ORIGINAL ARTICLE

The influence of posture on the estimation of daily salt intake by the second morning urine method

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The second morning urine (SMU) method was developed to evaluate daily salt intake, but the posture that should be adopted until the SMU collection remains unclear. This study investigated the influence of posture in hypertensive patients who underwent this test. The subjects were 100 patients who could collect 24-h urine samples correctly and were on a diet containing 7 g of salt per day. Their daily salt intake was estimated for three consecutive days in the recumbent, sitting, and sitting and standing positions (one posture each day). Estimated salt intake in the recumbent position ($10.9 \pm 2.4 \text{ g day}^{-1}$) was higher than in the sitting position ($7.5 \pm 2.0 \text{ g day}^{-1}$) and the sitting and standing position ($6.3 \pm 1.7 \text{ g day}^{-1}$). The salt intake estimated in the sitting and standing position was similar to that obtained by 24-h urine collection ($6.3 \pm 1.6 \text{ g day}^{-1}$) and was significantly ($r=0.44$, $P<0.05$) correlated with the 24-h urine value. The actual difference in estimated salt intake between the two methods was $0.0 \pm 1.7 \text{ g day}^{-1}$. There were no significant differences in estimated salt intake between the two methods in patients taking different classes of antihypertensive drugs. In conclusion, adopting the sitting and standing position until the SMU collection is important for the correct estimation of daily salt intake, and this method could replace the 24-h collection method because of its convenience, especially in outpatients.

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INTRODUCTION

Guidelines for the management of hypertension from various countries,^{1,2} including Japan,³ recommend the restriction of salt intake as an important dietary modification to lower blood pressure. The INTERSALT study⁴ estimated salt intake by 24-h urine collection at 52 centers in 32 countries and showed that the mean daily salt intake was 9.2 g whereas the average value obtained from three Japanese centers was 11.0 g, suggesting that the Japanese have a higher than average salt intake. Residents of Morioka in the Tohoku District of Japan have an even higher salt intake with a mean daily salt intake of approximately 13 g.^{5–7} This markedly exceeds the daily intake recommended by the Japanese guideline ($<6 \text{ g}$),³ and salt restriction is especially important in areas with high salt intake, such as Morioka. Although the estimation of daily salt intake is important to provide appropriate advice about salt restriction, estimation by interview, the diary method, or 24-h urine collection is inconvenient for general use.⁸ In fact, a survey showed that 88% of general physicians did not estimate the daily salt intake of hypertensive patients attending their outpatient clinics.⁹ Kawasaki *et al.*¹⁰ developed the second morning urine (SMU) method to evaluate daily salt intake from the second urine specimen collected in the morning before breakfast. This method is based on the assumption that 24-h creatinine excretion can be predicted from demographic factors (sex, age, height and body weight), and the sodium:creatinine ratio of the 24-h urine specimen is

proportional to that of the SMU specimen. Accordingly, the 24-h sodium excretion is calculated as the sodium:creatinine ratio of the SMU specimen multiplied by the predicted 24-h creatinine excretion. Daily sodium excretion values obtained by the SMU method show a strong correlation with those estimated by the 24-h collection ($R=0.73$). The usefulness of the SMU method has been confirmed in population studies^{5,11,12} and in hypertensive patients.¹³ Although the posture that should be adopted for the SMU method was not specified by the original authors,¹⁰ posture is known to affect the urinary sodium:creatinine ratio^{14,15} and could possibly influence the estimation of daily salt intake by this method. Therefore, this study was designed to assess the effect of posture on the estimation of daily salt intake by the SMU method compared with the method of 24-h collection in hospitalized patients with hypertension on a salt-restricted diet.

METHODS

Subjects

We recruited patients with hypertension who were undergoing lifestyle modification (diet and exercise) as inpatients of our hospital. A total of 116 patients satisfied the following three criteria. First, they were assessed at our clinic during a 2-month period before admission, undergoing blood pressure measurements and laboratory tests. Second, their dietary salt intake was limited to 7 g daily during admission to the hospital. Third, sodium and creatinine

excretion were measured by 24-h urine collection at the end of the first hospital week. Approval for the study was granted by the ethics committee of the Iwate Prefectural Central Hospital. All subjects were given detailed information about the protocol before they agreed to enroll, and written consent was obtained in all cases.

