ORIGINAL

Nutritional counseling regulates interdialytic weight gain and blood pressure in outpatients receiving maintenance hemodialysis

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Abstract : Maintenance hemodialysis outpatients must limit salt and water intake to maintain electrolyte balance and blood pressure. In Kawashima Hospital, nationally registered dietitians provide hemodialysis patients with monthly nutritional counseling. We investigated whether nutritional counseling affects interdialytic weight gain (IDWG) and blood pressure. We investigated 48 hemodialysis patients whose monthly average IDWG ratio to dry weight exceeded 5.1% and who had not had a long-term hospital admittance of >1 month. After the 48-month nutritional counseling period, the IDWG ratio had improved in 37 of the patients (77.1%), significantly decreasing from 6.0±0.7 to 5.3±0.9%. Estimated salt and water intake decreased significantly from 13.3±2.7 to 11.8±2.4 g/day and 2528±455 to 2332±410 ml/day, respectively. During the intervention period, normalized protein catabolic rate and body mass index did not change substantially. Pre-hemodialysis systolic and diastolic blood pressures had significantly decreased from 149±19 to 134±18 mmHg, and 82±13 to 75±10 mmHg for 48 months after study initiation, respectively. The dosage of antihypertensive drugs had significantly decreased in the group that experienced improvement in the IDWG ratio. Long-term nutritional counseling by nationally registered dietitians may improve the IDWG ratio and blood pressure of hemodialysis patients by decreasing their salt and water intake. J. Med. Invest. 64 : 129-135, February, 2017

Keywords **:** *hemodialysis, hypertension, interdialytic weight gain, nutritional counseling, salt and water restriction*

INTRODUCTION

Hypertension is very common in patients receiving hemodialysis (1, 2), and it is an important risk factor for cardiovascular diseases (3, 4). Cardiovascular disease is responsible for approximately half the deaths of patients receiving hemodialysis (5). Although approximately 86% of patients receiving hemodialysis with hypertension take antihypertensive drugs, only 30% have well-controlled blood pressure (BP). (6). Thus, despite the high rate of antihypertensive drug use, BP control remains unsatisfactory. In addition to BP, interdialytic weight gain (IDWG) is also a useful prognostic marker for kidney failure. The United States Renal Data System study found that a high IDWG was associated with shorter survival (7). Furthermore, a report in Japan revealed that survival was lower if the IDWG to dry weight ratio was ≤2% or ≥6% (8).

Hypertension is closely related to IDWG (9) ; it is therefore important to reduce IDWG to improve hypertension in patients receiving hemodialysis. IDWG is generally considered to be a consequence of salt and water intake between two consecutive dialysis sessions. Excessive salt and water intake expands extracellular volume, thereby increasing the risk of developing hypertension and left ventricular hypertrophy. Salt restriction with reduced use of antihypertensive drugs to manage high BP may reduce the prevalence of left ventricular hypertrophy and left ventricular dysfunction in hemodialysis patients (10-12). However, few systematic studies have demonstrated that dietary therapy or nutritional counseling have beneficial effects on hypertension and IDWG in Japan. Therefore, we investigated whether long-term nutritional counseling by a nationally registered dietitian could improve IDWG and blood pressure in hemodialysis patients.

METHODS

Patient selection

All of the patients who participated in the study received hemodialysis at Kawashima Hospital (Tokushima, Japan). The concentration of dialysate sodium during hemodialysis was maintained at 140 mEq/L in accordance with standard methods. Eligibility criteria for the study included : (i) IDWG ratio > 5.1%, the clinical parameter of Kawashima Hospital ; (ii) receiving hemodialysis therapy without regular nutritional counseling in Kawashima Hospital for > 5 years ; (iii) receiving hemodialysis routinely three times/week (scheduled as 12 hours/week) ; (iv) receiving hemodialysis for ≥5 years ; and (v) no residual renal function for > 5 years. Fifty-five patients met the eligibility criteria out of 469 hemodialysis outpatients at Kawashima Hospital. Seven patients were excluded for the following reasons : one patient died, two changed hospitals, and four had a long hospitalization of > 1 month during the study. The remaining 48 patients participated in the study.

