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Seasonal Variation of Nutritional Intake from 24-Hour Urine Collection and Adherence in Patients with Chronic Kidney Disease

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Abstract

Background: For appropriate diet therapy, it is desirable to determine urine volume and excreted urinary components using 24-hour urine volume (24hUV) and compare these data with indications. 24hUV allows an accurate measurement of excreted urinary protein, glucose, and salt per day, which are important for assessment of renal function and diet intake. In particular, urine volume may be seasonal variations because of the effect of perspiration.

Methods: The subjects were 37 (29 males and 8 females) outpatients with chronic kidney disease (CKD) who underwent 24-hour urine collection and were given nutrition education (consultation) continuously for 2 years or more. The survey period was January 2012 to July 2014. Patients were divided into 3groups according to their adherence to indicated intake as A, <15% difference, B, ≥15%.

Results: There was no significant difference in 24hUV and urinalysis between seasons. Mean Na throughout the year was 82±29 mEq/L, and Mean K throughout the year was 20.4±9.4 mEq/L. Estimated protein and salt intake were lower in group A throughout the year.

Conclusion: Urine 24hUV and urinalysis were not influenced by seasonal variations, and these findings were due to the influence of diet intake.

Key Word: diet therapy; estimated intake; protein; salt; energy

Introduction

Protein intake restriction is widely used in patients with renal impairment as therapy for inhibiting disease progression. A low-protein diet inhibits progression of renal impairment and introduction of dialysis through relief of uremia and release from Glomerular hyper filtration [1, 2]. Effects of renin-angiotensin system inhibitors, sodium bicarbonate and phosphorus adsorbents have also been found and these drugs are widely used; however, protein intake restriction remains important, and is described and recommended in worldwide and Japanese guidelines [3]. Salt intake restriction is involved in prevention of hypertension and cardiovascular disease in patients with Chronic Kidney Disease (CKD). In patients with chronic nephritis and diabetic nephropathy, salt intake correlates with excreted urine protein, and salt intake restriction has been suggested to degrade progression of nephropathy [4].

Given the above findings, it is important for patients with CKD to have a diet that focuses on protein and salt intake restriction. For appropriate diet therapy, it is desirable to determine urine volume and excreted urinary components using 24-hour urine volume (24hUV) and compare these data with indications [5]. Such assessment and estimation using spot urine is possible, but most urinary components increase during the day and decrease at night, and are influenced by diet, posture and movement. Kawasaki et, al. examined salt intake using spot urine, and found that the T method was most accurate for estimating excreted urinary sodium using urine during a hospital visit. However, the difference between estimation of excreted urinary sodium and salt intake exceeding 2 g/day was 45% in all tests, which indicates a problem obtaining accurate data [6]. In contrast, 24hUV allows an accurate measurement of excreted urine volume, urine protein and urine glucose per day, which are important for accurate assessment of renal function and diet intake [7]. However, 24hUV may be a cause of nosocomial infection and many specialists do not use this approach because of an increased burden on patients [8, 9].

Estimation of dietary intake is limited because salt intake per day cannot be accurately determined due to acute changes in salt intake, severe diarrhea and vomiting, and the start or discontinuation of diuretics. Spot 24hUV in healthy subjects has been shown not to match mean daily sodium excretion [10]. In particular, urine volume depends on perspiration volume and there may be seasonal variations in urine volume [11]. Few studies have examined the relationship of 24hUV with seasonal

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variations in patients with CKD, but accurate assessment through improvement of the accuracy of 24hUV test is necessary to establish appropriate diet therapy in these patients.

Methods

The subjects were male and female outpatients with CKD who underwent 24-hour urine collection and were given nutrition education (consultation) continuously for 2 years or more. The survey period was 2 months from July to August 2014 and clinical data were obtained from medical records of 201 patients (127 males and 74 females) for 2 years from January 2012 to July 2014. Of these patients, the subjects in the final analysis were 37 patients (29 males and 8 females) with data for four seasons from January 2012 to July 2014.

