณ 24-hour urinary sodium excretion มากกว่า 175 mmol พบว่ามีความขุ่นของภาวะความดันโลหิตสูงเพิ่มขึ้นอย่างมีนัยสำคัญ, อายุ (OR = 1.100, 95% CI = 1.041-1.613) และ 24-hour urinary sodium excretion มากกว่า 175 mmol (OR = 2.028, 95% CI = 1.262-3.259) เป็นปัจจัยเสี่ยงของการเกิดภาวะความดันโลหิตสูง

สรุป: 24-hour urinary sodium excretion ที่สูงขึ้นมีผลต่อการเกิดภาวะ systolic และ diastolic blood pressure, เพศ และ 24-hour urinary sodium excretion มากกว่า 175 mmol เป็นปัจจัยเสี่ยงของการเกิดภาวะความดันโลหิตสูง นอกจากนี้ยังพบว่าระดับของ 24-hour urinary sodium excretion มากกว่า 175 mmol มีผลต่อการเพิ่มขึ้นของความขุ่นของความดันโลหิตสูง

คำสำคัญ: ปริมาณของโซเดียมในปัสสาวะที่เก็บภายใน 24 ชั่วโมง, ความดันโลหิตสูง