Data collection

We collected the following clinical data from the patients' medical records during both the control (the 48-month period prior to

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the beginning of the intervention period) and intervention periods : sex, age, duration of hemodialysis, diabetes mellitus status, height, dry weight, IDWG, and normalized protein catabolic rate (nPCR). We also recorded antihypertensive drug use. We measured body weight with a scale. Dry weight was the post-dialysis body weight below which the patient developed symptomatic hypotension or muscle cramps in the absence of edema.

We measured pre- and post-dialysis systolic and diastolic BP with an aneroid sphygmomanometer. BP was averaged from three hemodialysis sessions at the end of each month. Measurements were classified based on the 2004 Japanese Society of Hypertension guidelines (13). Intradialytic hypotensive episodes were defined as a decrease in systolic BP of >20 mmHg requiring saline infusion. We recorded symptomatic intradialytic hypotensive episodes that occurred during the 12 hemodialysis sessions at the beginning of each month on the patients' charts for 6 months.

We defined IDWG as body weight just before hemodialysis minus body weight just after previous hemodialysis. The IDWG ratio was calculated as follows : IDWG ratio (%) = average of 12 measurements (three times/week $\times$ 4 weeks) of IDWG/dry weight $\times$ 100. We defined a decrease or increase in the IDWG ratio as a change of $>0.5\%$ at 48 months compared to the start of the intervention period, and we defined a decrease or increase in the dosage of medicated antihypertensive drugs as a change at 48 months compared to the start of the intervention period. Borah's formula was used to calculate the PCR (14). This method adds the measured dialysis protein loss to the measured urine and dialysis urea appearance rate. The latter is adjusted to obtain the PCR by a function of the linear correlation between the urea appearance rate and the PCR calculated from nitrogen mass balance measurements in hemodialysis patients. We then divided the PCR value by the patient's dry weight (kg) to yield the nPCR, measured as g/kg (dry weight)/day. The estimated salt intake was calculated with Kimura's formula (15) as follows : estimated salt intake (g/day) = interdialytic sodium intake (mmol) $\times$ 58.5/1000 $\times$ 24/hours from previous post-dialysis to pre-dialysis, where interdialytic sodium intake (mmol) + 1 = (serum sodium concentration of pre-dialysis $\times$ total body fluid volume of pre-dialysis) - (serum sodium concentration of previous post-dialysis $\times$ total body fluid volume of previous post-dialysis) + 1.

Estimated water intake was calculated as follows : estimated water intake (mL/day) = body weight gain for a week (g) $\times$ water density (ml/g)/6.5 (day) + volume of insensible water loss + estimated water volume in stool = body weight gain for a week/6.5 + 15 $\times$ dry weight + 200. Estimated water intake except food was calculated as follows : estimated water intake except food (mL/day) = estimated water intake (mL/day) - volume of water in the food intake (mL/day) = estimated water intake (mL/day) - 1000 (mL/day)

Nutritional counseling intervention

Before we began the nutritional counseling intervention, we made a checklist of each potential area of concern, such as salt and/or fluid restriction, to ensure that the counseling intervention was standardized. The written materials used for counseling were provided by each registered dietitian.

We started offering nutritional counseling in June 2002. At each session, the registered dietitian assessed the patient's clinical data to identify potential problems. The dietitian then provided the patient with monthly nutritional counseling at their bedside during hemodialysis. The educational contents of the dietitian to each patient were the following items : relationship between sodium and IDWG, sodium and/or water-rich foods, high-calorie foods, and so on. For example, we advised that they had better to avoid taking miso soup, one-pot cooking and stock sauce for noodle, while they had better to consume seasoning without salt. If the patient's clinical data had not improved by the next session, the dietitian made a special effort to listen carefully to the patient to determine how best to assist them.

At the beginning of the nutritional counseling intervention, we set the target reduction in salt and water intake to 1.5 g/day (about 1 cup of miso soup or 1 pickled plum) and 200 ml/day (1 cup of water), respectively. Nutritional counseling sessions lasted for an average of 20 minutes/session. The nutritional counseling intervention continued monthly for 4 years.

Ethical considerations

The study was approved by the Kawashima Hospital Ethics Committee, and informed consent was obtained from all patients. The study was designed to be a prospective observational study with self and historical control.

