

EFFECT OF RENAL SPECIFIC ORAL NUTRITION (ONCE RENAL) ON DIETARY INTAKE AND SERUM ELECTROLYTES IN CHRONIC KIDNEY DISEASE STAGE IV

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Abstract

Background and Objective: Low nutritional intake is common in advanced chronic kidney disease (CKD) and poses a direct risk for malnutrition. Our study evaluated the effects of a renal specific oral nutrition (ONCE Renal) supplement concerning nutritional status, minerals and electrolytes among patients with stage IV CKD.

Methods: A total of 32 patients with CKD with an estimated glomerular filtration rate 16-29 mL/min/1.73 m², well-nourished subjects and anticipated good compliance with the diet received the ONCE Renal diet instead of 1 meal daily for 30 days. Dietary protein and energy intake, body compositions, and serum concentrations of urea, creatinine, calcium, magnesium, phosphate and albumin were assessed at baseline, and at 30 days. A dietary intake by three-day food record was also evaluated by a registered dietitian.

Results: At the end of 30 days, significant improvements in energy, fat, fiber and magnesium intake by dietary interview were noted. In addition, the patients also increased body weight and body mass index after supplement. No significant changes in renal function, serum electrolytes, calcium, phosphorus, magnesium concentration and other nutritional markers including serum albumin, body compositions and protein equivalence of total nitrogen appearance were observed during study. The compliance with the ONCE Renal diet was good among enrolled patients and no adverse reactions were found.

Conclusion: Renal specific oral diet supplement can improve energy intake, body weight and maintain serum electrolyte concentrations among patients with stage IV CKD.

Keywords: Renal specific oral nutrition, Low protein diet supplement, Chronic kidney disease, Serum electrolytes, Nutritional status

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INTRODUCTION

Malnutrition and chronic inflammatory state are common among patients with advanced chronic kidney disease (CKD) and are associated with increased hospitalization and mortality rates.^(1, 2) Strong relationships exist among malnutrition, inflammation and atherosclerosis in CKD. The major causes of malnutrition in CKD include reduced food intake and appetite due to effects of uremia, reduced absorption of nutrients, metabolic acidosis, increased protein loss from chronic inflammation and oxidative stress.^(3, 4)

Suboptimal dietary intake and resting energy expenditure is increased among patients with advanced CKD and hemodialysis with severe hyperparathyroidism.⁽⁵⁻⁷⁾ Therefore, these populations are susceptible to insufficient energy intake with energy intakes below 30 kcal/kg/day.⁽⁸⁾ Oral nutritional supplementation is one of treatment options in these populations. Specific renal diets, designed to increase caloric and fiber intake without high protein, electrolytes and mineral load, are expected to improve energy intake and nutrition status without significant electrolyte abnormality.

Early evaluation and intervention concerning dietary intake may help to prevent malnutrition and CKD progression before and after commencing renal replacement therapy. Currently, dietary supplements among patients with advanced CKD can be challenging to health care teams and patients. Most patients with advanced CKD and undergoing hemodialysis have lower than normal dietary energy intake, and oral nutrition supplements are further needed to achieve intake recommendations.^(9,10) Currently, no consensus guidelines exist on the specific type of oral nutrition supplements and dietary approaches mentioned and strong evidence remains lacking.⁽¹¹⁾ This study aimed to determine the effects of a renal specific oral nutrition (ONCE Renal) diet on biochemical intake, calcium, magnesium, phosphate metabolism, nutrition markers and compliance with the prescribed diet among patients with advanced CKD for 30 days.

MATERIALS AND METHODS

Our prospective interventional study was

conducted at Phramongkutklo Hospital, Bangkok, Thailand, from August to December 2018. All patients were recruited from the outpatient center, examined by the same physician and counseled by the same registered dietitian during the study. This project was approved by the *institutional review board* of the *Royal Thai Army Medical Department* (S005h/61) and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from participants.

Inclusion criteria for subjects with CKD aged 18 to 75 years was estimated glomerular filtration rate (eGFR) of 15 to 29 mL/min/1.73 m² (stages 4 CKD) and those who had <10% change in GFR within 3 months, well-nourished subjects (Subjective Global Assessment score A/B and serum albumin ≥ 3.5 g/dL) and consented to participate in the study. Patients with CKD with active malignancy, severe heart, lung or liver disease, chronic HIV, hepatitis B virus or hepatitis C virus infection, malnourished conditions defined as a loss of $\geq 5\%$ body weight over the past 3 months or serum albumin concentration <3.5 g/dL were excluded from the study.