Sex, age, height, body weight, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were collected on the survey, and primary disease, complications, diuretics and prescription data were obtained from clinical records. Body mass index (BMI) was calculated from height and body weight. Blood and urine data determined at the beginning of the survey in July 2014 were also taken from clinical records. The hematological and biochemical test data included Red Blood Cell Count (RBC), Hemoglobin (Hb), Hematocrit (Ht), White Blood Cell Count (WBC), Platelet Count (Plt), Total Protein (TP), Serum Albumin (Alb), Total Cholesterol (TC), Low-Density Lipoprotein Cholesterol (LDL-C), Fasting Plasma Glucose (FPG), Gamma-Glutamyl Transpeptidase (γ-GTP), Blood Urea Nitrogen (BUN), Serum Creatinine (Cr), Uric Acid (UA), Estimated Glomerular Filtration Rate (eGFR), Serum Sodium (Na), Serum Potassium (K), Calcium (Ca), Serum Inorganic Phosphorus (P), Voluntary Cr (Spot Urine), and Urine Protein (UP) (spot urine).

Blood pressure, hematology, urine volume and urinalysis data from January 2012 to July 2014 were obtained from clinical records. These data included SBP, DBP, WBC, TP, Alb, BUN, Cr, UA, TC, triglyceride (TG), hemoglobin A1c using the National Glycohemoglobin Standardization Program (HbA1c (NGSP)), Na, K, Ca and P. The urine data included 24hUV, UP, urea nitrogen (UN), Cr, UA, Na, K and P.

Indicated energy per day (E: kcal), E intake (kcal), E assessment, indicated protein (Pro: g), Pro intake (g), Pro assessment, indicated salt (NaCl: g), NaCl intake (g) and NaCl assessment were obtained from nutrition education records. E, Pro and NaCl were assessed from the difference between the indication and intake, with groups defined based on this difference as A, <15%; B, ≥15%. Patients in group A had good adherence to diet and those in group BC had poorer adherence.

Nutrition education was offered as close as possible to tests for blood pressure, hematology, urine volume and urinalysis within the same season. Four seasons were chosen before July 2014, the date of the survey. The classification of seasons referred to the website of the Japan Meteorological Agency: 3 months (July to September) with a high mean temperature in 2012 and 2013 were defined as summer, 3 months (December to February) with a low temperature were defined as winter, and then March to June was defined as spring, and October to November as autumn [12].

Characteristics of patients and test results for blood pressure, hematology, urine volume and urinalysis are shown as mean ± standard deviation or with a range (minimum to maximum). The number and percentage of patients for primary disease, complications and prescribed diuretics are shown in cross tabulations. Statistical analysis was performed using "4 Step Excel Statistics" (OMS publishing Inc.). Results for blood pressure, hematology, 24hUV and urinalysis by season were analyzed by one-way analysis of variance, Kruskal-Wallis test and multiple comparisons. The same results and adherence to the indicated diet were analyzed by two-way analysis of variance for repeated measures. Differences in test results by adherence were analyzed by F test. The significance level was 5% in all statistical tests.

This study was approved by the research ethics committee of Tokyo Medical University (No. 2716, June 3, 2014). Patients were informed by attending physicians that information in clinical records could be used in a study. Information was posted in the outpatient department stating that patients could exclude themselves from the study based on their decision or that of their family. The study results are presented as tables with elimination of personal information.

Results

The characteristics of the patients are shown in Table 1. The mean age of the subjects in the survey was 67±11 years old (range: 37 to 88 years), mean BMI was 24.2±3.3 kg/m2 (19.0 to 30.6 kg/m2), and obesity assessed by BMI was normal, but 15 (41%) subjects were considered to be obese based on BMI ≥25.0 kg/m2 and no subject was lean [13]. Mean SBP was 129±16 mmHg (88 to 185 mmHg) and mean DBP was 73±10 mmHg (44 to 109 mmHg), which is within the hypotensive goal for patients with CKD (SBP: 130 mmHg, DBP: 80 mmHg) [14].