Statistical analysis

We performed statistical analyses with Excel Statistics 2006 (Microsoft Japan, Tokyo, Japan) for Windows. Data are expressed as the mean $\pm$ standard deviation (SD) of 48 individual outpatients. Paired t-test was used to analyze differences in the IDWG ratio and pre-dialysis systolic or diastolic BP. A P value of <0.05 (two-sided) was considered significant. The Cochran-Armitage test was used to analyze the correlation between the dosage of antihypertensive drugs and the IDWG ratio. A P value of <0.05 (two-sided) and Cramer's coefficient of association (Cramer's V-value) of $0<V<1$ were considered significant.

RESULTS

General clinical data

Table 1 lists the subjects' baseline clinical data. There were approximately 1.7 times more men than women ; 63% of the men received nocturnal dialysis and worked. The subjects were on average 10 years younger the average age of the patients in the 2005 report of The Japanese Society for Dialysis Therapy (2). The average BMI of the subjects was 20.9 ± 2.6, close to the standard value of 22 kg/m^2. The IDWG ratio was 1% higher than the IDWG clinical parameter used at Kawashima Hospital. The nPCR was 1.19 ± 0.17 g/kg/day, which met the criteria of the Japanese Society for Dialysis Therapy. The ratio of antihypertensive drug use and pre- or post-dialysis BP was similar to the measurements reported in 2005 by the Japanese Society for Dialysis Therapy, except for post-dialysis systolic BP. The primary diseases of the study participants were as follows : chronic glomerulonephritis (29/48), type II diabetes mellitus (9/48), toxemia of pregnancy (3/48), polycystic kidney disease (1/48), chronic pyelonephritis (1/48), obstructive uropathy (1/48), and cause unknown (4/48). We did not observe any cases of hypertensive nephrosclerosis. During the control period, most of the subjects had not received nutritional counseling.

Changes in salt and water intake

Salt and water intake increased significantly from 48 months prior to the intervention period (-48 months) to the beginning of the intervention period (0 months). After 48 months of intervention (48 months), salt and water intake had decreased significantly compared to 0 months, but it did not decrease to the level noted at -48 months (Table 2).

Changes in the interdialytic weight gain ratio

The participants' mean IDWG ratio increased with repeated seasonal variations during the control period. We did not observe a significant decrease in the IDWG ratio until 6 months after the intervention period had started. After 12 months, the IDWG continued

Table 1. Baseline clinical data of the study participants.

Characteristics	Values	JSDT2005
Men/women	30/18	
Age, years	52.9±9.7	63.9±12.8
Duration of hemodialysis, years	12.2±5.7	
Diabetes mellitus	11 (23)	(31)
Height, cm	161.4±9.0	
Dry weight, kg	54.6±9.9	
Body mass index, kg/m^2	20.9±2.6	
Interdialytic weight gain ratio, %	6.0±0.7	
Normalized protein catabolic rate, g/kg/day	1.19±0.17	
Antihypertensive drug use	30 (63)	(66)
Blood pressure		
Pre-dialysis systolic, mmHg	149±19	153±24
Pre-dialysis diastolic, mmHg	82±13	79±14
Post-dialysis systolic, mmHg	127±18	139±25
Post-dialysis diastolic, mmHg	72±7	74±14

Values are mean±standard deviation or *n* (%) of 48 patients.
JSDT2005, The 2005 report from The Japanese Society for Dialysis Therapy.

Table 2. Effects of nutritional counseling on normalized protein catabolic rate (nPCR) and estimated salt and water intake.

	-48 months	0 months	48 months
nPCR, g/kg/day	1.16±0.15	1.19±0.17	1.14±0.17
Estimated salt intake, g/day	10.7±3.0*	13.3±2.7	11.8±2.4*
Standardized estimated salt intake, g/kg of dry weight/day	0.20± 0.04	0.24±0.03	0.22±0.04
Estimated water intake, mL/day	2209±463*	2528±455	2332±410*
Standardized estimated water intake except food, ml/kg of dry weight/day	22±6*	28±4	24±5*

*$P<0.05$ between 0 months and -48 months or 48 months.

to decrease significantly with repeated seasonal variations (Figure 1).

