《Original article》

Estimation of previous-day salt intake by a regression equation using the overnight urinary sodium/potassium ratio and conductivity

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Abstract

Background

Patients with hypertension need restrictions of salt in meals. Several methods for assessing daily salt intake have been established, which have some difficulties in accuracy, simplicity or promptness. Recently, we have developed a new estimation formula (Sumikama's formula) of daily salt intake using the overnight urinary sodium (Na)/potassium (K) ratio. In this study, we re-evaluated the accuracy of a new Sumikama's estimation formula in comparison with a widespread used formula, Tanaka's formula.

Methods

Ten young adults (4 males and 6 females) were enrolled as subjects from May to July 2021. Amounts of salt in meals varied every 5 days, 15 g, 5 g, 10 g, 10 g, 5 g, and 15 g during experimental period for 30 days. The salt-adjusted meal was prepared daily by the subjects themselves, and all subjects consumed the same menu. Overnight urine samples were collected daily during the experimental period. Concentrations of Na, K, and creatinine in urine, urine specific gravity, electrical conductivity (conductivity), and urine weight were measured. To evaluate the accuracy of the estimation formulas, we calculated the estimated salt intake using Sumikama's and Tanaka's formulas for each experimental diet period and compared the agreement rate between the estimated and actual daily salt intakes.

Results

Estimated daily salt intakes on the previous day using Sumikama's and Tanaka's formulas for each diet period were 7.6 ± 1.6 g and 6.8 ± 1.7 g for the 5g-salt periods, 9.3 ± 1.8 g and 8.1 ± 1.8 g for the 10g-salt periods, and 11.0 ± 2.6 g and 9.2 ± 1.8 g for the 15g-salt periods, respectively. The percentages of the estimated values within ±30% of the actual salt intake by Sumikama's and Tanaka's formulas were 57.3% and 49.3%, respectively.

Conclusion

The present findings suggest that the accuracy of Sumikama's formula is acceptable compared with Tanaka's formula in estimation of daily salt intake. Further validation studies of Sumikama's formula for another age groups are necessary for clinical practical use.

Keywords: salt intake, urinary Na/K ratio, overnight urine, urine conductivity

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Introduction

At present, there are approximately 9.94 million patients with hypertension in Japan, the largest number among all diseases[1]. Among patients with hypertension, essential hypertension accounts for 90% and secondary hypertension for 10%. Hypertension is a risk factor for many diseases, including stroke (cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage), heart disease, kidney disease, and stomach cancer[2-7]. Previous studies have reported that excessive salt intake increases blood pressure, and salt restrictions are considered necessary to prevent various diseases[8].

In clinical practice, salt intake is assessed using various methods. The interview methods, including 24-hour recall method, have the advantage of a relatively low patient burden, while the accurate assessment of salt intake estimated by interview methods is sometimes difficult, because of inaccurate patient's memory and inexperienced dietitian's interview skills. The 24-hour urine collection method, measuring urinary excretion of sodium directly, is considered the gold standard, but it is not suitable for practical use because of high burden on patients collecting all amount of urine. Therefore, estimation methods using spot urine such as Tanaka's formula[9], Kawasaki's formula[10], and INTERSALT's formula[11] have been developed. Tanaka's formula uses casual urine, while it needs correction by urinary creatinine. Kawasaki's formula is relatively difficult because it needs the second urine after waking in the morning fasting. The INTERSALT formula is based on the data collected from several countries in North America and Europe in the 1980s, which differs from the current Japanese, so it may be a limitation. In addition, these formulas are intended to estimate salt intake for populations, so they are inappropriate for assessing sodium intake for individuals. An accurate, rapid, and simple method for evaluation of sodium intake for individuals is needed.

Therefore, we previously developed a regression formula (Sumikama's formula) for estimating a patient's previous-day salt intake using the overnight urinary sodium (Na)/potassium (K) ratio, which can easily be evaluated in the first urine. Sumikama's formula is unnecessary for the correction by urinary creatinine, so daily salt intake of patients can be determined and we can use it for nutritional guidance on the day of collection. Furthermore, Sumikama's formula needs a little burden on the patient for collection of urine sample because the first urine after waking is used.

Although we developed Sumikama's formula to estimate an individual's previous-day salt intake using the overnight urinary Na/K ratio in our previous study, it has not yet been validated in other populations. Therefore, in this study, we tested the accuracy of Sumikama's formula in another subjects taking test meals containing a wide range of salt.

