Effect of Salt Intake on Renal Excretion of Water in Humans

Feng J. He, Nirmala D. Markandu, Giuseppe A. Sagnella, Graham A. MacGregor

Abstract—Two studies were performed to determine the quantitative relationship between salt intake and urinary volume (\(U_v\)) in humans. In study 1, 104 untreated hypertensives were studied on the fifth day of a high- and a low-salt diet. The 24-hour \(U_v\) was 2.2 L (urinary sodium \([U_{Na}]\) 277 mmol) on the high-salt diet and decreased to 1.3 L (\(P<0.001\)) \([U_{Na}]\) 20.8 mmol) on the low-salt diet. The reduction in 24-hour \(U_v\) was significantly related to the decrease in 24-hour \([U_{Na}]\) \((P<0.001)\) and predicts that a 100-mmol/d reduction in salt intake would decrease 24-hour \(U_v\) by 367 mL. In study 2, 634 untreated hypertensives were studied on their usual diet. There was a significant relationship between 24-hour \(U_v\) and \([U_{Na}]\) \((P<0.001)\). This predicts that a 100-mmol/d reduction in salt intake would decrease 24-hour \(U_v\) by 454 mL. The International Study of Salt and Blood Pressure (INTERSALT) of 1731 hypertensives and 8343 normotensives on their usual diet showed that 24-hour \(U_v\) was significantly related to \([U_{Na}]\) \((P<0.001)\) and predicted that a 100-mmol/d reduction in salt intake would decrease 24-hour \(U_v\) by 379 and 399 mL in hypertensives and normotensives, respectively. These findings document the important effect that salt intake has on \(U_v\). The recommended reduction in salt intake in the general population is from 10 to 5 g/d. This would reduce fluid intake in the population by \(\approx350\) mL/d per person. This would have a large impact on the sales of soft drinks, mineral water, and beer. (Hypertension. 2001;38:317-320.)

Key Words: sodium, dietary ■ urinary volume ■ human

There is much evidence that salt intake plays an important role in regulating blood pressure.\(^1\) However, there is little evidence about the relationship between salt intake and urinary volume (\(U_v\)). Studies in animals have shown that a high salt intake significantly increases renal excretion of water due to increased water intake,\(^4\) whereas in humans, the extent to which salt intake determines \(U_v\) is not clear. We therefore performed 2 analyses to compare the relationship between salt intake and \(U_v\) in patients with essential hypertension. In the first study, dietary salt intake was deliberately altered from a high- to a low-salt diet to document the change in \(U_v\), with a defined change in salt intake. In the second study, patients were studied on their usual diet to document the relationship between usual salt intake and \(U_v\).

The International Study of Salt and Blood Pressure (INTERSALT) Cooperative Research Group kindly provided us with data on \(U_v\) and urinary sodium \([U_{Na}]\) to allow us to compare our findings with a much larger group of people from different parts of the world with both normal and raised blood pressure.

Methods

Study 1: Experimental Study

One hundred four patients with essential hypertension who had not had previous treatment or in whom treatment had been stopped for at least 3 months were studied on the fifth day of high salt intake of \(\approx350\) mmol/d and then on the fifth day of a low salt intake of 10 to 20 mmol/d. There was no washout period between the 2 diets. There were 48 men (33 white, 15 black) and 56 women (38 white, 18 black). Mean age was 48 years (range, 19 to 70 years). A high salt intake was achieved by supplementing their usual diet with 20 Slow Sodium tablets (200 mmol/d). The low-salt diet was provided by the metabolic unit kitchen under the supervision of the metabolic dietitian. The potassium, protein, and calorie intakes were not altered for either diet. Subjects were permitted free access to fluid. Two 24-hour urine samples were collected during the last 2 days of each dietary period for measurement of volume, sodium, potassium, and creatinine. Blood was also taken at the end of each dietary period for measurement of electrolytes, creatinine, plasma renin activity,\(^10\) and aldosterone.\(^11\) Blood pressure was measured in the same arm by nurses using semiautomatic ultrasound sphygmomanometers with attached recorders (Arteriosonde). Blood pressure was the mean of 5 readings taken at 1- to 2-minute intervals. All subjects gave informed consent. The study was approved by the local hospital ethics committee.

Study 2: Cross-Sectional Observational Study

Six hundred thirty-four patients with essential hypertension were studied on their usual diet and were instructed to collect a 24-hour urine sample for measurement of volume, sodium, potassium, and creatinine. There were 328 men (170 white, 88 black, 33 Asian) and 304 women (165 white, 61 black, 28 Asian). In 2 subjects gender was not recorded, and in 89 subjects ethnic group was not clear. Mean age was 47 years (range, 19 to 87 years). Patients had not received previous treatment or treatment had been stopped for at least 3 months.