Changes in pre-dialysis blood pressure and antihypertensive drug use

BP remained near constant during the control period (Figure 2), but the number of antihypertensive drugs increased (Figure 3A). However, we observed a significant decrease in BP 24 months into the intervention period (Figure 2), and the percentage of participants taking two or more antihypertensive drugs decreased from 45.8 to 18.7% after 48 months (Figure 3A). The percentage of patients who did not need antihypertensive drugs decreased by approximately 20%, from 58.2 to 37.5%, at 0 months compared to -48 months. However, 48 months into the intervention, half of the subjects no longer required antihypertensive drugs. In the pre-intervention control period, use of all types of antihypertensive drugs increased. Once the intervention period began, use of all types of antihypertensive drugs decreased, except for angiotensin II-receptor blockers (ARB) (Figure 3B).

Changes in cardiothoracic ratio, dry weight, normalized protein catabolic rate, and hemoglobin $A_{1}c$

The mean cardiothoracic ratio was similar at -48, 0, and 48 months : 49±4.7, 50.3±4.9, and 49.5±4.8%, respectively. We did not observe any edema in the participants at any of these times. Dry weight did not change significantly at -48, 0, and 48 months : 54.8±9.4, 54.6±9.9, and 54.2±9.6 kg, respectively. The nPCR also remained nearly the same (Table 2). The mean hemoglobin $A_{1}c$ of the patients decreased slightly, but the change was not significant : 6.4±1.1, 6.3±1.0, and 6.0±0.5%, respectively, at -48, 0, and 48 months.

Classification of participants based on 2009 Japanese Society of Hypertension guidelines, and frequency of hypotension

We classified the subjects in accordance with the Japanese Society of Hypertension Guidelines 2009 (Table 3). The percentage of patients with normal BP decreased to less than half during the control period. This was a far lower rate than that reported by the Japanese Society for Dialysis Therapy. Moreover, patients with high-normal BP increased 1.6-fold and patients with III grade hypertension increased 2.5-fold during the control period. After 48 months of intervention, none of the participants had grade III hypertension. Furthermore, the percentage of patients with grade II hypertension decreased to approximately one-fifth and the percentage of patients with normal blood pressure increased approximately 4-fold. The mean frequency of hypotension during 12 consecutive dialysis sessions (three times/week×4 weeks) was 2.3±3.0, 2.4±2.9, and 2.5±2.9 times at -48, 0, and 48 months, respectively. The change in the mean frequency was no significant.

Correlation between weekly dosage of antihypertensive drugs and interdialytic weight gain ratio

Both increased and decreased antihypertensive drug dosages significantly correlated with the IDWG ratio after 48 months of intervention compared to 0 months (Table 4). The IDWG of seven

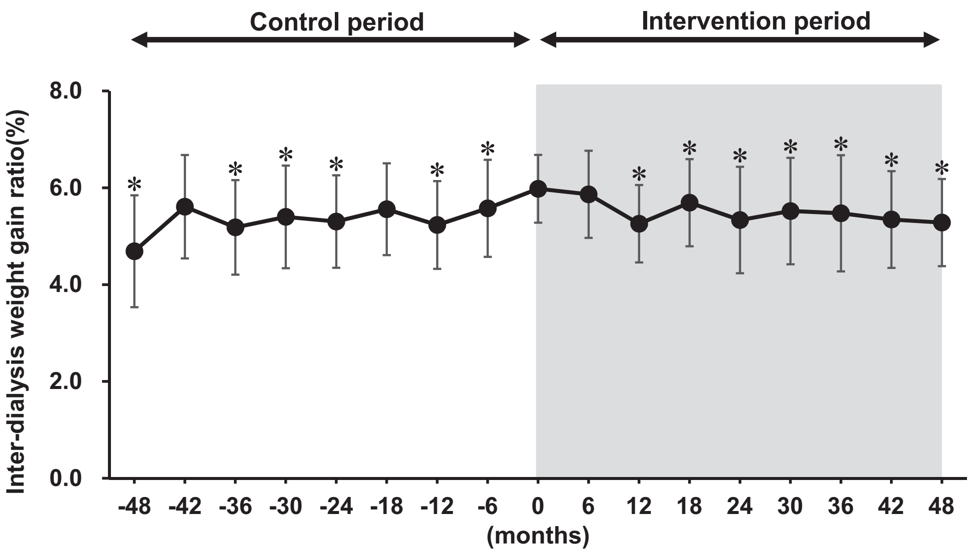

Figure 1. Changes in the interdialytic weight gain ratio during the control and intervention periods. Values are mean±standard deviation of 48 patients. *$P < 0.05$ compared to 0 months.