Procedures

Before admission to the hospital, the blood pressure of each subject was measured at our outpatient clinic on at least three occasions, and blood and urine samples were collected before breakfast on at least one occasion. Figure 1 shows the protocol used to assess the validity of the SMU method. During hospital admission, patients were placed on a daily diet of 7 g of salt. Their daily salt intake was assessed by 24-h urine collection at the end of the first hospital week, as equilibration of the sodium balance requires approximately 1 week.¹⁶ On three consecutive days during the second week of admission, each patient arose at 0600 h and discarded the first voided urine. Then, the second voided urine was collected before breakfast at 0800 h. Until the second voiding after awakening, patients remained in the recumbent position on the first day, in the sitting position on the second day, and in the sitting and standing position (both sitting and standing equally) on the third day. In the standing position, subjects were allowed to walk but not run. A 24-h urine collection was carried out with an Automatic Urine Collection System (PZ-50AZ; Koken, Tokyo) that allows fractional urine sampling. During admission, patients were advised to only adhere to the hospital diet and eat nothing else. Water and weak Japanese tea were available to drink *ad libitum*.

Measurements and calculations

Using the second voiding urine specimen, daily sodium excretion was measured by the SMU method,¹⁰ which utilizes the patient's gender, age, body weight, height, and the sodium and creatinine concentrations of the urine sample. As approximately 90% of a person's sodium intake is excreted in the urine,¹⁷ daily sodium excretion was considered to be equal to daily salt intake and was expressed as grams of sodium chloride (NaCl) per day as suggested by the Japanese guideline.³ The formula for estimating the salt intake (grams of NaCl per day) was $0.96 \times ((\text{UNa}/\text{UCr}/10) \times \text{predicted daily creatinine excretion})^{0.5}$, where UNa is the urinary sodium concentration (mEq l^{-1}), and UCr is the urinary creatinine concentration ($\text{mg } 100 \text{ ml}^{-1}$).

The formula¹⁸ for estimating daily creatinine excretion from demographic data was $15.1 \times \text{body weight (kg)} + 7.4 \times \text{height (cm)} - 12.6 \times \text{age (years)} - 79.9$ for men and $8.6 \times \text{body weight (kg)} + 5.1 \times \text{height (cm)} - 4.7 \times \text{age (years)} - 75.0$ for women. The 24-h urine specimen was also used to calculate the daily excretion of sodium and creatinine. The albumin concentration of each urine specimen was measured by SRL Laboratories (Tokyo, Japan). Hypertension, diabetes and dyslipidemia were diagnosed according to the Japanese guidelines for hypertension,³ diabetes¹⁹ and atherosclerosis.²⁰ Blood pressure was defined as the mean of the values obtained at the last two clinic appointments. Subjects who were already on antihypertensive medications were classified as having hypertension regardless of their actual blood pressure. When the calculated creatinine

excretion was outside $\pm 30\%$ of the predicted creatinine excretion, patients were considered to have performed the urine collection incorrectly.²¹ A total of 16 patients had creatinine excretion values that were more than 30% below the predicted value, and these patients were excluded. Accordingly, 100 patients were subjected to further analysis.