The major primary disease was glomerulonephritis in 16 (43%) subjects, followed by diabetic nephropathy in 11 (30%), connective tissue disease in 6 (16%), nephrotic syndrome in 4 (11%), nephrosclerosis in 3 (8%), and renal artery stenosis in 2 (5%). The major complication was hypertension in 35 (95%) subjects, followed by dyslipidemia and diabetes mellitus in 21 (57%), hyperuricemia in 19 (51%), and renal anemia 17 (46%).

Diuretics were prescribed in 12 subjects (33%) in spring, 12 (32%) in summer, 11 (29%) in autumn, and 10 (26%) in winter; and all were given as monotherapy. Furosemide was prescribed in 4 subjects (11%) in spring and 3 (8%) in summer, autumn and winter. Azosemide was prescribed in 3 (8%) in spring, summer and winter, and 2 (5%) in autumn. Trichlormethiazide was prescribed in 3 (8%) in spring, summer and autumn, and 2 (5%) in winter. Blood and urine data determined at the beginning of survey are shown in Table 2.

Results for 24hUV and urinalysis by season are shown in Table 3. There was no significant difference in 24hUV and

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Table 1: Patients profile

		Total(n=37)				
		M	±	SD	Max	Min
Age	(years old)	67	±	11	88	37
Height	(cm)	164.1	±	6.7	174.5	152.0
Weight	(kg)	65.3	±	10.6	92.0	45.0
BMI	(kg/m^2)	24.2	±	3.3	30.6	19.0
SBP	(mmHg)	129	±	16	185	88
DBP	(mmHg)	73	±	10	109	44

urinalysis between seasons. The mean 24hUV was 1785±491 mL/day throughout the year, 1850±446 mL/day in spring, 1690±479 mL/day in summer, 1785±576 mL/day in autumn, and 1815±457 mL/day in winter. All these volumes were higher than the reference range of 1500 mL/day [15]. Mean Na throughout the year was 82±29 mEq/L, within the reference range of 40-90 mEq/L. Mean K throughout the year was 20.4±9.4 mEq/L, which was also within the reference range of 20-60 mEq/L except in summer [16].

Results for 24hUV and urinalysis by season and adherence to the indicated E are shown in Table 4. There was no significant difference in 24hUV and urinalysis by season and adherence to indicated E among seasons. In comparison by adherence to the E indication, UN in Group A was 281±118 mg/dL in spring, 300±121 mg/dL in summer, 329±166 mg/dL in autumn, and 290±120 mg/dL in winter, while UN in Group B was 429±169 mg/dL in spring, 376±160 mg/dL in summer, 378±157 mg/dL in autumn, and 390±124 mg/dL in winter. Thus, UN in Group A was significantly lower in all seasons ($p<0.001$). Similarly, urine K in Group A was all significantly lower than those in Group B. Variance of all was significantly higher in Group A than in Group B.

Results for 24hUV and urinalysis by season and adherence to the indicated Pro are shown in Table 5. There was no significant difference in 24hUV and urinalysis by season and adherence to Pro indication among seasons. In comparison by adherence to Pro indication, UN in Group A was significantly lower than those in Group B, and urine Na and K in Group A in all seasons were significantly lower than those in Group B. Variance of 24hUV in autumn was significantly higher in Group A than in Group B.

Results for 24hUV and urinalysis by season and adherence to indicated NaCl are shown in Table 6. There was no significant difference in 24hUV and urinalysis by Season and adherence to NaCl indication among seasons. In comparison by adherence to NaCl indication, UN, urine Na, K in all seasons in Group A were significantly lower than those in Group B.