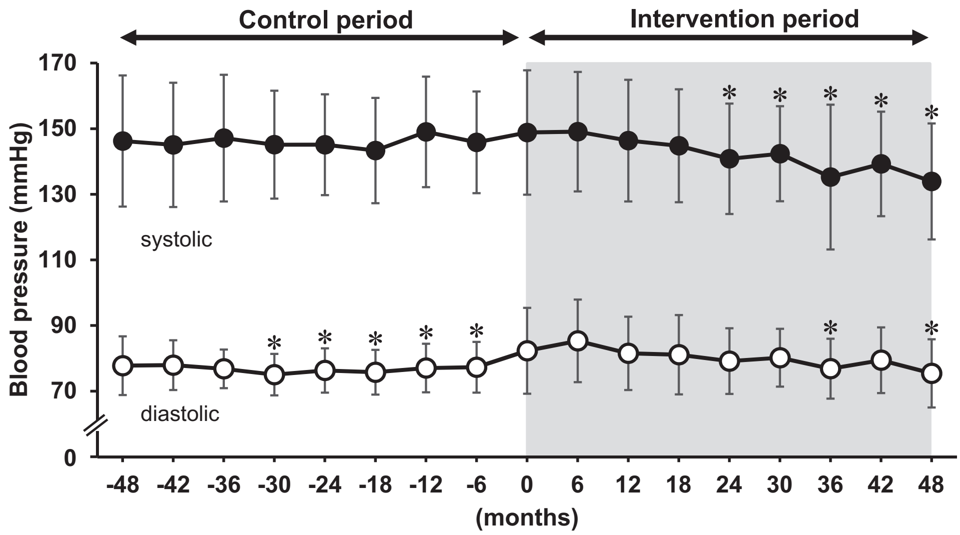

Figure 2. Changes in pre-dialysis systolic and diastolic blood pressure during the control and intervention periods. Values are mean±standard deviation of 48 patients. *$P < 0.05$ compared to 0 months.

female participants did not decrease. These subjects were underweight (BMI 18.5±1.6 kg/m^2) and did not have diabetes.

DISCUSSION

Despite the high prescription rate for antihypertensive drugs among patients receiving dialysis, most have poor control of their BP. In Japan, pre-dialysis BP is as high as 153±24/79±14 mmHg in 66% of dialysis patients who are taking antihypertensive drugs (2). We included maintenance hemodialysis patients whose IDWG ratios were > 5.1% in the present study. However, 63% of these patients took antihypertensive drugs. Several studies (10-12) have reported that patients can control their BP without antihypertensive drug use by strict restriction of salt and water intake. Therefore, we investigated whether long-term nutritional counseling by nationally registered dietitians could improve IDWG and BP in patients receiving hemodialysis.

During counseling sessions in which we offered nutritional guidance on salt and water restrictions, we paid marked attention to whether nPCR and dry weight were maintained properly, because there is a close relationship between IDWG and nutritional status in hemodialysis patients (16). Moreover, IDWG and nPCR values decrease over long interdialytic intervals (17). This indicates that many hemodialysis patients intentionally reduce food intake to control their IDWG, which could lead to malnutrition.