Materials and Methods

Protocols and salt-adjusted diets

This study was conducted from May 19 to July 23, 2021, with 10 students (4 males and 6 females) as subjects. Profile characteristics of subjects are shown in Table 1. Amount of salt intake was varied every 5 days for a total of 30 consecutive days as follows: 15 g on days 1–5, 5 g on days 6–10, 10 g on days 11–20, 5 g on days 21–25, and 15 g on days 26–30. The salt-adjusted diets were prepared by the participants themselves daily. All subjects consumed the same menu to ensure that there were no extreme changes in amounts of salt intake. However, additional or leftover food intake was allowed, even where the nutritional amounts could be accurately calculated. Water was the only freely consumed beverages to ensure 1–2 liters of water intake per day. In addition, to prevent sodium loss due to sweating, the subjects were restricted from strenuous exercise of more than 5 metabolic equivalents (METs). This study protocol

Table 1. Characteristics

		Male(n=4)	Female(n=6)
Age	(years)	22.5 ± 1.3	21.3 ± 0.5
BMI	(kg/m^2)	20.1 ± 2.9	21.1 ± 1.5
Body-fat	(%)	13.4 ± 5.4	26.8 ± 5.0
SBP	(mmHg)	115 ± 7	98 ± 6
DBP	(mmHg)	70 ± 10	66 ± 6

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure.

was approved by the Research Ethics Committee of Nagoya University of Arts and Sciences (No. 499), and written informed consent was obtained from all subjects before the study began.

Urine analysis

Overnight urine samples were collected daily during the experimental period, and urine specific gravity, electrical conductivity, and urine weight were measured. A pocket urine specific gravity refractometer (PAL-09S; ATAGO Co., Ltd, Tokyo, Japan) was used to measure urine specific gravity, and a compact electrical conductivity meter (LAQUAtwin; HORIBA) was used to measure electrical conductivity. Subjects were checked to be able to operate the measuring devices correctly prior to the experiment. Overnight urine samples were collected in 10 mL tubes (sample volume 8–9 mL) and frozen at –20°C. All samples were analyzed by the Nagoya Medical Cooperative Association Nagoya Clinical Laboratory Center. Urinary sodium, potassium, chlorine, and creatinine concentrations were measured. Body weight and blood pressure were measured daily during the experimental period to confirm the health condition of the subjects.

Statistics analysis

To evaluate the accuracy of the estimation formulas, we calculated the estimated salt intake for each diet period using Sumikama's and Tanaka's formulas, and compared the agreement between the estimated and actual salt intake values.

Sumikama's formula: previous-day salt intake (g) = 0.64 × Na/K ratio + 0.18 × conductivity (mS/cm) – 0.43 × sex (male 0, female 1) + 3.62

Relative error (%) was calculated as [(estimated value – actual sodium intake) / actual sodium intake] × 100, and these values were classified into five levels: less than ±10%, ±10% to 20%, ±20% to 30%, ±30% to 40%, and ±40% or more. Statistical analysis was performed using EZR ver.1.54. P value < 0.05 was statistically significant.

Results

Nutrient intake and urine measurements

Data of nutrients intake and urine measurements are shown in Table 2. For nutrient intake, actual salt

Table 2. Nutrient intake and urine measurements

Intake					
		Overall (n=300)	5g (n=100)	10g (n=100)	15g (n=100)
Energy	kcal	1841 ± 129	1814 ± 108	1837 ± 129	1873 ± 143
Proteins	g	76.4 ± 4.3	73.8 ± 4.0	76.4 ± 3.5	79.1 ± 3.7
Fat	g	63.3 ± 11.1	60.7 ± 7.5	69.7 ± 12.8	59.6 ± 9.7
Carbohydrate	g	257.8 ± 32.6	258.7 ± 24.6	242.7 ± 32.3	272.1 ± 33.6
Salt	g	9.9 ± 4.0	**5.2 ± 0.1**	**9.7 ± 0.3**	**14.9 ± 0.3**
Na	mg	3927 ± 1559	2055 ± 37	3867 ± 117	5858 ± 127
K	mg	2622 ± 86	2605 ± 80	2591 ± 74	2669 ± 84
Na/K	mol/mol	2.54 ± 0.98	**1.34 ± 0.04**	**2.54 ± 0.10**	**3.74 ± 0.10**

