ORIGINAL RESEARCH

Spot Urine-guided Salt Reduction in Chronic Kidney Disease Patients

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Objective: Dietary salt restriction is important in patients with chronic kidney disease (CKD) to reduce hypertension, cardiovascular events, progression of CKD, and mortality. However, recommending salt reduction for patients is difficult without knowing their actual sodium intake. This study evaluated the effectiveness of spot urine-guided salt reduction in CKD outpatients.

Design: A prospective cohort study was used.

Subjects: This study included a total of 127 adult outpatients (aged 60 ± 18 years, 80 males) with CKD. Their baseline estimated glomerular filtration rate was 51.4 ± 25.1 (mL/minute/1.73 m^2), and 64 (50%) of them were with CKD stage 3a or 3b (both 32 [25%]).

Intervention: We informed the patients of their individual spot urine-estimated salt intake every time they visited the outpatient clinic. Based on the data, the nephrologist encouraged the patients to achieve their salt restriction goal.

Main Outcome Measure: The primary outcome was the estimated salt excretion, and the secondary outcome was the urinary protein-to-Cr ratio (UPCR). Multiple regression analyses were performed to clarify the contributing factors of changes in both outcomes.

Results: Over a follow-up of 12 months, the median number of patients' visits was 7 (5-8). The estimated salt intake was significantly reduced from 7.98 ± 2.49 g/day to 6.77 ± 1.77 g/day ($P < .0001$). The median UPCR was also reduced from 0.20 (0.10-0.80) to 0.10 (0.10-0.48) ($P < .0001$). On multiple regression analysis, a reduction in UPCR was positively associated with the baseline UPCR and a reduction in systolic blood pressure significantly ($P < .0001$ and $P < .01$, respectively) as well as positively correlated with a reduction in the estimated salt intake, with borderline significance ($P = .08$).

Conclusions: Providing spot urine-estimated salt intake feedback effectively motivated CKD patients to reduce their salt intake. Spot urine-guided salt reduction may slow CKD progression through decreased urinary protein excretion.

Introduction

MANY OBSERVATIONAL AND interventional studies have shown that a reduction in salt intake lowers blood pressure.[1,2] In particular, patients with chronic kidney disease (CKD) are likely to develop salt and water retention, which leads to a high prevalence of hypertension among such patients.[3] Some studies have shown that a high salt intake in CKD patients was associated with higher blood pressure and higher risks of CKD progression and all-cause mortality.[4] Although the Japanese Society of Nephrology has recommended the daily salt intake to be in the range of 3 to 6 g,[5] the target attainment rate is extremely low in our country, despite general awareness of the need to reduce salt intake.[6]

Therefore, we hypothesized that evaluating and informing patients of their actual salt intake could provide greater encouragement to achieve the salt restriction goal. Twenty-four-hour home urine collection and measurement of urinary sodium (Na) excretion is the most reliable method for the estimation of the daily salt intake[7]; however, the method is difficult for outpatients to repeat in clinical practice, whereas estimation with spot urine is very simple and takes very little time for outpatients.[8] We performed a prospective study to evaluate the effectiveness of spot urine-guided salt reduction in CKD outpatients.

Methods

We enrolled all 128 adult pre-dialysis patients who met the CKD criteria and visited 1 nephrologist in the outpatient nephrology clinic of our hospital between June 2015 and December 2015. We used a modification of the CKD Epidemiology Collaboration Equation for Japanese to calculate the estimated glomerular filtration rate (eGFR).[9] One patient with enteral nutrition who could not adjust the salt intake was excluded.

At each visit, the nephrologist reviewed the patients' records of home blood pressure and body weight. Laboratory tests, including urinary Na, creatinine (Cr), and protein, were also measured. The urinary protein-to-Cr ratio (UPCR) was assessed as a marker of proteinuria. The nephrologist gave feedback of the individual data, including spot urine-estimated salt intake, to the patients every time they visited the outpatient clinic and encouraged them to

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achieve their salt-restriction goal. The patients were prospectively followed for 12 months from the first measurement, and changes in estimated salt excretion and UPCR were measured as primary and secondary endpoints, respectively. The period between every patient visit varied from 1 to 6 months, and we set the last follow-up 12 months from the first visit. Therefore, the follow-up period has a range of 12 ± 2 months.

Medications, including antihypertensive drugs, were freely changed as necessary.

