ORIGINAL RESEARCH

Improvement in Nutritional Status in Patients With Chronic Kidney Disease-4 by a Nutrition Education Program With No Impact on Renal Function and Determined by Male Sex

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Objective: Protein–energy wasting (PEW) is associated with increased morbidity and mortality and a rapid deterioration of kidney function in patients with chronic kidney disease (CKD). However, there is little information regarding the effect of nutrition intervention. The aims of this study were to evaluate the efficacy and safety of a nutrition education program (NEP) in patients with nondialysis dependent CKD (NDD-CKD), based on the diagnostic criteria for PEW proposed by the International Society of Renal Nutrition and Metabolism. The design of the study was a 6-month longitudinal, prospective, and interventional study. The study was conducted from March 2008 to September 2011 in the Nephrology Department of La Paz University Hospital in Madrid, Spain.

Subjects: A total of 160 patients with NDD-CKD started the NEP, and 128 finished it.

Intervention: The 6-month NEP consisted of designing an individualized diet plan based on the patient's initial nutritional status, and 4 nutrition education sessions.

Main Outcome Measures: Changes in nutritional status (PEW) and biochemical, anthropometric and body composition parameters.

Results: After 6 months of intervention, potassium and inflammation levels decreased, and an improved lipid profile was found. Body mass index lowered, with increased muscle mass and a stable fat mass. Men showed increased levels of albumin and prealbumin, and women showed decreased proteinuria levels. The prevalence of PEW decreased globally (27.3%-10.9%; $P = .000$), but differently in men (29.5%-6.5%; $P = .000$) and in women (25.4%-14.9%; $P = .070$), 3 of the women having worsened. Kidney function was preserved, despite increased protein intake.

Conclusion: The NEP in NDD-CKD generally improved nutritional status as measured by PEW parameters, but individual poorer results indicated the need to pay special attention to female sex and low body mass index at the start of the program.

Introduction

PROTEIN–ENERGY WASTING (PEW) is defined as "the state of decreased body pools of protein with or without fat depletion or a state of diminished functional capacity, caused at least partly by inadequate nutrient intake relative to nutrient demand and/or which is improved by nutritional repletion."[1]

Among the primary causes of PEW in patients with nondialysis-dependent chronic kidney disease (NDD-CKD) are inadequate nutrient intake due to the anorexia caused by kidney function deterioration, difficulties in adhering to dietary restrictions or to social and economic factors, and hypercatabolism caused by the disease itself or by comorbidities, oxidative stress, and acidemia.[2]

Uremic malnutrition in predialysis patients is associated with increased morbidity and mortality,[3] as well as a poorer quality of life[4] and greater deterioration of kidney function,[5] which affects the prognosis of patients on dialysis.[6]

Both the National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines[7] and the International Society of Renal Nutrition and Metabolism (ISRNM)[8] expert committee recommend nutritional intervention during the treatment of predialysis patients. There are few studies, however, that assess the effect of nutritional intervention on these patients,[9-12] and we have not found any studies that use the ISRNM criteria to define PEW; its prognostic value in terms of survival in advanced CKD has therefore been clearly underanalyzed, despite its existence and wide acknowledge.

The potential reversing effects of early intervention on PEW are hypothesized here.

The aims of this study were to evaluate the efficacy of a nutritional education program at the predialysis stage, based

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on the diagnostic criteria for PEW proposed by ISRNM, and to assess its safety, relative to kidney function deterioration.

Methods

Study Participants

The initial number of participants in the NEP was 160, with 128 completing the study. The reasons for dropout were as follows: 14 required dialysis therapy, 8 failed to attend subsequent visits, 6 changed hospital, and 4 died. The recruitment period was from March 2008 to September 2011.

The inclusion criteria were creatinine clearance $<$20 mL/minute/1.73 m^2 in stages 4 and 5, not 5d (20 patients had creatinine clearances $<$30 mL/minute/1.73 m^2); age $\geq$18 years; no deterioration of cognitive abilities; and signed informed consent. Exclusion criteria were patients with active neoplasia, active infection, or severe lung disease; any patients who had begun kidney replacement therapy; or patients who had been hospitalized during the study period.

The study was approved by the Ethics Committee of La Paz University Hospital and was conducted according to the guidelines of the Declaration of Helsinki. The patients signed a written informed consent before inclusion.