urine measurement					
		Overall (n=300)	5g (n=100)	10g (n=100)	15g (n=100)
Na/K	mol/mol	5.18 ± 3.69	**3.85 ± 2.79**	**4.84 ± 3.16**	**6.62 ± 4.13**
Na	mmol/L	57.47 ± 34.89	46.38 ± 27.03	51.2 ± 26.71	74.46 ± 41.22
K	mmol/L	15.73 ± 11.38	16.75 ± 11.92	15.14 ± 11.19	15.53 ± 11.11
Cl	mmol/L	46.97 ± 33.50	36.12 ± 26.43	41.36 ± 26.62	62.96 ± 38.45
Cr	mg/dL	74.97 ± 49.39	82.22 ± 57.70	70.08 ± 43.97	74 ± 46
Aldsterone	μg/L	4.3 ± 5.1	6.5 ± 6.7	3.9 ± 4.2	2.7 ± 2.7
Cor	μg/L	56.3 ± 46.4	64.78 ± 67.9	54.15 ± 30.77	51.56 ± 29.27
conductivity	mS/cm	14.5 ± 5.2	13.0 ± 67.1	14.1 ± 4.98	16.6 ± 5.7
specific gravity		1.02 ± 0.01	1.02 ± 67.11	1.01 ± 0.01	1.02 ± 0.01
heavyweight	g	384 ± 169	368 ± 67	383 ± 157	389 ± 181

Nutrients intake and urinalysis measurements are shown with means and standard deviations for salt intake of each 5g, 10g and 15g.

intakes during the 5 g, 10 g, and 15 g salt-adjusted diet phases were 5.2 ± 0.1 g, 9.7 ± 0.3 g, and 14.9 ± 0.3 g, respectively, and potassium intakes were 2605 ± 80 mg, 2591 ± 74 mg, and 2669 ± 84 mg, respectively. Salt intake varied in the range of 5–15 g with salt-adjusted meal, but potassium intake varied within a narrow range. The Na/K ratios of the ingested meals during the 5 g, 10 g, and 15 g salt-adjusted diet phases were 1.34 ± 0.04, 2.54 ± 0.10, and 3.74 ± 0.10, respectively.

Sodium concentrations in overnight urine varied substantially among salt-adjusted diets with different amounts of sodium, whereas potassium concentrations in overnight urine were approximately same. Overnight urinary Na/K ratios varied according to amounts of sodium in each salt-adjusted diet.

Evaluation of regression equations to estimate previous-day sodium intake

Actual and estimated previous-day salt intake as calculated by Sumikama's and Tanaka's formulas were compared for each salt-adjusted diet period (Figure 1). Mean salt intake during the 5-g, 10-g, and 15-g salt-adjusted diet periods in this study were 5.2 ± 0.1 g, 9.7 ± 0.3 g, and 14.9 ± 0.3 g, respectively. The estimated values of the previous day's salt intake by Sumikama's and Tanaka's formulas for each salt-adjusted diet period were 7.6 ± 1.6 g and 6.8 ± 1.7 g

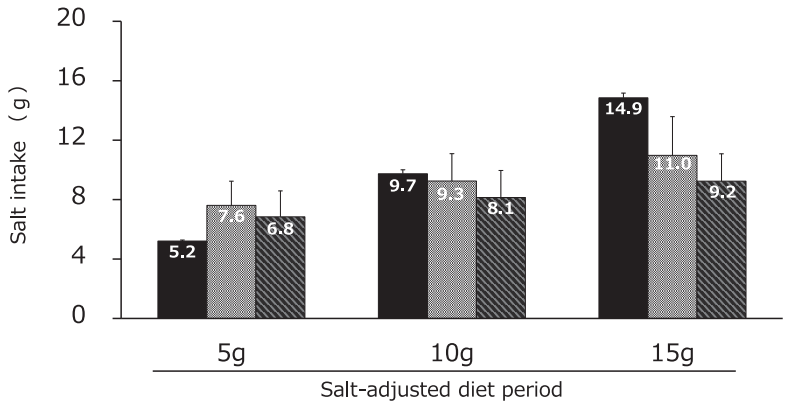

Figure 1. Comparison of salt intake and estimate values for each salt diet period. Actual salt intake and estimates by Sumikama's and Tanaka's formulas are shown for each level of salt intake.
■: Actual salt intake. ▒: Estimated values from Sumikama's formula. ▨: Estimated values from Tanaka's formula.