Statistical methods

Results are expressed as mean $\pm$ s.d. The χ^2 -test was used for the comparison of diabetes mellitus, dyslipidemia and administration (none, monotherapy and combination therapy) of antihypertensive drugs between men and women. Differences in other parameters between men and women were analyzed by the Mann-Whitney *U*-test. Differences between the three postures (recumbent, sitting, and sitting and standing) and differences between the SMU and 24-h urine data were analyzed by Wilcoxon's signed rank test. Correlations between the SMU and 24-h data were assessed by univariate analysis. In all analyses, a probability (*P*) value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics of men and women in this study are presented in Table 1. Body weight, hemoglobin A_{1c} and serum creatinine were significantly higher in men than women whereas high-density lipoprotein cholesterol was significantly higher in women. The effect of posture on the estimation of salt intake from the second urine collection by the SMU method is shown in Table 2. For all 100 patients, the estimated salt intake was $10.9 \pm 2.4 \text{ g day}^{-1}$ in the recumbent position, $7.5 \pm 2.0 \text{ g day}^{-1}$ in the sitting position, and $6.3 \pm 1.7 \text{ g day}^{-1}$ in the sitting and standing position. It was found that assessment in the recumbent position led to the highest estimated salt intake, followed by assessment in the sitting position and then the sitting and standing position in both men and women. The estimated salt intake in the sitting and standing position was similar to that obtained from the 24-h urine collection ($6.6 \pm 1.5 \text{ g day}^{-1}$ for men, $6.0 \pm 1.6 \text{ g day}^{-1}$ for women, and $6.3 \pm 1.6 \text{ g day}^{-1}$ for all patients). Figure 2 shows that the estimated salt intake obtained by 24-h urine collection was not significantly different from that estimated by the SMU method in the sitting and standing position but was significantly lower than that obtained in the sitting position or the recumbent position for both men and women. As there were no significant differences between men and women with regard to the estimated salt

Figure 1 Protocol for assessing the validity of the second morning urine (SMU) method.

Table 1 Baseline characteristics of the patients

Variable	Men	Women
Number	53	47
Age (years)	58 $\pm$ 14	61 $\pm$ 12
Body weight (kg)	69.2 $\pm$ 12.5	58.7 $\pm$ 12.9*
Body mass index (kg m^{-2})	24.8 $\pm$ 3.8	25.2 $\pm$ 5.1
Systolic blood pressure (mm Hg)	143 $\pm$ 14	144 $\pm$ 14
Diastolic blood pressure (mm Hg)	83 $\pm$ 10	81 $\pm$ 9
Hemoglobin A _{1c} (%)	8.1 $\pm$ 1.8	7.3 $\pm$ 2.0*
Low-density lipoprotein cholesterol ($\text{mg } 100 \text{ ml}^{-1}$)	116 $\pm$ 31	121 $\pm$ 31
High-density lipoprotein cholesterol ($\text{mg } 100 \text{ ml}^{-1}$)	46 $\pm$ 15	56 $\pm$ 17*
Triglycerides ($\text{mg } 100 \text{ ml}^{-1}$)	116 $\pm$ 31	119 $\pm$ 64
Creatinine ($\text{mg } 100 \text{ ml}^{-1}$)	0.85 $\pm$ 0.24	0.57 $\pm$ 0.19*
Urinary albumin (mg g^{-1} creatinine)	100 $\pm$ 229	101 $\pm$ 210
Diabetes mellitus, number (%)	44 (83)	28 (88)
Dyslipidemia, number (%)	37 (70)	18 (56)
Antihypertensive drugs		
None, number (%)	13 (25)	9 (19)
Monotherapy, number (%)	24 (45)	21 (45)
Combination therapy, number (%)	16 (30)	17 (36)

**P* < 0.05 compared with men by the Mann-Whitney *U*-test.

Table 2 Influence of posture on the estimated daily salt intake obtained by the second morning urine method

Sex	Parameter	Recumbent position	Sitting position	Sitting and standing position
Men	Sodium (mEq l ⁻¹)	83.1 ± 36.2*,**	75.7 ± 35.7*	66.2 ± 25.7
	Creatinine (mg 100 ml ⁻¹)	110.2 ± 62.3*,**	194.1 ± 98.4*	242.3 ± 104.4
	Sodium:creatinine (mEq mg ⁻¹)	92.4 ± 50.4*,**	47.2 ± 29.3*	33.6 ± 22.1
	Intake (g day ⁻¹)	10.4 ± 2.5*,**	7.5 ± 2.0*	6.2 ± 1.7
Women	Sodium (mEq l ⁻¹)	86.3 ± 40.8*,**	76.2 ± 28.6*	72.3 ± 25.6
	Creatinine (mg 100 ml ⁻¹)	59.3 ± 32.0*,**	130.4 ± 61.9*	157.8 ± 40.1
	Sodium:creatinine (mEq mg ⁻¹)	163.4 ± 70.7*,**	71.3 ± 37.3*	53.6 ± 28.3
	Intake (g day ⁻¹)	11.4 ± 2.3*,**	7.4 ± 2.1*	6.5 ± 1.7

Sodium and creatinine are expressed as concentrations of second voided urine samples for measurements of daily salt intake.