Table 2: Clinical laboratory data of the patients at registration

		Total(n=37)		
		M	±	SD
RBC	(×10^2/μL)	3.8	±	0.6
Hb	(g/dL)	11.8	±	1.7
Ht	(%)	35.0	±	4.8
WBC	(×10^3/μL)	6.0	±	1.7
PLt	(×10^2/μL)	200.7	±	72.0
TP	(g/dL)	6.7	±	0.4
Alb	(g/dL)	3.9	±	0.4
TC	(mg/dL)	181	±	35
LDL-C	(mg/dL)	97	±	25
FPG	(mg/dL)	129	±	61
γ-GTP	(U/L)	29	±	18
BUN	(mg/dL)	38.4	±	18.2
Cr	(mg/dL)	3.22	±	1.88
UA	(mg/dL)	7.0	±	1.3
eGFR	(mL/min/1.73m^2)	22	±	16
Na	(mEq/L)	141	±	2
K	(mEq/L)	4.7	±	0.6
Ca	(mg/dL)	8.6	±	0.5
P	(mg/dL)	3.7	±	0.7
Cr(spot urine)	(mg/dL)	89.6	±	34.1
TP(spot urine)	(mg/dL)	117	±	102

Discussion

Seasonal variations of blood pressure, hematology, 24hUV and excreted urinary components and the relationship with adherence to diet therapy in patients with CKD were examined in this study. The mean age of the subjects was 67±11 years old, and the accuracy of 24hUV in such elderly patients is likely to be low, which may cause errors in the results. However, the subjects measured 24hUV for 2 years or longer; therefore, they were a population with a good technique of urine collection with less error. There were no significant differences in blood pressure, hematology, urine volume, and urinalysis by season. These results show that the test data determined by 24hUV in patients with CKD were not influenced by seasonal variations.

There were seasonal variations of blood pressure, hematology, urine volume and urinalysis, and adherence to diet indication. For adherence to the energy indication, BUN, urine UN, K in Group A were significantly lower than those in Group B, and Na also showed a decreasing tendency. These results show that subjects with good adherence to the indicated energy had low excreted urinary components. Energy intake in Group B varied, which

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Table 3: 24hUV and urinalysis by season

		Total(n=37×4)					Spring(n=37)					Summer(n=37)					Autumn(n=37)					Winter(n=37)					
		M	±	SD	Max	Min	M	±	SD	Max	Min	M	±	SD	Max	Min	M	±	SD	Max	Min	M	±	SD	Max	Min	p value*
24hUV	(mL/ day)	1785	±	491	2910	570	1850	±	446	2710	970	1690	±	479	2910	990	1785	±	576	2900	570	1815	±	457	2780	1150	0.370
TP	(mg/dL)	71	±	64	290	0	75	±	63	262	0	62	±	57	239	0	70	±	65	253	0	78	±	73	290	0	0.647
UN	(mg/dL)	355	±	149	838	70	361	±	164	822	82	335	±	143	838	70	360	±	160	694	122	366	±	129	613	129	0.764
Cr	(mg/dL)	66.0	±	21.4	135.7	23.0	64.6	±	20.6	115.5	34.3	69.8	±	23.2	128.4	25.9	65.8	±	22.6	135.7	30.3	63.8	±	19.2	113.1	23.0	0.728
UA	(mg/dL)	15.1	±	8.3	45.2	4.2	15.0	±	8.9	43.2	5.0	14.8	±	7.1	32.5	4.2	16.2	±	10.1	45.2	5.3	14.4	±	7.0	35.1	4.2	0.993
Na	(mEq/L)	82	±	29	173	26	82	±	30	146	37	79	±	29	135	30	80	±	30	173	26	85	±	27	140	41	0.763
K	(mEq/L)	20.4	±	9.4	61.3	6.5	20.5	±	11.0	61.3	6.5	19.9	±	7.8	35.8	6.5	20.2	±	10.2	56.6	8.2	20.9	±	8.5	51.4	7.8	0.823
P	(mg/dL)	31.3	±	13.7	113.8	13.2	32.3	±	17.5	113.8	14.2	30.5	±	10.9	60.2	13.7	31.5	±	15.1	90.2	13.2	31.0	±	10.7	57.2	15.2	0.977