Study Design

A 6-month longitudinal, prospective, and interventional study, performed on a total of 160 patients. The complete population was selected from patients in the advanced kidney disease care program at the Nephrology Department of La Paz University Hospital.

Nutrition Education Program

Selected patients were included in a nutrition education program (NEP), consisting of the design of an individualized diet plan based on the patient's initial nutritional status, attendance at 4 nutrition education sessions and nutritional assessment, and monitoring over a period of 6 months.

The intervention was administered by a single dietitian, aimed at providing a personalized dietary prescription (including energy [25-35 kcal/kg/day] and protein [0.75-1.0 g/kg/day]).[7]

In the nutrition education sessions, the patients were addressed over protein and energy intake, content of phosphorus and potassium in foods, cooking techniques, and a fourth issue chosen according to the patient's specific needs; for example, content of fat, cholesterol, or sucrose in foods. We also elaborated a dietary plan after obtaining information from a 3-day dietary record. We used photographic albums as material support to estimate portions size or to explain patients how to read and understand food labels.

Thirty-two patients (25%) required specific nutritional support (oral supplementation).

During the program, the patients continued with their usual medical treatment.

Clinical data were collected at the beginning of the NEP.

Laboratory Parameters

Preprandial blood samples were collected: albumin, prealbumin, creatinine clearance, serum creatinine, serum potassium, serum phosphorus, C-reactive protein, total lymphocyte count, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides. Also collected were 24-hour urine variables: diuresis volume and proteinuria levels. The analysis of biochemical parameters was performed according to the standardized method used in the Biochemistry Unit Laboratory of La Paz University Hospital.

Normalized protein nitrogen appearance (nPNA) was calculated using the formula proposed by the National Kidney Foundation.[7]

Anthropometrics and Body Composition

Anthropometric measurements were performed using standard techniques following the recommended international regulations (World Health Organization, 1976). These measurements were taken with the patients in underwear and barefoot. Weight was measured using a single frequency body composition analyzer (TANITA BC-420 MA; Biológica Tecnología Médica S.L., Barcelona, Spain). Height was measured using a measuring rod with pinpoint accuracy (range: 80-200 cm). The mid-arm circumference (MAC) was measured using a stretchable measuring tape. The tricipital skinfold (TSF) was measured using a Holtain caliper with a jaw-width of 20 cm and sensitivity of 0.2. The mid-arm muscle circumference (MAMC) was calculated, in centimeters, as follows: $MAMC = MAC - (3.14 \times TSF)$.

Body mass index (BMI) was calculated on the basis of the weight and height measurements (weight [kilogram]/height^2).[7]

Measures of body composition included bioimpedance analysis (BIA-101; Akern Systems, Florence, Italy) at 50 kHz.

Dietary Intake

The overall dietary intake of each patient was recorded in a food intake record for 3 consecutive days, listing all food intake (including hydration); 1 of these days was on a weekend. The caloric and nutritional value of the diet was quantified using DietSOURCE®3.0 nutritional software. The values obtained were compared with current recommendations in the Kidney Disease Outcomes Quality Initiative guidelines.[7]

Nutrition Assessment

The nutritional assessment was performed according to PEW criteria proposed by the ISRNM.[1]

To determine nutritional status according to ISRMN criteria, the patient must have met 1 criterion out of 3 in the 4 categories that determine the presence of PEW, maintaining it over a period of 2 months:

- Biochemical category: <3.8 g/dL; prealbumin <30 mg/dL body mass; cholesterol <100 mg/dL without lipid-lowering medication (in our case, this criterion was not used, given that a total of 147 patients consumed such medication).
- Body mass category: BMI <23 kg/m^2; unintentional 5% weight loss over the last 3 months or of 10% over the last 6 months.
- Muscle mass category: Loss of 10% of MAMC muscle mass in relation to percentile 50.
- Intake category: Protein catabolism rate (nPNA) < 0.6 g; energy intake <25 kcal/kg adjusted to weight/day.

Adherence

Adherence was assessed on completion of the intervention, using a score of 0 to 10 based on the compliance with the guidelines and the effort invested. We asked: "*How would you score the effort invested to 0- 10?*" and, "*How would you score the compliance of the recommendations to 0-10?*". A visual analog scale was used as material support.