Salt intake is expressed as g of NaCl per day. * $P < 0.05$ vs. sitting and standing, ** $P < 0.05$ vs. sitting by the Wilcoxon signed-rank test.

Figure 2 Comparison of salt intake estimated by the second morning urine (SMU) method with various postures and the 24-h urine collection method in men (open columns) and women (closed columns). * $P < 0.05$ vs. 24-h urine in men, # $P < 0.05$ versus 24-h urine in women by the Wilcoxon signed-rank test.

intake obtained by the SMU method with any posture or by 24-h collection, we carried out further data analysis for men and women combined. The predicted creatinine excretion showed a strong correlation ($r=0.92$, $P < 0.01$) with the creatinine excretion measured by 24-h urine collection (Figure 3, left). The actual difference in creatinine excretion between the two methods was 16 ± 154 mg day⁻¹. The salt intake estimated by the SMU method with the sitting and standing posture also showed a significant correlation ($r=0.44$, $P < 0.01$) with that obtained by 24-h urine collection (Figure 3, right), and the actual difference of salt intake between the two methods was 0.0 ± 1.7 g day⁻¹.

The effect of antihypertensive therapy on the estimation of salt intake by the SMU method in the sitting and standing position was assessed by comparison with the 24-h collection method. The following antihypertensive drugs were being used: calcium channel blockers (daily doses: amlodipine 5–10 mg, manidipine 20–40 mg, cilnidipine 10–20 mg, benidipine 4–8 mg and nifedipine retard 20–60 mg), angiotensin II receptor blockers (candesartan 8 mg, losartan 25 mg, telmisartan 40–80 mg, olmesartan 20 mg and valsartan 80–160 mg), diuretics (indapamide 0.5–1 mg), angiotensin-converting enzyme inhibitors (enalapril 5–10 mg and imidapril 5–10 mg), β -blockers (atenolol 25–50 mg, betaxolol 10–20 mg and bisoprolol 5 mg),

α -blockers (doxazosin 2–4 mg and urapidil 60 mg), α/β -blockers (carvedilol 5 mg), central sympatholytic agents (guanabenz 1–2 mg) and a combined preparation (losartan 50 mg and hydrochlorothiazide 12.5 mg). The diuretics and the combined preparation were administered once daily in the morning; the central sympatholytic agent and α/β -blocker were administered twice a day (morning and evening); and the other antihypertensive drugs were administered in the morning or in the morning and evening. There were no significant differences in the estimated salt intake between the SMU and 24-h collection methods among patients without antihypertensive therapy (6.9 ± 1.4 g day⁻¹ vs. 6.9 ± 1.6 g day⁻¹), patients on monotherapy (6.1 ± 1.7 g day⁻¹ vs. 6.3 ± 1.5 g day⁻¹) and patients on combination therapy (6.3 ± 1.7 g day⁻¹ vs. 6.3 ± 1.6 g day⁻¹). The patients were also divided into six groups by the different classes of antihypertensive drugs. Angiotensin II receptor blockers and/or angiotensin-converting enzyme inhibitors were used by 55 patients, calcium channel blockers by 43 patients, diuretics by 13 patients, β -blockers by 10 patients, α -blockers by 9 patients and central sympatholytic agents by 5 patients. Patients who took the α/β -blocker were counted in both the α -blocker group and the β -blocker group. Patients who received the combined preparation were counted in both the angiotensin II receptor blockers group and the diuretic group. There were no significant differences in the estimated salt intake between the SMU and 24-h collection methods in the angiotensin II receptor blockers and/or angiotensin-converting enzyme inhibitors group (6.2 ± 1.7 g day⁻¹ vs. 6.2 ± 1.5 g day⁻¹), the calcium channel blocker group (6.2 ± 1.9 g day⁻¹ vs. 6.1 ± 1.5 g day⁻¹), the diuretic group (5.7 ± 1.8 g day⁻¹ vs. 5.3 ± 1.7 g day⁻¹), the β -blocker group (5.6 ± 1.0 g day⁻¹ vs. 5.7 ± 1.5 g day⁻¹), the α -blocker group (6.5 ± 1.7 g day⁻¹ vs. 6.4 ± 1.5 g day⁻¹) and the central sympatholytic group (6.4 ± 1.7 g day⁻¹ vs. 6.8 ± 1.1 g day⁻¹) (Figure 4).