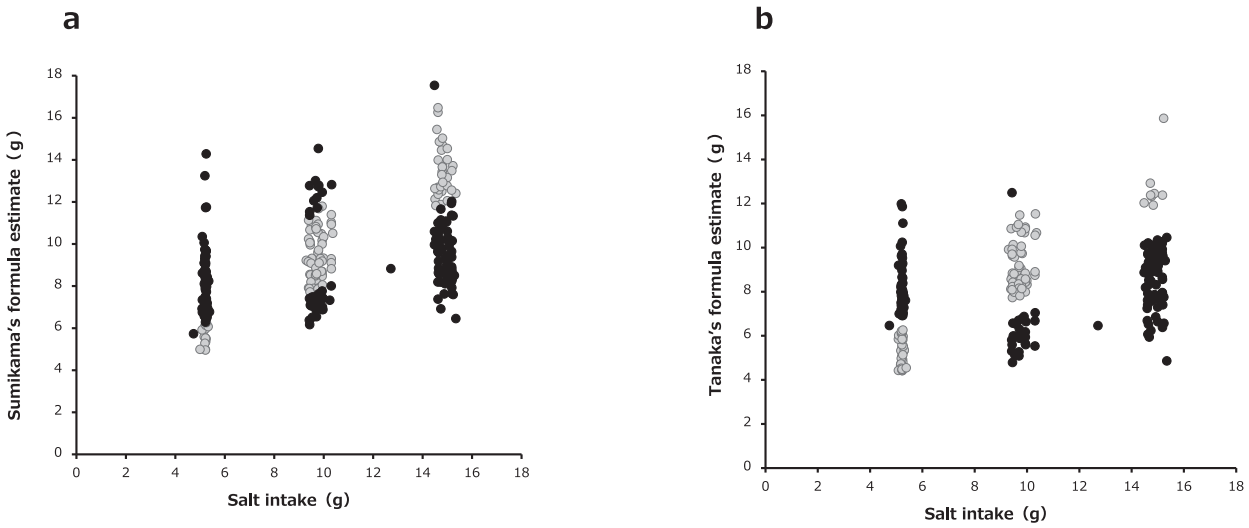

Figure 2. Relative error between salt intake and estimates for each salt diet period.
(a) Relationship between salt in take estimated by Sumikama's formula and actual salt intake. (b) Relationship between salt intake estimated by Tanaka's formula and actual salt intake. Black plot: relative difference > 30%, gray plot: relative difference ≤ 30%.

for the 5-g period, 9.3 ± 1.8 g and 8.1 ± 1.8 g for the 10-g period, and 11.0 ± 2.6 g and 9.2 ± 1.8 g for the 15-g period, respectively. A comparison of the error ranges for the estimated salt intake by Sumikama's and Tanaka's formulas is shown in Figure 2. The percentages of relative errors within ±30% by Sumikama's and Tanaka's formulas were 57.3% and 49.3%, respectively.

Discussion

In our previous study, we newly developed Sumikama's formula to estimate salt intake using the overnight urinary Na/K ratio and conductivity. In the present study, we tested the accuracy of Sumikama's formula in another subjects taking test meals containing a wide range of salt, comparing Tanaka's formula which is mostly used formula in Japan to assess daily salt intake. In our previous study, each subject consumed meals containing various amounts of salt for different periods. In the present study, each subject consumed test meal containing strictly adjusted amounts of salt for the same period. The percentages of errors within ±30% from the actual salt intake were 64.2% in our previous study, and 57.3% in the present study, both of which were superior over the accuracy by Tanaka's formula.

In the present study, test meals containing strictly adjusted three amounts of salt were consumed daily during the experimental period. The correlation between actual salt intake and the estimated values for the previous day was examined by a regression equation. Comparing the estimated previous-day salt intakes as calculated by Sumikama's and Tanaka's formulas for each salt-adjusted diet period, a trend toward overestimation was seen at 5-g period, and underestimation at 15-g period. As these formulas are likely to be used for patients with hypertension, cardiovascular diseases, or renal diseases requiring salt restrictions, underestimation during a 15-g high-salt diet phase may lead to misunderstanding the patient's salt intake. Further validation may be necessary.

In the present study, the correlation coefficients between the actual and estimated values of previous-day salt intake by Sumikama's and Tanaka's formulas were 0.553 and 0.481, respectively. Cogswell et al.[12] evaluated the validity of estimated 24-hour Na excretion in 207 individuals using Kawasaki's formula, INTERSALT's formula, Tanaka's formula, and Mage's formula[13], and reported that the correlation coefficients of estimated 24-hour Na excretion from early morning urine and that from 24-hour urine storage were 0.52, 0.47, 0.50, and 0.51, respectively. In addition, Zhou et al.[14] evaluated the validity of Kawasaki's formula, INTERSALT's formula, and Tanaka's formula for estimated 24-hour urinary Na excretion at the individual level using urine from 141 Chinese adults. The correlation coefficients between the 24-hour urinary sodium excretion and the estimated values by Kawasaki's, INTERSALT's, and Tanaka's formulas were 0.31, 0.25, and 0.35, respectively ($p < 0.01$). The correlation coefficient of Sumikama's formula was higher than those reported in previous studies, suggesting the high accuracy of Sumikama's formula.