Statistical Analysis

Qualitative variables are described using absolute frequencies and percentages; for quantitative variables, the mean and standard deviations (X ± SD) are used.

The comparison of qualitative variables between 2 groups was performed using the chi-squared test, test and/or Fisher's exact test, depending on the data distribution. Wilcoxon test (quantitative variables) and McNemar test (qualitative variables) were performed to compare differences between the beginning and the end of the program in each individual. The comparison of quantitative variables between 2 groups was performed using the Mann–Whitney U test or Student's *t*-test, depending on the data distribution.

All the statistical tests were bilateral, with a significance level of 0.05. Statistical analysis was performed using the SPSS 17.0 statistics program.

Results

General Characteristics of the Population

A total of 128 patients with a mean age of 67 ± 14.8 years, 52.3% (*n* = 67) women, completed the NEP. The primary etiology of CKD was diabetes mellitus (54 patients; 42.2%); 4 patients (3.1%) had type I diabetes, followed by nephroangiosclerosis (21 patients; 16.4%), glomerulonephritis (16 patients; 12.5%), polycystic kidney disease (14 patients; 10.9%), unknown etiologies (12 patients; 9.4%), and other (11 patients; 8.6%). General characteristics of the studied population are summarized in Table 1.

Laboratory Parameters Follow-up

At completion, the NEP process was associated with a mild increase in kidney function (creatinine clearance 17.4 ± 3.9 vs. 19.5 ± 6.4 mL/minute; $P < .001$) and decreased levels of urea (136.6 ± 45.1 vs. 133.6 ± 41.2 mg/dL; $P = .048$ mg/dL), nPNA (1.3 ± 0.4 vs. 0.3 ± 1.2 g/kg/day; $P < .001$), and proteinuria at the limit of significance (1.7 ± 2.1 vs. 1.6 ± 2.0 g/24 hours; $P = .060$). Serum potassium (4.8 ± 0.6 vs. 4.6 ± 0.5; $P = .040$) also decreased. The lipid profile showed minor global changes (decreased total cholesterol and low-density lipoprotein cholesterol).

Table 2 shows the follow-up of kidney, metabolic, and inflammation parameters separated by sex; kidney function in both men and women remained stable, with a slight upward trend, and with stable proteinuria levels. Serum potassium and polymerase chain reaction (PCR) levels decreased.

Regarding biochemical parameters related to nutritional status, increases in albumin and prealbumin values were observed in men, whereas increases in total lymphocyte count were observed in women.

Anthropometric and Body Composition Parameter Follow-up

BMI significantly dropped (27.6 ± 5.0 vs. 27.1 ± 4.3; $P = .001$), whereas body composition improved. Muscle mass increased (38.7 ± 9.4 vs. 40.3 ± 9.0; $P = .001$), fat mass remained stable, and the distribution of body fluid

Table 1. Comorbidities and Pharmacological Treatment in the Studied Patients

Comorbidities		Pharmacologic Treatment	
CHF or unresolved ischemia	41 (32%)	Antihypertensive antiproteinuric medication (ACE inhibitors, ARBs, or selective renin inhibitors)	99 (77.3%)
Peripheral arterial disease	40 (31.2%)	Other antihypertensive	77 (66.1%)
Functionally severe physical sequelae	5 (3.9%)	Hypolipidemic agents	99 (77.3%)
Cerebrovascular accident	10 (7.8%)	Phosphate binders	14 (10.9%)
COPD	8 (6.2%)	Potassium binders	16 (12.4%)
DM	54 (42.2%)	Insulin	31 (24.6%)

ACE inhibitors, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptors blockers; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus.

Values are presented as percentages.