DISCUSSION

Although 24-h urine collection is considered to be the most reliable method for assessing daily salt intake,^{4,8,10} complete and accurate collection is not easy to achieve. We excluded 16 patients with incomplete collection and a deviation of creatinine excretion by more than 30% of the predicted value and then compared the SMU and 24-h collection methods in 100 hypertensive patients with a daily salt intake of 7 g during hospital admission. Our findings clearly indicated that the posture adopted until the collection of the SMU influenced the estimate of the daily salt intake by the SMU method. Data obtained in the sitting and standing position were most similar to the salt intake obtained by 24-h urine collection, so adoption of the sitting and standing position was important for the accurate

Figure 3 Correlation between predicted creatinine excretion and measured creatinine excretion ($r=0.92$, $P<0.05$) (left panel). Correlation between salt intake estimated by the second morning urine (SMU) method and the 24-h urine collection method ($r=0.44$, $P<0.05$) (right panel). The plots show data from 100 hypertensive patients. Salt intake was estimated by the SMU method in the sitting and standing position.

Figure 4 Effect of each class of antihypertensive agents on the estimation of daily salt intake by the second morning urine (SMU) method (open columns) or the 24-h urine collection method (closed columns). There were no significant differences in the estimated salt intake between the two methods (Wilcoxon's signed-rank test). ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; CCB, calcium channel blockers.

estimation of salt intake by this method, and salt intake was overestimated in the recumbent position. There are several possible mechanisms by which changes in urinary sodium excretion occur in response to postural changes. Standing up from the recumbent position causes fluid to shift into the interstitial spaces in the lower limbs²² and results in an increase in colloid osmotic pressure, which leads to a decrease in the glomerular filtration rate and an increase in the fractional tubular reabsorption of sodium.²³ Standing also alters sympathetic tone^{24,25} and the production of hormones related to the sodium balance, including the renin-angiotensin system,²⁶ endothelin²⁷ and atrial natriuretic peptide,²⁸ resulting in changes in urinary sodium excretion.

The SMU method was originally developed using healthy subjects¹⁰ who did not lie down after awakening until the SMU collection. To examine whether the SMU method is applicable for hypertensive patients, previous clinical studies have been done using hospital patients on a constant salt intake, but these patients often spend a considerable amount of time in bed and tend to lie down until voiding the SMU, resulting in an overestimation of salt intake. This may also

help to explain why the SMU method is not widely used to estimate the salt intake of hypertensive patients at present. Owing to a difference of approximately 1 g daily between the salt intake obtained in the sitting position versus the sitting and standing position, and because of daily salt intake that varies in normal life,²⁹ it is not practical to advise outpatients undergoing this test to spend their time equally in the sitting position and standing position; however, it is useful to advise them not to lie down. In the Japanese guideline, a spot urine method developed by Tanaka *et al.*³⁰ is recommended for the general estimation of daily salt intake because urine collection can be done at any time to measure the sodium:creatinine ratio. However, the estimation of salt intake by the spot urine method could also be affected by the posture adopted before urine collection.