Baseline information including age and sex of participants was obtained. All participants were interviewed, physically examined, and investigated for underlying medical illness. Weight was measured using a weighing scale and height was measured using a stadiometer to the nearest centimeter with subjects before and after treatment. The body mass index (BMI) was calculated using the formula: $\text{Weight}/(\text{Height})^2$ (kg/m²). Casual systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using a standard mercury sphygmomanometer applied on the same arm after a 10-minute rest in the sitting position.

About 7 mL of venous blood after an 8-hour fast was obtained from patients to perform biochemical tests including fasting plasma concentrations of blood urea nitrogen (BUN), creatinine, electrolytes, calcium, phosphorus, magnesium and albumin before and after treatment. All participants performed self-directed 24-hour urine collections for protein, sodium, potassium, magnesium and chloride. Serum and urine creatinine samples were analyzed using the enzymatic method. GFR, using the CKD-EPI equation based on serum creatinine, was calculated.

Table 1. Contents of the ONCE Renal Supplement

Macronutrient	1 serving or 76 g (360 kcal)
Caloric Distribution of Macronutrients (%)	
- Protein	8%
- Carbohydrate	52%
- Fat	40%
Source	
Protein	7.19 g
1. Casein	3.595 (50%)
2. Soy protein isolate	3.595 (50%)
Carbohydrate	48.25 g (fiber 2.99 g)
1. Maltodextrin	31.3 (64.88%)
2. Isomaltulose	9.97 (20.66%)
3. Fructose	3.99 (8.27%)
4. Fibersol	1.99 (4.13%)
5. Fructooligosaccharides	1.00 (2.06%)
Fat	15.95 g
1. Canola oil	6.98 (43.74%)
2. High oleic safflower oil	2.99 (18.77%)
3. Medium chain triglycerides oil	5.98 (37.49%)
Micronutrient	
Vitamins & Minerals	
Vitamin A (mcg RE)	67.43
Vitamin D (IU)	15.20
Vitamin C (mg)	36.27
Calcium, mg	143.6
Phosphorus, mg	143.6
Magnesium, mg	39.06
Potassium, mg	197.4
Sodium, mg	132.8
Carnitine, mg	99.71
Others	As Thai RDI recommendation

Body composition was evaluated using direct segmental multi-frequency bioelectrical impedance analysis (DSM-BIA, In-Body (720) body compositions analyzer). The spectrum of electrical frequencies was used to predict the body composition, total fat mass, intracellular (ICW) and extracellular water (ECW) compartments of the total body water (TBW) in the various body segments. Body composition was assessed at baseline and at the end of the study period.

Dietary Intervention

All participants were provided 360-kcal sachets of ONCE Renal supplement containing 7.19 g of proteins, 48.25 g of carbohydrate with fiber 2.99 g, 15.95 g of fat, 143.6 mg of calcium, 143.6 mg of phosphorus, 197.4 mg of potassium and 132.8 mg of sodium (Table 1) instead of 1 meal daily for 30 days. Additional 30 ONCE Renal supplement sachets were provided at first visits, and empty sachets were collected to determine compliance.

All participants kept a 3-day food record and underwent dietary interviews by a registered dietitian, before and after the study period. Nutrient composition of the diets was analyzed

using the standard national food database program (Inmucal Version 3.2). Daily protein intake was determined using the calculated protein equivalence of total nitrogen appearance (PNA).

Statistical Analysis

Data were analyzed using the statistical package for social sciences (SPSS), Version 16.0 (SPSS, Chicago, IL, USA). Continuous variables were presented as means and standard deviation and discrete variables were presented as percentages. Comparisons against the baseline measurements were evaluated using the paired *t*-test while *P* values <0.05 were considered significant.

RESULTS

We reviewed the eligibility criteria of 62 patients, and 32 patients were recruited during the period of study, consisting of 15 men and 17 women with mean age 66.4± 11.9 years. Hypertension (84.4%), dyslipidemia (81.3%) and type 2 diabetes (33.3%) were common comorbid diseases. Baseline participant characteristics are shown in **Table 2**.