Table 2. Kidney, Metabolic, and Inflammation Parameters by Sex

Variable	Men 61 (47.7%)			Women 67 (52.3%)		
	Month 0	Month 6	*P*	Month 0	Month 6	*P*
Albumin (g/dL)	3.5 ± 0.5	3.7 ± 0.4	**.040**	3.5 ± 0.4	3.6 ± 0.3	.146
Prealbumin (mg/dL)	30.0 ± 7	32.1 ± 6.2	**.040**	29.9 ± 6.2	30.7 ± 5.6	.309
Creatinine (mg/dL)	4.0 ± 1.2	3.8 ± 1.3	**.014**	3.5 ± 0.9	3.3 ± 1	.110
ClCr (mL/min)	18.4 ± 3.4	21.1 ± 6.4	**.020**	16.4 ± 4.0	17.8 ± 6	**.013**
Urea (mg/dL)	137.2 ± 49.8	131.1 ± 42.5	.732	136 ± 40.7	136.0 ± 40.1	.956
Volume diuresis (mL/d)	2462.4 ± 632.5	2445.7 ± 710.4	.543	2142.1 ± 682.3	2179.4 ± 711.4	.174
Proteinuria (g/24 h)	1.9 ± 1.7	1.9 ± 1.7	.373	1.5 ± 2.4	1.3 ± 2.2	**.039**
nPNA (g/kg/d)	1.3 ± 0.3	1.1 ± 0.2	**.023**	1.3 ± 0.3	1.2 ± 0.3	**.001**
Potassium (meq/L)	4.8 ± 0.6	4.6 ± 0.5	**.038**	4.8 ± 0.6	4.6 ± 0.4	**.007**
Phosphorous (mg/dL)	4.0 ± 1.0	3.9 ± 0.8	.294	4 ± 0.8	3.9 ± 0.6	.239
CRP (mg/L)	5.0 ± 8.2	3.5 ± 3.9	**.040**	4.4 ± 5.3	3.4 ± 3.9	**.004**
Total lymphocyte count (lymph/cc)	1745.9 ± 718.4	1732.3 ± 675.5	.454	1636 ± 491.8	1965.7 ± 238.3	**.013**
Cholesterol (mg/dL)	172 ± 48.5	157.5 ± 36.0	**.009**	184.2 ± 43,6	180.8 ± 38	.625
LDL-C (mg/dL)	107.4 ± 34.6	100.1 ± 23.9	**.049**	116.8 ± 33.1	110 ± 31.6	**.044**
HDL-C (mg/dL)	45.6 ± 13.6	44.0 ± 13.6	.065	53.2 ± 13.7	53 ± 12.5	.790
TG (mg/dL)	136.6 ± 52.5	121.4 ± 31.8	**.046**	138.2 ± 66.3	126.8 ± 48.4	**.040**

ClCr, creatinine clearance; CRP, C-reactive protein; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; nPNA, normalized protein nitrogen appearance; TG, triglycerides.

Values are presented as mean ± standard error of the mean. *P* was calculated by Wilcoxon test. Significant differences are highlighted in bold.

improved with a reduction in the Na/K exchange ratio (1.2 ± 0.3 vs. 1.1 ± 0.2; $P = .045$).

Table 3 shows the follow-up of the anthropometric and body composition parameters by sex. BMI dropped, and muscle mass increased in men. Women showed a slight drop in body weight, maintaining stable body composition. A reduction in extracellular water and an increase in intracellular water were observed in both the men and the women.

PEW Outcome

The NEP contributed toward a significant improvement in nutritional status by reducing the number of patients in a PEW state from 35 patients (27.3%) to 14 (10.9%) ($P = .001$). Nineteen patients (59.7%) with PEW required oral supplementation.

An improvement in the unintentional weight loss criteria was observed; at the start of the program, 59 patients (46.15%) met these criteria, whereas none of them met it