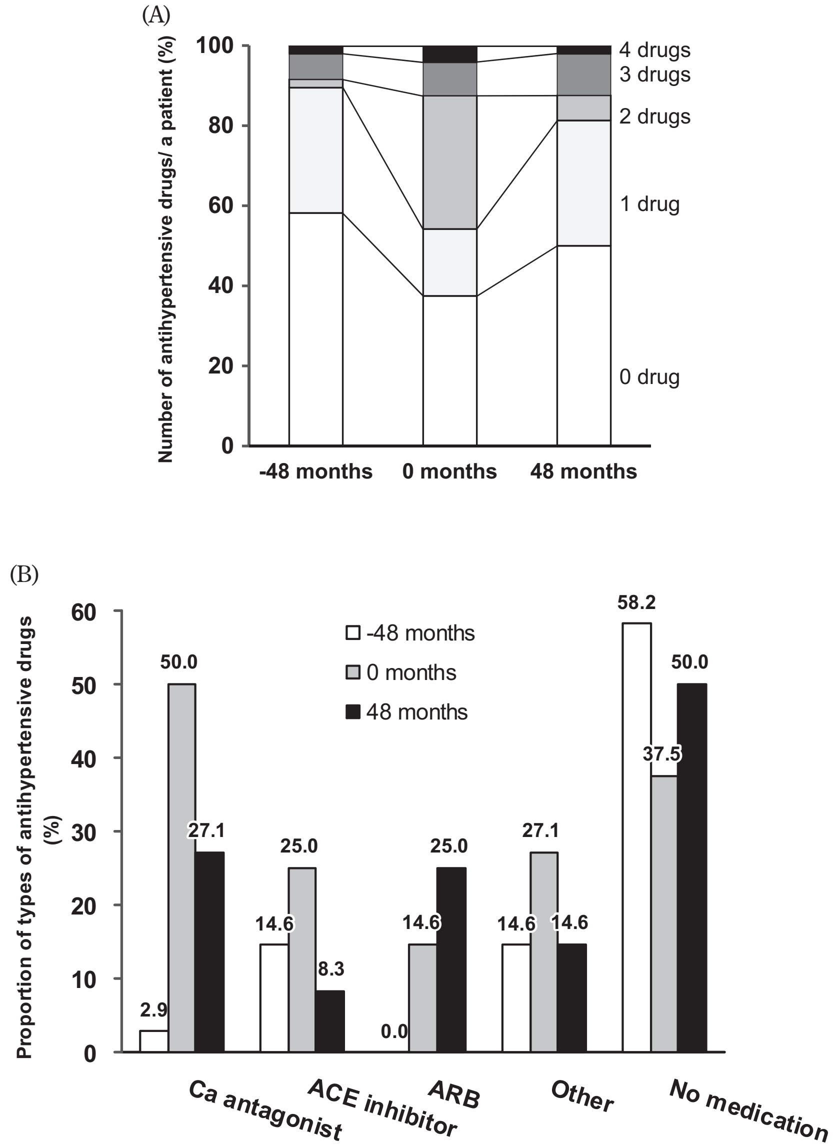

Figure 3. The percentage of patients taking number (A) and types (B) of prescribed antihypertensive drugs during the control and intervention periods. ACE, angiotensin-converting enzyme ; ARB, angiotensin II receptor blocker.

Table 3. Classification of outpatients based on The Japanese Society of Hypertension guidelines 2009.

	-48 months	0 months	48 months	JSDT2005
Normal blood pressure (<130/85 mmHg)	18.8	8.3	33.2	14.5
High normal blood pressure (systolic < 130-139 or diastolic < 85-89 mmHg)	10.4	16.7	31.3	11.2
Grade I hypertension (systolic < 140-159 or diastolic < 90-99 mmHg)	43.7	41.7	31.3	32.5
Grade II hypertension (systolic < 160-179 or diastolic < 100-109 mmHg)	22.9	22.9	4.2	26.9
Grade III hypertension (systolic ≥ 180 or diastolic ≥ 110 mmHg)	4.2	10.4	0.0	14.9

Values are presented as percentages of 48 patients.
JSDT2005, The 2005 report from The Japanese Society for Dialysis Therapy.

Table 4. Correlation between weekly dosage of antihypertensive drugs and interdialytic weight gain ratio.