Table 2. Characteristics of the study population

Characteristics	N=32
Men (N, %)	15 (46.9%)
Age (yr)	66.4± 11.9
Height (cm)	161.0±8.9
Body weight (kg)	66.4±13.6
Body mass index (kg/cm ²)	25.5±3.5
Blood urea nitrogen (mg/dL)	34.6±11.7
Serum creatinine (mg/dL)	2.6±0.6
Estimated glomerular filtration rate (mL/min/1.73 m ²)	22.1±6.0
Serum albumin (g/dL)	4.4±0.3
Comorbid disease (N, %)	
- Diabetes mellitus	11 (33.3%)
- Hypertension	27 (84.4%)
- Gout	8 (24.2%)
- Dyslipidemia	26 (81.3%)

Values presented as n (%) and mean±SD.

Table 3. Dietary intake with three-day food record at baseline and the end of one month follow-up

Per day	Nutritional Recommendation in CKD stage III-IV	Baseline	End	Mean Change (95%CI)	p-value
Energy (kcal)	-	1292.9±392.6	1462.3±281.1	169.4 (57.1 to 281.7)	0.004
Energy (kcal/kg/day)	30-35	19.8±6.1	22.5±5.3	2.7 (0.9 to 4.5)	0.005
Protein (g)	-	49.2±15.1	47.4±15.9	-1.8 (-4.2 to 7.7)	0.551
Protein (g/kg/day)	0.6-0.8	0.7±0.2	0.7±0.3	0.02 (-0.1 to 0.1)	0.595
Carbohydrate (g)	-	190.4±56.4	201.7±45.1	11.3 (-4.5 to 23.7)	0.114
Fat (g)	Saturated fat <7% Trans fat <1%	40.7±14.9	50.9±15.2	10.1 (4.9 to 14.3)	<0.001
Fiber (g)	25-38	8.8±3.2	11.0±3.7	2.2 (0.8 to 3.2)	<0.001
Sodium (mg)	<2,300	2331.1±1016.7	2112.6±1278.1	207.4 (-297.9 to 712.7)	0.409
Potassium (mg)	<1,500 with hyperkalemia	1242.6±537.7	1219.9±353.9	29.6 (-143.9 to 203.2)	0.730
Calcium (mg)	-	372.7±171.2	415.5±198.0	49.1(-123.7 to 25.6)	0.190
Phosphorus (mg)	<800-1,000 with hyperphosphatemia	518.9± 227.1	600.2±188.3	81.2 (-167.4 to 5.1)	0.064
Magnesium (mg)	-	56.5±45.9	80.6± 26.3	25.0 (10.4 to 39.7)	0.001

Values presented as Mean±SD. and Mean change (95%CI). p-value corresponds to Paired t-test.

Table 4. Comparison of two regular meals per day without the ONCE renal supplement at aseline and at the end of study

Per day	Baseline	End	Mean Change (95%CI)	p-value
Energy (Kcal)	900.8 ± 287.7	923.2 ± 287.6	22.3 (-104.8, 60.2)	0.585
Energy (kcal/kg/day)	13.9 ± 4.8	13.9 ± 4.1	0.05 (-12.9, 1.2)	0.935
Protein (g)	38.1 ± 19.9	41.5 ± 23.9	3.3 (-7.7, 1.1)	0.133
Protein (g/kg/day)	0.8 ± 0.3	0.6 ± 0.3	0.04 (-0.1, 0.02)	0.229
Carbohydrate (g)	126.4 ± 55.1	120.7 ± 49.4	-5.6 (-7.2, 18.5)	0.378
Fat (g)	26.6 ± 10.3	30.3 ± 14.1	3.67 (-8.2, 0.8)	0.106

Values presented as Mean±SD. and Mean change (95%CI). p-value corresponds to Paired t-test.

Energy and Nutrient Intake

Table 3 shows the mean values for estimated energy and nutrient intake at baseline and at week 4. A significant increase in energy intake from 19.8±6.1 to 22.5±5.3 kcal/kg/day ($p=0.005$), fat intake from 40.7±14.9 to 50.9±15.2 g/day ($p<0.001$) and fiber intake from 8.8±3.2 to 11.0±3.7 g/day ($p<0.001$) were observed during the study. No significant change was found in

dietary protein, carbohydrate, sodium, potassium, calcium and phosphorus intake after intervention except significant increase in magnesium intake [25.0 (95% CI 10.4 to 39.7) g/day, $p=0.001$]. We also determined that energy and nutrient intake from regular food (2 meals daily) was similar at baseline and at the end of the study (**Table 4**).