Table 3. Anthropometric and Body Composition Parameters by Sex

Variable	Men 61 (47.7%)			Women 67 (52.3%)		
	Month 0	Month 6	*P*	Month 0	Month 6	*P*
Weight (kg)	77.3 ± 10.7	75.5 ± 9.5	**.010**	65 ± 13.4	64.4 ± 11.7	**.017**
Height (m)	167.2 ± 6.4			153.9 ± 7.3		
BMI (kg/m^2)	27.7 ± 3.7	27.0 ± 3.1	**.010**	27.5 ± 5.9	27.3 ± 5.3	.134
TSF (mm)	15.5 ± 5.9	15.2 ± 5.8	**.043**	22 ± 7.3	21.7 ± 7.1	.053
MAMC (mm^2)	23.9 ± 3.7	24 ± 3.7	.459	22.3 ± 4.2	22.5 ± 3.9	.236
Resistance (Ω)	463.6 ± 57.1	484.1 ± 64.6	**.019**	543 ± 88	543.2 ± 85.7	.680
Reactance (Ω)	41.8 ± 12.3	45.6 ± 11.7	**.019**	41.7 ± 10.5	44.5 ± 9.1	**.029**
Phase angle (°)	5.2 ± 1.3	5.4 ± 1.2	**.040**	4.4 ± 1	4.7 ± 0.8	**.003**
Exchange Na/K	1.2 ± 0.3	1.1 ± 0.2	.612	1.3 ± 0.3	1.2 ± 0.2	**.010**
Body cell mass (%)	45.5 ± 8.1	46.4 ± 6.5	.330	43.2 ± 8.5	46.8 ± 7.9	**.040**
Total body water (%)	57 ± 6.1	56 ± 5.4	**.045**	51.1 ± 7.4	50 ± 6.6	.830
Extracellular water (%)	50.1 ± 6.7	48.7 ± 6.1	**.006**	55.2 ± 6.3	52.5 ± 4.2	**.002**
Intracellular water (%)	49.9 ± 6.7	51.2 ± 6.0	**.018**	44.7 ± 6.2	47.9 ± 4.4	**.001**
Fat mass (%)	27.4 ± 8.7	27.6 ± 8.9	.626	35.8 ± 9.2	36.6 ± 8.8	.681
Fat-free mass (%)	71.8 ± 10.6	72.8 ± 8.2	.910	64.2 ± 9.2	63.5 ± 8.9	.670
Muscle mass (%)	41.6 ± 8.5	43.2 ± 7.4	**.043**	36 ± 9.7	37.7 ± 9.7	**.001**
Body cellular mass index	8.7 ± 2.3	8.9 ± 2.1	.118	7.1 ± 1.9	7.7 ± 2.1	**.003**

BMI, body mass index; MAMC, mid-arm muscle circumference; TSF, tricipital skinfold.

Values are presented as mean ± standard error of the mean. *P* was calculated by Wilcoxon test. Significant differences are highlighted in bold.

on program completion. The same was the case with the nPNA criteria <0.6 (6.3% vs. 0%).

Table 4 shows the evolution of the protein energy wasting state by sex. We found significant differences between the response to nutritional intervention between men and women. Men improved their nutritional status significantly, with only 4 men (6.5%) of 18 (29.5%) having remained in the PEW state. On the contrary, 10 women (14.9%) remained in PEW status (dropping from 17 [25.4%]). The nutritional state actually worsened in 3 of these women after intervention (Fig. 1).

The common criteria of the 4 men at the start of the NEP who remained in a PEW state were older age (78.5 ± 7.1 vs. 69.1 ± 10.6; *P* = .045), lower serum albumin levels (2.8 ± 0.3 vs. 3.3 ± 0.32; *P* = .016), BMI (23.2 ± 1.1 vs. 26.2 ± 2.7; *P* = .002), and body cellular mass index (6.5 ± 2.1 vs. 8.2 ± 2.1; *P* = .045). When we removed the BMI variable from the PEW criteria, only 1 man and 3 women remained in this state, with one of them actually worsening.

Adherence

The analysis of adherence variables showed differences in effort score regarding nutritional intervention by sex (men 8.0 ± 1.3 vs. women 7.1 ± 3.1; *P* = .030), but not in terms of compliance (men 6.7 ± 1.5 vs. women 6.7 ± 2.0; NS).

Characteristics of Women Who Improved Their Nutritional Status

Although we began with a global analysis of results, the different behavior of women in relation to the intervention requires a separate analysis.

We evaluated the female patients demonstrating an improved nutritional status if they did not have PEW at any point during the intervention.

The women classified as having improved their nutritional status maintained their levels of albumin and prealbumin and showed a slight increase in kidney function with a slight reduction in inflammation, measured by C-reactive protein (CRP). As for anthropometric and body composition parameters, BMI dropped and body composition improved. This was determined by a fat deposit reduction with muscle mass increase. Total body water remained stable, with an improvement in the distribution of body fluid, a reduction in extracellular water, and an increase in intracellular water and phase angle.

Comparison of Women in PEW State to Women Who Improved After Nutritional Intervention

Of the 67 women in the study, 10 (14.9%) overcame the wasting state, 7 (10.4%) remained in it, and 3 (4.5%) entered it at the end of the NEP.