This study indicated that the formula predicting daily creatinine excretion for healthy subjects was also applicable to hypertensive patients because the values calculated with the formula strongly correlated with the measured value for creatinine excretion (Figure 3, left). The correlation of estimated salt intake between the SMU method and the 24-h urine method was significantly weaker in our hypertensive patients ($r=0.44$) than that reported in healthy subjects ($r=0.73$).¹⁰ This difference may be related to the measurement conditions (a single measurement versus the mean value of three to five measurements) or the admission status (hospitalized versus not hospitalized). Hypertensive patients can be divided into dippers and non-dippers based on the circadian rhythm of their blood pressure and the change of sodium excretion, which differs between these two types because of movement from the supine to upright position,³¹ so the heterogeneity of our subjects may explain the weaker correlation in this study.

Calcium channel blocker,³² angiotensin-converting enzyme inhibitors³³ and diuretics all have a natriuretic effect that could potentially influence the estimation of daily salt intake by the SMU method by altering the circadian rhythm of sodium secretion.³⁴ However, this method can actually be used in patients receiving antihypertensive therapy because there were no differences between the SMU and 24-h collection methods for any class of antihypertensive (Figure 4). These findings agreed with our previous results.¹³ Chronic administration of diuretics was considered most likely to interfere with the SMU method because these drugs have the strongest natriuretic effect among

antihypertensive agents. However, diuretics were used at comparatively low doses (indapamide 0.5–1 mg day⁻¹ and hydrochlorothiazide 12.5 mg day⁻¹) probably because the Japanese guideline³ recommends low-dose diuretic therapy to avoid adverse effects. The SMU method was carried out to assess salt intake at 24 h after diuretic administration in this study, which may have allowed useful data to be obtained in patients taking diuretics, but further studies will be necessary to examine the influence of higher doses of diuretics.

Although the SMU method seems to be applicable to most hypertensive patients, it theoretically cannot be used in some patients. In patients who have muscle atrophy, such as those with long-term bed rest, the SMU method cannot be employed because the predicted value may overestimate their actual creatinine excretion. Also, if the sodium:creatinine excretion ratio of the second morning urine is not correlated with the ratio for the 24-h urine, the SMU method cannot be applied. A change of posture from the recumbent position increases the re-absorption of sodium by the renal tubules mainly through sympathetic nerve stimulation.^{24,25} Patients with autonomic neuropathy, such as diabetic neuropathy and/or patients with renal tubular dysfunction, for example, interstitial nephritis, may not be appropriate for the SMU method. Further studies are needed to determine the patients who should be excluded from the SMU method to enhance reliability.

There were several limitations of our study. We only examined the reliability of the SMU method in patients with a daily salt intake of 7 g, so investigation at a higher salt intake is also needed. We previously studied³⁵ 22 patients with essential hypertension who had a salt intake of 17 g per day, followed by 7 g per day for 1 week each. The salt intake estimated at the end of each week by the SMU method was 8.0 ± 1.9 g day⁻¹ and 16.2 ± 2.3 g day⁻¹, respectively, although the posture adopted until the second urine collection was not specified. These findings suggest that the SMU method is effective for estimating a higher salt intake. We examined the effect of three different postures on the estimation of salt intake by the SMU method, but the order was not randomized to avoid errors, so bias was possible. Although the dietary salt intake was set at 7 g day⁻¹ during admission, there was a comparatively wide range of salt intake (2.5–9.7 g) shown by the 24-h urine collection method. The patient with the lowest intake did not eat miso soup containing 0.5 g of salt and did not use soy sauce containing salt as seasoning. If the study had been carried out in a metabolic ward, more precise results may have been obtained. This study was carried out in patients who wanted to initiate lifestyle modifications with diet and exercise, and they had relatively mild target organ damage. It remains unclear whether this method would be applicable in patients with severe target organ damage or an accelerated phase of hypertension.

In conclusion, the posture adopted before the second morning collection influenced the estimation of daily salt intake by the SMU method when the effect of posture was examined in inpatients with restricted salt intake (7 g day⁻¹). Maintaining the sitting and standing position until the SMU collection is advised to correctly estimate daily salt intake by the SMU method, and it is important for patients not to lie down. This method can be used in patients receiving antihypertensive therapy because there were no differences between the SMU and 24-h collection methods in patients receiving various drugs. The SMU method may replace the 24-h urine collection method because of its greater convenience, especially in outpatient clinics.

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