There was no significant difference (probability <0.05) in all measured items among 4 seasons

Table 4: 24hUV and urinalysis by season and adherence to the indicated energy

		Adherence group	Total(A=60 B=88)			pvalue *	Spring(A=17 B=20)			Summer(A=20 B=17)			Autumn(A=14 B=23)			Winter(A=9 B=28)			pvalue *
			M	±	SD		M	±	SD	M	±	SD	M	±	SD	M	±	SD	
24hUV	(mL/ day)	A	1822	±	466	0.368	2018	±	342	1680	±	462	1800	±	498	1804	±	566	0.446
		B	1759	±	508		1707	±	481	1702	±	512	1775	±	629	1819	±	429	
UN	(mg/dL)	A	299.9	±	129.6	0.001	281	±	118	300	±	121	329	±	166	290	±	120	<0.001
		B	393.0	±	149.4		429	±	169	376	±	160	378	±	157	390	±	124	
Na	(mEq/L)	A	76	±	29	0.054	67	±	27	79	±	31	80	±	33	80	±	26	0.060
		B	85	±	28		95	±	27	80	±	29	79	±	29	86	±	27	
K	(mEq/L)	A	17.1	**±**	6.8	0.001	16.4	**±**	7.7	17.5	**±**	7.3	18.6	**±**	6.1	15.5	**±**	4.9	<0.001
		B	22.6	**±**	10.3		24.0	**±**	12.3	22.7	**±**	7.7	21.1	**±**	12.0	22.7	**±**	8.7	

* express comparison between A and B

Table 5: 24hUV and urinalysis by season and adherence to the indicated protein intake

		Adherence group	Total(A=58 B=90)			P value *	Spring(A=17 B=20)			Summer(A=15 B=22)			Autumn(A=15 B=22)			Winter(A=11 B:26)			P value *
			M	±	SD		M	±	SD	M	±	SD	M	±	SD	M	±	SD	
24hUV	(mL/ day)	A	1746	±	421	0.519	1835	±	421	1705	±	473	1626	±	348	1826	±	445	0.441
		B	1810	±	532		1863	±	476	1680	±	494	1893	±	676	1810	±	471	
UN	(mg/dL)	A	275	±	143	<0.001	301	±	180	256	±	108	291	±	169	240	±	75	<0.001
		B	407	±	128		413	±	132	388	±	141	406	±	139	419	±	108	
Na	(mEq/L)	A	67	±	26	<0.001	69	±	30	68	±	30	66	±	26	64	±	19	<0.001
		B	91	±	26		94	±	27	87	±	27	89	±	29	93	±	25	
K	(mEq/L)	A	17.4	±	8.5	<0.001	18.2	±	10.8	17.0	±	6.5	18.2	±	9.6	15.4	±	5.6	0.002
		B	22.3	±	9.5		22.4	±	11.1	21.8	±	8.2	21.5	±	10.6	23.3	±	8.5	

* express comparison between A and B

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Table 6: 24hUV and urinalysis by season and adherence to indicated NaCl