All patients were carefully instructed both orally and by printed instructions on how to accurately collect a 2-hour urine sample and were carefully supervised by the Blood Pressure Unit research nurses.

Received December 8, 2000; first decision January 19, 2001; revision accepted February 23, 2001.

From the Blood Pressure Unit, St George’s Hospital Medical School, London, United Kingdom.

Correspondence to Professor G.A. MacGregor, Blood Pressure Unit, St George’s Hospital Medical School, Cranmer Terrace, London, SW17 0RE, UK.

E-mail g.macgregor@sghms.ac.uk

© 2001 American Heart Association, Inc.

Hypertension is available at http://www.hypertensionaha.org
## Statistical Analysis

Results are reported as mean±SEM. Differences in 24-hour Ur, and other variables between the high- and low-salt diets were analyzed by paired t tests. Multiple regression was used to examine the association of 24-hour Ur, and UrNa with adjustment for potential confounders. All statistical analyses were performed by the Statistical Package for the Social Sciences (SPSS).

## Results

### Experimental Study

The Table shows the results obtained on the final day of the usual diet, on the fifth day of high salt intake, and on the fifth day of low salt intake. Because the study was designed to determine the changes from high to low salt intake, we used a paired t test to compare the difference between the 2 salt intakes.

From the high- to the low-salt diet, there was a reduction of 0.9±0.09 L/24 h (P<0.001) in Ur, with a decrease of 256.2±11.9 mmol/24 h (P<0.001) in UrNa excretion (Figure 1). The reduction in 24-hour Ur, from the high- to the low-salt diet was significantly correlated with the decrease in 24-hour UrNa (r=0.496, P<0.001). On average, Ur decreases by 367 mL for a 100-mmol reduction in salt intake (Figure 2). The relationship between 24-hour Ur, and UrNa remained significant when adjusted for age, gender, race, changes in body weight, mean arterial pressure, urinary potassium, and urinary creatinine excretion (r=0.58, P<0.001). The effect of the adjustment for these variables was to change the estimate of the decrease in Ur per 100-mmol reduction in salt intake from 367 to 452 mL.

From the fifth day of high salt intake to the fifth day of low-salt diet, there was a reduction of 1.82 kg (P<0.001) in body weight, an increase of 1.92 ng/mL per hour (P<0.001) in plasma renin activity, and an increase of 423.3 pmol/L (P<0.001) in plasma aldosterone. All of these changes would suggest sodium and volume loss with salt restriction.

### Cross-Sectional Observational Study

In the 634 hypertensive patients studied on their usual salt intake, the average 24-hour Ur, was 1.77±0.03 L, with a 24-hour UrNa of 143±2.7 mmol. There was a highly significant positive correlation between 24-hour Ur, and 24-hour UrNa (r=0.38, P<0.001). For a reduction of 100 mmol/d in salt intake, this predicted a reduction in 24-hour Ur, of 454 mL (Figure 3). The relationship between 24-hour Ur, and UrNa remained significant after adjustment for age, gender, race, body weight, mean arterial pressure, and urinary potassium and creatinine excretion (r=0.26, P<0.001; n=540). The effect of the adjustment for these variables was to change the estimate of the decrease in Ur, per 100-mmol reduction in salt intake from 454 to 345 mL.

---

### Table: Urine, Blood Pressure, and Other Laboratory Data on Usual Diet and Different Salt Intake in the Experimental Study