		Interdialytic weight gain ratio	
		Improvement (n=37)	No improvement (n=11)
Weekly dosage of antihypertensive drugs	Decrease	18 (48.6)	2 (18.2)
	Increase	6 (16.2)	1 (9.1)
	No change	13 (35.2)	8 (72.7)

Values are n (%) of 48 patients. The Cochran-Armitage test between the dosage of antihypertensive drugs and the IDWG ratio : P= 0.0317, V=0.3203

During the control period, the subjects' mean IDWG increased, and repeated seasonal variations occurred. However, the mean IDWG gradually decreased after intervention by a dietitian, although the repeated seasonal variations continued. Thus, this change during the control period is an effect of increased and decreased perspiration due to changes in the temperature.

The beneficial effect that nutritional counseling significantly decreased the IDWG is partially explained by "the health belief model" devised by Rosenstock *et al.* (18, 19). In this model, the patients' sense that a health crisis is occurring will cause them to reduce their salt and water intake for a short time. However, when they perceived the unpleasant effects of restricted salt and water intake greater than its health benefits for a long time, they allowed themselves to receive the diets non-restricted salt and water. The nutritional counseling helps them to keep it in the mind that a health crisis was progressing even if they did not feel receiving beneficial effects from the diet restricted salt and water.

The estimated salt and water intake after 48 months of intervention was far from the dietary standards (The salt intake was less than 0.15 g/kg dry weight/day, and the water intake was less than 15 ml/kg dry weight/day) of Japanese Society of Nephrology in 1997, when our project started. However, this limitation was very difficult for peoples eating the diet non-restricted salt and water to complete. Therefore, we considered it necessary to optimize programs for longer-term follow-ups and nutritional counseling. Therefore, our initial targets of reducing salt intake and water intake were set at 1.5 g/day and 200 ml/day, respectively, which approximately correspond to the salt amount in 200 ml miso soup, and realized. In the present study, such mild limitation of salt and water intake was able to decrease the mean vale of IDWG of our hemodialysis out patients. In addition, our participants continued to keep this limitation of salt and water intake even after the study. Thus, we recommend that the limitation of salt and intake for hemodialytic outpatients should not be too strict.

Hemodialysis patients with diabetes can improve their IDWG by controlling blood glucose (20). In this study, the hemoglobin $A_{1}c$ percentage in diabetic patients did not change significantly over the course of 8 years. However, current guidelines recommend the use of glycoalbumin values to manage blood glucose in diabetic patients undergoing dialysis. However, our intervention period took place when blood glucose was still being managed based on hemoglobin $A_{1}c$ levels ; thus, we are uncertain whether blood glucose was strictly managed. For hemodialysis patients with diabetes mellitus, it may be necessary to augment nutritional counseling to include information about managing blood glucose. Our underweight female participants found it difficult to decrease their IDWG. Thin hemodialysis patients have more severe salt and water restrictions than other patients and may benefit more from high-calorie and -protein diets than strict salt and water restrictions. In our study, although the percentage of patients taking multiple antihypertensive drugs increased, the number of subjects with normal BP decreased and the number of patients with grade III hypertension patients increased in the control period. As reported in previous studies (21), patients receiving hemodialysis may have difficulty lowering their BP, even if they are taking multiple antihypertensive drugs. Two years into the intervention period, the mean pre-dialysis systolic BP had decreased significantly. Concurrently, the percentage of patients taking multiple antihypertensive drugs decreased. This result is in concordance with that of a previous study (10-12), which found that salt and water restrictions are important in the treatment of hypertensive hemodialysis patients.

Agarwal *et al.* (22) reported that it is important for BP management of hemodialysis patients to measure their BP at home. However, our study began before their results were published and thus most of our patients did not measure their BP at home. In the future, it may be beneficial to tailor counseling on the basis of the results of home BP monitoring. Moreover, in this study, few patients underwent ongoing echocardiographic examinations. Thus, we could not investigate changes in cardiac function. We hope to do so in future studies.

CONCLUSION

Our findings suggest that long-term nutritional counseling by a nationally registered dietitian may improve the IDWG ratio and BP of hemodialysis patients by decreasing their salt and water intake.

CONFLICT OF INTEREST STATEMENT

None declared.

ACKNOWLEDGMENTS

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LIST OF ABBREVIATIONS

ACE inhibitor, angiotensin-converting enzyme inhibitor ; ARB, angiotensin II-receptor blocker ; IDWG, inter-dialysis weight gain ; nPCR, normalized protein catabolic ratio

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