		Adherence group	Total(A=58 B:90)				Spring(A=12 B=25)			Summer(A=18 B=19)			Autumn(A=16 B=21)			Winter(A=12 B=25)			
			M	±	SD	p value *	M	±	SD	M	±	SD	M	±	SD	M	±	SD	p value *
24hUV	(mL/day)	A	1744	±	450	0.421	1932	±	394	1658	±	480	1758	±	540	1669	±	286	0.425
		B	1811	±	516		1811	±	472	1721	±	489	1805	±	613	1885	±	510	
UN	(mg/dL)	A	269	±	114	<0.001	255	±	122	277	±	123	259	±	119	282	±	95	<0.001
		B	411	±	142		412	±	158	389	±	142	436	±	146	406	±	125	
Na	(mEq/L)	A	64	±	25	<0.001	60	±	24	66	±	29	61	±	23	71	±	24	<0.001
		B	93	±	25		93	±	27	92	±	24	94	±	26	91	±	25	
K	(mEq/L)	A	16.8	±	6.7	<0.001	14.3	±	5.9	18.4	±	7.9	15.7	±	5.4	18.1	±	7.2	<0.001
		B	22.7	±	10.1		23.5	±	11.7	21.2	±	7.7	23.6	±	11.7	22.3	±	8.9	

*express comparison between A and B

suggests that these subjects mixed excessive and low energy intake. Consequently, there was no significant difference in energy intake between Groups A and B.

For adherence to protein indication, WBC, BUN, TC, LDL-C, UP, UN, UA, Na, K and P in Group A were significantly lower than those in Group B. These results show that good adherence to the indicated protein kept excreted urinary components low. Protein intake in Group A was significantly lower than that in Group B (34±8 vs. 51±11 g/day). Thus, protein intake in Group B was excessive, which led to high BUN, UN, K and P. There was no significant difference in urine Cr by adherence to protein indication. An increase or decrease in urine Cr does not depend on diet or urine volume, but urine Cr is proportional to muscle development and momentum [13]. However, these results show that Cr is independent of protein intake.

For adherence to the salt indication, WBC, BUN, TC, LDL-C, UP, UN, UA, Na, K and P in Group A were significantly lower than those in Group B. These results show that good adherence to the salt indication maintained a low level of excreted urinary components. It is notable that items with a significant difference between Groups A and B by adherence to the salt indication were almost the same as those by adherence to the protein indication. In healthy subjects, energy correlates strongly with salt intake and there is a relationship between salt and protein intake [14]. Based on these results, good adherence to protein indication appears to be proportional to that for salt indication, leading to similar results for excreted urine components.

The results of this study show that blood pressure, hematology, 24hUV and urinalysis in patients with CKD did not show seasonal variations, and it suggested diet intake of the subjects were stable throughout year. Healthy subjects have seasonal variety of food intake in daily life, but nutrients except vitamin C and iron have no seasonal variation [15]. Diet intake may effect on urine volume by amount of water intake, but water intake obtained from diet in healthy elderly people has been shown not to change in summer and winter [16, 17]. Subjects in Group A were in compliance with the dietary indication and the mean age was 67±11 years old; therefore, seasonal variations due to diet appeared to be few, similarly to the results of the previous study. The subjects in this study were given nutrition education continuously for 2 years or more, and this may have kept a stable dietary intake, leading to less seasonal variation. Dietary intake in Group A was close to the indication throughout the year. Based on the above, 24hUV in patients who maintain appropriate diet therapy shows accurate dietary contents.

A several limitations are considered in this study. First, the patients recruited in this study were well-trained to our procedure to 24h urine collection. Therefore, the present results may not be applied to the general patients. Secondly season was defined by calendar month. Temperature and humidity that relate much to sweating were not considered in data analysis.

Conclusion

This study was conducted to examine seasonal variations of blood pressure, hematology, 24hUV, excreted urinary components, and their relation with adherence to diet therapy in patients with CKD. The results showed that blood pressure, hematology, urine 24hUV and urinalysis were not influenced by seasonal variations, and these findings were due to the influence of diet. In patients with CKD who require diet therapy, diet is stable throughout the year, and consequently, urine volume and excreted urinary components showed no seasonal variations. On the other hand, some hematology items depended on adherence to diet therapy, and these results in Group A with good adherence were significantly lower than those in Group BC. Dietary intake in Group A was close to the diet indication throughout the year. Based on these findings, hematology determined by 24hUV in patients who maintain an appropriate diet gives accurate dietary contents.

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