<table>
<thead>
<tr>
<th>Variables</th>
<th>Usual Diet</th>
<th>High-Salt Diet</th>
<th>Low-Salt Diet</th>
<th>Difference Between High- and Low-Salt Diets</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Urine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume, L</td>
<td>1.6±0.05</td>
<td>2.2±0.09</td>
<td>1.3±0.05</td>
<td>−0.9†</td>
</tr>
<tr>
<td>Sodium, mmol/24 h</td>
<td>146.9±4.6</td>
<td>277.0±11.6</td>
<td>20.8±1.3</td>
<td>−256.2†</td>
</tr>
<tr>
<td>Potassium, mmol/24 h</td>
<td>61.0±2.1</td>
<td>57.3±1.9</td>
<td>46.6±1.3</td>
<td>−10.6†</td>
</tr>
<tr>
<td>Creatinine, mmol/24 h</td>
<td>10.6±0.6</td>
<td>11.4±1.3</td>
<td>10.4±0.5</td>
<td>−1.0</td>
</tr>
<tr>
<td><strong>Plasma</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium, mmol/L</td>
<td>139.4±0.2</td>
<td>140.5±0.2</td>
<td>137.6±0.3</td>
<td>−2.89†</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>4.0±0.04</td>
<td>3.8±0.04</td>
<td>3.9±0.04</td>
<td>0.1*</td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>84.5±1.6</td>
<td>83.7±1.7</td>
<td>93.3±1.9</td>
<td>9.64†</td>
</tr>
<tr>
<td>Renin activity, ng·mL⁻¹·h⁻¹</td>
<td>0.89±0.07</td>
<td>0.54±0.05</td>
<td>2.47±0.22</td>
<td>1.92†</td>
</tr>
<tr>
<td>Aldosterone, pmol/L</td>
<td>428.4±24.7</td>
<td>316.3±19.2</td>
<td>739.6±52.3</td>
<td>423.3†</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>73.3±1.3</td>
<td>73.9±1.3</td>
<td>72.0±1.3</td>
<td>−1.82†</td>
</tr>
<tr>
<td><strong>Supine blood pressure, mm Hg</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>175±2</td>
<td>173±2</td>
<td>155±2</td>
<td>−18†</td>
</tr>
<tr>
<td>Diastolic</td>
<td>110±1</td>
<td>109±1</td>
<td>102±1</td>
<td>−7†</td>
</tr>
</tbody>
</table>

*P<0.05; †P<0.001, low-salt vs high-salt diet.

---

**Figure 1.** Ur, and UrNa on high- and low-salt diets in the experimental study. *P<0.001, low-salt vs high-salt diet.
Comparison Between the Experimental and Cross-Sectional Observational Studies

To compare the quantitative relationship of salt intake and $U_v$ between the cross-sectional observational study and the experimental study, we plotted the change in $U_v$ against the change in $U_{Na}$ from the experimental study and superimposed the data of the observational study. Figure 4 shows that the age- and gender-adjusted slopes were very similar in the 2 studies. A change of 100 mmol/d in salt intake predicted a change of 24-hour $U_v$ of 367 mL in the experimental study and 454 mL in the cross-sectional study. After adjustment for age and gender, these estimates changed to 357 and 462 mL in the experimental and cross-sectional studies, respectively.

Discussion

In the experimental study, in which salt intake was deliberately decreased from a high- to a low-salt diet, there was a reduction in $U_v$. The relationship between salt intake and $U_v$, found in this study was similar to that found in a larger group of patients studied on their usual salt intake. Therefore, our results demonstrate that salt intake is a major factor in controlling $U_v$ in patients with essential hypertension when on their usual salt intake.

The INTERSALT study, which made careful standardized measurements of 24-hour urinary collections to assess both sodium excretion and volume, included 1731 hypertensive patients (systolic blood pressure $\geq$140 mm Hg or diastolic blood pressure $\geq$90 mm Hg or on treatment for high blood pressure) and 8343 nonhypertensive persons from 52 centers around the world. In a within-sample analysis, $U_v$ was significantly related to $U_{Na}$. Importantly, the relationship between $U_{Na}$ and $U_v$ was very similar between hypertensives and nonhypertensives. A reduction of 100 mmol/d in salt intake predicted a reduction in 24-hour $U_v$ of 379 mL ($P<0.001$) in hypertensive patients and 399 mL ($P<0.001$) in nonhypertensive persons (adjusted for age and gender). After further adjustment for body mass index, systolic blood pressure, alcohol intake, urinary potassium, creatinine, calcium, magnesium, and nitrogen excretion, there was still a significant relation between $U_v$ and $U_{Na}$. The adjustment of these variables changed the estimate of the decrease in $U_v$ per 100-mmol reduction in salt intake from 379 to 334 mL in hypertensive patients ($n=1720$) and from 399 to 339 mL in nonhypertensive persons ($n=8300$) (data not corrected for regression dilution bias). In a random sample of 805 men and women who had a repeated 24-hour urinary specimen collected, the difference in $U_v$ was significantly correlated with the difference in $U_{Na}$ ($r=0.612$, $P<0.001$). A change of 100 mmol in salt intake predicted a change of 466 mL in $U_v$.

When the results from the INTERSALT study were superimposed on our own results, it gave a similar regression line (Figure 4). The consistent results between our experimental, observational study and the INTERSALT study demonstrate that salt intake is an important factor in controlling $U_v$ not only in hypertensive patients but also in normotensive persons.