Table 5. Nutritional, electrolyte, mineral and renal parameters at baseline and at the end of four-week follow-up

Variables	Baseline	End	Mean Change (95%CI)	p-value
Nutrition parameters and body compositions				
Body weight (kg)	66.4±13.6	66.9±13.3	0.45 (0.74 to 0.84)	0.021
Body mass index (kg/cm ²)	25.5±3.5	25.6±3.4	0.17 (0.22 to 0.32)	0.026
Serum albumin (g/dL)	4.4±0.3	4.5±0.3	0.03 (-0.12 to 0.65)	0.557
Percentage of total body water (%)	46.9±5.9	46.7±5.5	-0.25 (-0.42 to 0.90)	0.453
Percentage of body fat (%)	30.4±8.2	30.8±7.6	0.39 (-1.48 to 0.70)	0.466
Muscle mass (kg)	43.9±10.8	42.6±10.5	-1.36 (-1.38 to 4.10)	0.319
Bone mass (kg)	3.2±3.7	3.2±3.8	0.01 (-0.09 to 0.66)	0.748
Protein equivalence of total nitrogen appearance (g/kg/day)	0.7±0.2	0.7±0.2	-0.06 (-0.01 to 0.12)	0.095
Renal function, serum electrolytes and minerals				
Blood urea nitrogen (mg/dL)	34.6±11.7	34.3±11.3	-0.34 (-1.64 to 2.33)	0.726
Serum creatinine (mg/dL)	2.6±0.6	2.5±0.6	-0.07 (-0.15 to 0.01)	0.109
Estimated glomerular filtration rate (mL/min/1.73 m ²)	22.1±6.0	22.9±6.3	0.77 (-2.56 to 1.02)	0.387
Sodium (mEq/L)	137.5±22.6	140.9±1.7	3.46 (-11.50 to 4.58)	0.387
Potassium (mEq/L)	4.6±0.4	4.5±0.5	-0.09 (-0.05 to 0.24)	0.193
Bicarbonate (mg/dL)	23.8±2.5	24.3±2.6	0.55 (-1.34 to 0.25)	0.171
Calcium (mg/dL)	9.4±0.5	9.3±0.4	-0.02 (-0.11 to 0.16)	0.718
Phosphorus (mg/dL)	3.7±0.5	3.7±0.5	0.03 (-0.18 to 0.13)	0.701
Magnesium (mg/dL)	2.8±3.6	2.2±0.2	-0.65 (-0.66 to 1.96)	0.316
24-hr urine protein, electrolytes and minerals				
Protein (g/day)	0.9±1.1	1.0±1.3	0.06 (-0.22 to 0.10)	0.472
Sodium (mEq/day)	90.4±36.2	97.7±67.1	7.37 (-31.04 to 16.30)	0.530
Potassium (mEq/day)	17.3±7.3	17.3±7.3	-0.01 (-2.76 to 277)	0.998
Magnesium (mEq/day)	3.8±1.8	3.9±1.7	0.05 (-0.62 to 0.51)	0.858
Chloride (mEq/day)	71.4±34.7	78.7±71.5	7.33 (-34.23 to 16.57)	0.582

Values presented as Mean±SD. and Mean change (95%CI). p-value corresponds to Paired t-test.

Nutrition and body compositions

A significant increase in body weight with a mean difference of 0.45 (95% CI 0.74 to 0.84, $p=0.021$) kg and BMI with a mean difference of 0.17 (95% CI 0.22 to 0.32, $p=0.026$) kg/cm² were observed after 30 days. No significant changes in serum albumin, PNA and body compositions were found at the study endpoint (**Table 5**).

Serum and Urine Biochemical Measurement

At the end of the study, the treatment did not significantly change the concentrations of renal function, serum sodium, potassium, bicarbonate, calcium, phosphorus, and magnesium.