A reason why Sumikama's formula can estimate previous-day superior over other formulas estimating daily salt intake is using both overnight urinary Na/K ratio and conductivity. The Na/K ratio is affected by fluctuations of both Na and K in urine. In other words, Na/K ratio in urine increases as a result of increased Na excretion or decreased K excretion. As conductivity reflects the electrolyte concentration in urine, an elevation Na/K ratio due to K excretion is corrected in Sumikama's formula. Increased dietary intake of K enhances urinary Na excretion[15]. Therefore, Sumikama's formula can be more accurate than pre-existing formulas, which do not take account of the effect of K. Tanaka's formula is reported to be not suitable for estimating individual Na and K excretion, but useful for estimating population mean levels of 24-h Na and K excretion.

Several limitations of the present study warrant mention. First, the subjects including in the present study were only young adults. The prevalence of hypertension increases with aging, the applicability of Sumikama's formula should be validated in elder

ages with an increased frequency of hypertensin, cardiovascular diseases, or renal diseases. In future, the accuracy of estimation in middle-aged and older age groups should be examined. Second, timing of meals in the present study was not limited strictly, and varied among the subjects. Nishida et al.[16] reported that a certain amount of ingested Na and K are excreted in the urine until bedtime if dinner is consumed at 18:30, but not until the next morning if dinner is consumed at 23:30 (they tend to be stored in the body). Furthermore, Kaneko et al.[17] reported a higher Na/K ratio in postprandial urine. In other words, individual differences in Na and K excretion are expected to occur depending on timing of meals. As timing of the urine measurement also varied among subjects, it will be necessary to examine the influence of measurement timing on estimated values. Although this study protocol restricted strenuous exercise of more than 5 METs, the experiment was conducted during the hot months of June and July, which may have increased Na excretion in sweat and affected the accuracy of Na excretion measurements.

At present, Kawasaki's formula, INTERSALT's formula, and Tanaka's formula are commonly used to estimate previous-day salt intakes using urine. However, all these methods need urinary creatinine excretion for adjustment of estimation, which is inconvenient because of the time and cost required for measurement. On the other hand, Sumikama's formula use only the first urine Na/K ratio and conductivity measurements to estimate salt intake. In other words, salt intake can be quickly assessed by spot urine only. It is convenient to know daily salt intake then and there for patients visiting a health center for nutritional guidance.

Conclusion

A new developed Sumikama's formula is a more accurate, simple, and rapid formula for estimating daily salt intake than another pre-existing formula. However, further validation of Sumikama's formula for various age groups is necessary for practical use.

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《原著》

第一尿の Na/K 比と尿伝導度を用いた1日塩分摂取量推定式（Sumikama の式）の検討

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要旨

【目的】早朝第一尿の Na/K 比と伝導度を用いた前日の塩分摂取量の推計式（Sumikama の式）の精度を検証するため様々な量の塩分を含む試験食を用いて検討した。
【方法】10名の大学生（男性 4 名、女性 6 名）を対象に、5 g、10g、15g の塩分を含む試験食をそれぞれ 2 回ずつ 5 日間、計30日摂食してもらった。早朝第一尿の Na、K、クレアチニン濃度、伝導度、尿比重、尿重量等を測定した。スポット尿を用いた 1 日塩分摂取量推定式である既存の Tanaka の式と本研究室で近年開発した Sumikama の式による推定値と実際の塩分摂取量とを比較し、その精度を検証した。
【結果】Sumikama の式と Tanaka の式から算出した 1 日塩分摂取量の推定値は、5 g 塩分食では7.6 ± 1.6 g、6.8 ± 1.7 g、10 g 塩分食では9.3 ± 1.8 g、8.1 ± 1.8 g、15 g 塩分食では11.0 ± 2.6 g and 9.2 ± 1.8 g であった。実際の塩分摂取量と比較して推定値が ± 30% の範囲内であったのは、Sumikama の式は57.3%、Tanaka の式は49.3% であった。
【結論】Sumikama の式による 1 日塩分摂取量の推定値は臨床に使用可能な範囲であると考えられた。今後は塩分制限が必要となる疾患を有する患者での検証が必要である。

キーワード：1 日塩分摂取量、早朝第一尿、尿中 Na/K、尿伝導度

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