Guyton et al. in 1974, proposed that renal function curve and $U_v$ load (the rate of fluid intake minus the rate of nonrenal fluid loss) were 2 primary determinants of arterial blood pressure, and it has been suggested that fluid intake per se may play a role in regulating blood pressure. However, a study in humans with short-term but large changes in water intake showed no effect on blood pressure, whereas changing salt intake had a significant effect on blood pressure. These results in conjunction with the results of our present

**Figure 2.** Relationship between change in $U_v$ and decrease in $U_{Na}$ excretion on high- and low-salt diets in the experimental study.

**Figure 3.** Relationship between $U_v$ and $U_{Na}$ excretion in hypertensive patients on their usual diet in the cross-sectional observational study.

**Figure 4.** Relationship between difference in $U_v$ and decrease in $U_{Na}$ excretion (adjusted for age and gender) in the experimental, cross-sectional, and INTERSALT (within-sample analysis in 10,074 men and women) study.
study strongly suggest that any relationship between fluid intake, UI, and blood pressure is due to the differences in salt intake, which affect both blood pressure and UI.

Our findings when the salt intake was deliberately changed are in agreement with studies in animals. However, a study in healthy young men (age 19 to 32 years) did not show a significant change in UI, or in water intake when dietary salt intake was altered from 20 to 400 mmol/d. It is difficult to explain these findings, but they may be due to the relatively small sample size (24 men) and a large fluid intake at baseline (≈2 L/d). Although there was no significant change in UI, or water intake in this small study, there was a graded increase in body weight with the increase in salt intake, indicating sodium and volume retention.

One potential bias of the cross-sectional observational study is incomplete collection of urine or overcollection of urine. If a 24-hour urine collection is incomplete, both the 24-hour volume and the 24-hour sodium will be low, but the proportionate relationship between them will not be seriously affected. However, in the experimental study the 24-hour urinary creatinine excretion was similar on the high and low salt diets, indicating that the difference in UI was due to changes in salt intake and not due to differences in urine collection between the 2 diets. The cross-sectional observational study showed a very similar relation between UNa and urine collection between the 2 diets. The cross-sectional observational study strongly suggest that any relationship between salt intake and UI, is incomplete collection of urine or overcollection of urine.

Another confounding factor is vigorous exercise or a hot environment, which would cause water loss through sweating. In our study very few of the hypertensive patients were participating in vigorous exercise, and only a small proportion of patients were studied during the English summer.

It was not the purpose of our study to investigate the mechanism of the relationship between salt intake and UI, although, as expected, when salt intake was increased there was an increase in plasma sodium and an increase in plasma osmolality, which is known to stimulate thirst and antidiuretic hormone secretion. This increase in fluid intake will reduce plasma osmolality and will increase UI.

These studies demonstrate that in humans on their usual diet, the greater the salt intake, the greater the renal excretion of water. When salt intake is decreased from a high- to a low-sodium diet, there is a fall in UI, similar to that seen between different individuals on different salt intakes. These results clearly demonstrate that salt intake is a major factor in controlling UI, and therefore fluid intake.

Most western countries have now recommended that salt intake should be reduced from the current average of ≈10 to 5 g/d. This would reduce fluid intake in the whole population by ≈350 mL/d per person. Approximately 25% of fluid intake in the United Kingdom is in the form of soft drinks. This reduction in salt intake would reduce soft drink sales by ≈13 million soft drinks per day, which is 5 billion soft drink sales per year. In the United States these figures are larger, and a similar reduction in salt intake would reduce soft drink consumption by ≈40 billion soft drinks per year. Some soft drink companies own large snack companies that specialize in highly salted snacks. Some of these companies have been preeminent in trying to create an artificial controversy doubting the relationship between salt intake and blood pressure, presumably in the hope of stopping or slowing down any reduction in population salt intake to protect soft drink sales.

Acknowledgments

The analyses of the within-population INTERSALT data were kindly provided by Caroline Terrill (Imperial College, London) on behalf of the INTERSALT Cooperative Group. We thank Prof P. Elliott, Prof J. Stamler, and Prof A. Dyer for their support and helpful comments in preparing the manuscript. We also thank Dr C.G. Missouri and Dr M.B. Papavassiliou for their help in collecting the data.

References

Effect of Salt Intake on Renal Excretion of Water in Humans
Feng J. He, Nirmala D. Markandu, Giuseppe A. Sagnella and Graham A. MacGregor

Hypertension. 2001;38:317-320
doi: 10.1161/01.HYP.38.3.317

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/38/3/317

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located,
click Request Permissions in the middle column of the Web page under Services. Further information about
this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/