No significant differences were observed in 24-hour urine protein, electrolytes and minerals before and after treatment. During the study, no serious complications were observed especially electrolyte disturbances and fluid overload. At the study's completion, patient compliance, receiving the ONCE Renal supplementation on schedule, was 99.7%

Discussion

The results of our study showed that the daily use of a 360-kcal ONCE renal supplement for 30 days improved energy, fat, fiber, and body weight among patients with stage IV CKD, indicating

that the use of these supplement had beneficial effects on dietary nutrient intake without short term electrolytes disturbance.

Loss of appetite, poor food intake, anorexia and vomiting are more common symptoms among patients with advanced CKD; hence, predisposing them to malnutrition. Several studies have indicated that minimum calorie requirements were not met among patients with advanced CKD, despite dietary nutritional counseling.⁽⁸⁾ Enriched nutritional supplements might improve dietary intake and malnutrition. However, limited evidence exists pertaining to the impact of nutritional supplementation in preventing malnutrition and improving quality of life among patients with CKD and undergoing dialysis.^(12, 13) Most clinical guidelines preferred oral nutritional supplements as first line treatment to increase caloric and protein dietary intake at 25 to 30 kcal/kg/day and 0.55 to 0.6 g/kg/day in advanced CKD.^(14, 15) Our study indicated that the ONCE Renal diet significantly improved energy and fiber intake and maintained nutritional markers among patients with advanced CKD. This study was consistent with results found in other studies and a systematic review demonstrating effectiveness of renal dietary intervention for patients with advanced CKD and dialysis populations.⁽¹⁶⁻²⁰⁾ Studies are limited concerning the efficacy of specific renal supplement in a long term study and among significantly malnourished patients with CKD.

Medical nutrition therapy by a registered dietitian experienced in predialysis CKD improved nutrition-related biomarkers,⁽²¹⁾ but energy and dietary component targets may be difficult to achieve with dietary counseling alone.⁽²²⁾ An additional benefit of the ONCE Renal supplement is the low amount of protein (7.2 g/360 kcal), sodium (132 mg/360 kcal), phosphate (143 mg/360 kcal), potassium (197 mg/360 kcal) and magnesium (39 mg/360 kcal) content. As a consequence, serum potassium, magnesium and phosphate did not increase after treatment, which was of significant benefit to patients. Moreover, our study indicated that the ONCE Renal diet supplement instead of 1 regular meal could achieve the therapeutic targets of dietary intake with an average dietary sodium intake of 2.1 g/day,

average 24-hour urine sodium of 98 mEq/day, average dietary potassium intake of 1.2 g/day, average 24-hour urine potassium of 17 mEq/day, average dietary phosphorus intake of 0.6 g/day and average dietary magnesium intake of 80 mg/day in addition to dietary counseling. The ONCE Renal supplement did not increase risk of electrolyte abnormality among patients with advanced CKD.

Inadequate energy and excess protein intake were correlated with worsening renal function in CKD⁽²³⁾ and ensuring compliance is the main target for effective nutritional intervention.⁽²⁴⁾ Related studies have shown that about 40 to 50% of patients with CKD follow the recommended diets.^(25, 26) In contrast to our study, compliance was very good; 99% of patients complied with the ONCE Renal supplementation for 30 days, improving an average additional caloric intake with low amount of protein (7.2 g/360 kcal). The high percentage of compliance may reflect the type of patient selection in our study in that they received the intervention based on their excellent reputation for nutritional management. Therefore, the ONCE Renal diet was convenient for educated patients with CKD unable to choose an appropriate low protein renal diet to maintain adequate energy intake. However, patient compliance was limited by the relatively short period of follow-up.

The study had a few limitations. First, the study design was not randomized or placebo-controlled. Second, the INMUCAL program could not represent all micronutrients completely, especially magnesium (validity 36.3%).⁽²⁸⁾ Therefore, the amount of magnesium was shown lower than usual diets. Furthermore, the study was conducted in an outpatient clinic setting, and a 3-day dietary recall was used to estimate food intake. The validity of this method could be questioned because the day-to-day food intake may have varied, and it may not be representative of a usual diet.

In conclusion, the results provided some beneficial effects of a renal-specific oral nutritional support combined with nutritional counseling among patients with advanced CKD. The ONCE Renal diet improved energy, fiber and magnesium intake without significant short term abnormal electrolyte disturbance. This intervention might require larger studies in other groups of patients with CKD with longer duration of the ONCE Renal supplement.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

Individual clinical data used to support the findings of this study are available from the corresponding author upon request.

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