The study protocol was approved by the Clinical Research Ethics Committee of our hospital (approval number 740), and all the study procedures were in accordance with the Declaration of Helsinki. Informed consent was obtained from all the included patients.

Estimation of Urinary Salt Excretion (Estimated Salt Intake)

The estimated daily salt excretion was calculated from random urine according to the following equation:[8,10]

Twenty-four-hour urinary Na excretion (mEq/day) = 21.98 × (spot urine Na [mEq/L] ÷ spot urine Cr [mg/dL] ÷ 10 × estimated 24-hour urinary Cr excretion)$^{0.392}$, where the estimated 24-hour urinary Cr excretion (mg/day) is given by

Body weight (kg) × 14.89 + height (cm) × 16.14 − age × 2.04 − 2,244.45

Then, the estimated daily salt intake (gram/day), or 24-h urinary salt excretion (g/day), was calculated as follows: 24-h urinary Na excretion (mEq/day) × 58.5 ÷ 1,000.

The spot urine was collected at the time of the patients' clinic visits, between 08:00 and 12:00 hours.

Statistical Analysis

The analysis used data from all participants, consistent with the intention-to-treat principle. We performed the single imputation method of last observation carried forward (LOCF) in which the missing values of 6 of 127 participants with incomplete follow-up were replaced by their last observed values. We performed a paired t-test or Wilcoxon signed-rank test, depending on the data distribution, to compare baseline parameter values with those at follow-up. Subgroup differences were assessed by a paired t-test or 1-way analysis of variance with post-hoc Turkey's honestly significant difference test. For nominal values, McNemar's test was used. We also performed simple correlation analysis, followed by multiple linear regression analysis. A regression model was created to evaluate the association between the change in the estimated salt intake as the dependent variable, and age, body mass index (BMI), eGFR, systolic or diastolic blood pressure, urinary salt excretion, period from the first visit to the nephrologist (at baseline), and the number of follow-ups during the study period as the independent variables. We also evaluated the factors contributing to a decrease in UPCR. The regression model used variables thought to have a clinical effect on UPCR decrease, including baseline UPCR, decreases in BMI, eGFR, systolic or diastolic blood pressure, and estimated salt intake. A simple correlation analysis and Spearman's correlation were used for baseline salt excretion and UPCR decrease, respectively. Data are expressed as the means ± standard deviations, median and interquartile range, or percentages, as appropriate. All analyses were performed using R software for Mac OS X, ver. 3.2.3.

Results

Characteristics of the Patients and Changes in Parameters

A total of 127 CKD outpatients were included in the study, and 121 patients completed the 1-year follow-up (12 ± 2 months); 2 patients died, 1 withdrew due to induction of hemodialysis, 1 withdrew due to peritoneal dialysis, and 2 were lost to follow-up.

The baseline characteristics of the patients are shown in Table 1. The patients were followed for 11.7 ± 1.9 months, and the median number of visits was 7 (5-8). Antihypertensive drugs were increased in 22 (17%) patients, decreased in 28 (22%) patients, and unchanged in 77 (61%) patients during the study period.

Table 1. Baseline Characteristics of the Patients

Age (y)	60.1 ± 17.9
Sex (% male)	80 (63%)
Period from the first visit to the nephrologist (mo)	11.1 (5.3-19.7)
Follow-up period (mo)	11.7 ± 1.9
Number of visits during the study period	7 (5-8)
CKD stage	
G1	8 (6%)
G2	30 (24%)
G3a	32 (25%)
G3b	32 (25%)
G4	20 (16%)
G5	5 (4%)
UPCR (g/gCr)	
<0.15	55 (43%)
0.15–0.50	24 (19%)
>0.5	48 (38%)
Race/ethnicity	
Asian	127 (100%)
Primary disease	
Diabetes	23 (18%)
Nephrosclerosis	30 (24%)
Chronic glomerulonephritis	21 (17%)
ADPKD	13 (10%)
Drug use	
ACEI/ARB	71 (56%)
CCB	45 (35%)
Diuretics	23 (18%)

ACEI, angiotensin-converting enzyme inhibitor; ADPKD, autosomal dominant polycystic kidney disease; ARB, angiotensin II receptor blocker; BMI, body mass index; CCB, calcium channel blocker; CKD, chronic kidney disease; UPCR, urinary protein-to-Cr ratio.