Table 4. Protein–Energy Criteria (PEW) Criteria According to Sex

	Men 61 (47.7%)			Women 67 (52.3%)		
Protein–Energy Wasting (PEW) Criteria	Month 0	Month 6	*P*	Month 0	Month 6	*P*
(A) Serum chemistry						
Albumin <3.8 g/dL	40 (65.5%)	36 (59%)	.454	47 (70.1%)	45 (67.1%)	.854
Prealbumin <30 mg/dL (*N* = 102)	15 (24.5%)	11 (18%)	**.049**	19 (28.3%)	17 (25.4%)	.754
Patients meeting the biochemistry category	42 (68.8%)	41 (67.2%)	.900	49 (73.1%)	48 (71.6%)	.900
(B) Body weight and fat (body mass)						
BMI <23 kg/m^2	8 (13.1%)	6 (9.8%)	.625	19 (28.3%)	17 (25.4%)*	.625
Unintentional weight loss: 5% over 3 mo or 10% over 6 mo.	28 (45.9%)	0 (0%)	**.000**	31 (46.2%)	0 (0%)	**.000**
Fat mass <10%	2 (3.2%)	2 (3.2%)	1.000	1 (0.1%)	1 (0.1%)	1.000
Patients meeting body mass category	30 (49.1%)	6 (9.8%)	**.000**	33 (49.2%)	17 (25.4%)	**.000**
(C) Muscle mass						
MAMC: reduction >10% in relation to 50th percentile	25 (41%)	23 (36.7%)	.800	23 (34.3%)	24 (35.8%)	1.000
Reduced muscle mass: 5% over 3 mo	–	0 (0%)		–	0 (0%)	
Patients meeting the muscle mass category	25 (41%)	23 (36.7%)	.754	23 (40.3%)	24 (35.8%)	1.000
(D) Dietary intake						
nPNA <0.6	2 (3.2%)	0 (0%)	**.000**	6 (8.9%)	0 (0%)	**.000**
Unintentional low dietary energy intake <25 kcal/kg/d for 2 mo	22 (36.1%)	18 (29.5%)	.557	18 (26.8%)	17 (25.3%)	1.000
Patients meeting the protein intake category	22 (36.1%)	18 (29.5%)	.090	18 (26.8%)	17 (25.37%)	1.000
PEW	18 (29.5%)	4 (6.5%)	**.000**	17 (25.4%)	10 (14.9%)	.070
PEW (without BMI)	18 (29.5%)	1 (1.6%)	**.000**	14 (20.9%)	3 (4.3%)	**.001**

BMI, body mass index; MAMC, mid-arm muscle circumference; nPNA, normalized protein nitrogen appearance.
Values are presented as percentages. *P* was calculated by McNemar test. Significant differences are highlighted in bold.
*Significant differences at 6 months between women and men.

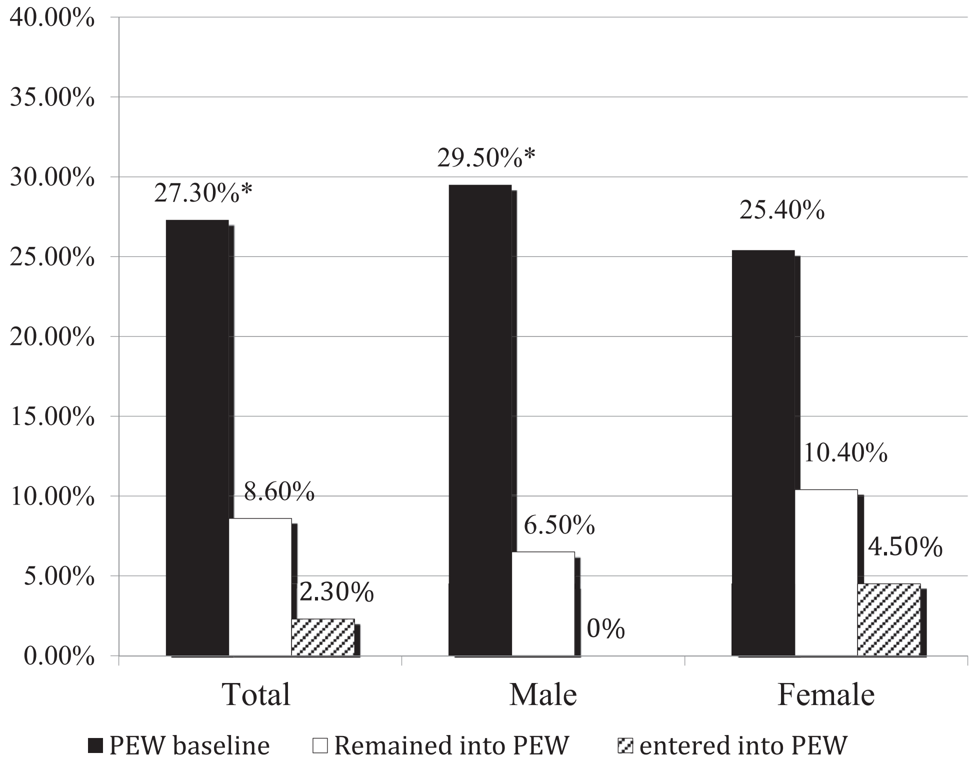

Figure 1. Protein–energy wasting evolution by sex. Percentage of subjects, total and by sex, with PEW at baseline and at the end of the nutrition intervention, and the subjects who entered into PEW during the intervention. *P* was calculated by the chi-squared test. *Statistically significant differences ($P < .05$) between baseline and the end of nutritional intervention.

Table 5 shows the variables that underwent a significant modification or that were approaching limits of significance in the 10 women who showed a reversed PEW state compared with those who maintained or entered into it.

The group of women who failed to reverse or who worsened their nutritional status showed a significantly lower BMI at starting NEP, with no other difference detected in baseline. After the program, a slight increase in kidney function and prealbumin levels were detected, along with a reduction in proteinuria, nPNA, and PCR levels.

Those who improved their nutritional status increased their levels of albumin and prealbumin, with no other biochemical variable change.

Among the anthropometric variables, weight increased in both groups, although significant differences were reached only when wasting status was reversed, with an improved distribution of body fluids. We did not find differences in the other variables analyzed.

The 3 women whose nutritional status worsened had a lower BMI (22.9 ± 4.4 kg/m^2) adjusted for age (65.4 ± 7.3 years), depletion of muscle mass at baseline, as well as low food intake over time in their dietary histories. No values changed after the intervention except energy and protein intake, which dropped.

Discussion

Few studies have investigated nutritional status in patients with NDD-CKD, although its importance is recognized. In our study, we found a malnutrition prevalence of 27.3%, which is higher than the 11% of this population found in Norway[13] and lower than the 63.7% found in Brazil,[14] although both studies use different scales to define the disorder.

There are also few studies evaluating the effect of nutritional intervention before commencing dialysis, with none using ISRNM criteria to define PEW, and their sample size and demographics being clearly different. Campbell et al.[4] performed a 4-month study on a control group of 27 patients who only received written material and on an intervention group of 24 who received individual nutritional education. The control group increased the proportion of patients with malnutrition measured by a subjective global assessment scale from 11% to 22%, whereas all the patients in the intervention group diagnosed with malnutrition (20.8%) reversed their situation. Concordantly, our study did show a reduction in patients with PEW, but we unexpectedly found that nutritional status actually worsened in 3 patients.

Table 5. Characteristics of Women Who Reverse and Do Not Reverse the Wasting Situation

	Women Who Reverse 10 (14.9%)			Women Who Do Not Reverse 10 (14.9%)		
Variable	Month 0	Month 6	*P*	Month 0	Month 6	*P*
Albumin (g/dL)	3.3 ± 0.3	3.6 ± 0.4	**.007**	3.5 ± 0.4	3.6 ± 0.3	.990
Prealbumin (mg/dL)	28.4 ± 6.6	29.5 ± 4.7	**.049**	26.6 ± 5.2	30.9 ± 6.2	**.020**
ClCr (mL/min)	14.0 ± 4.4	15.8 ± 6.0	.320	16.3 ± 4.5	17.0 ± 6.4	**.049**
Proteinuria (g/24 h)	1.2 ± 0.9	1.1 ± 1.9	.635	1.2 ± 0.8	0.6 ± 0.4	**.020**
nPNA (g/kg/día)	1.3 ± 0.5	1.2 ± 0.3	.530	1.3 ± 0.	1.1 ± 0.3	**.010**
CRP (mg/L)	3.4 ± 3.7	3.0 ± 3.4	.990	5.7 ± 6.7	3.1 ± 2.5	**.049**
Weight (kg)	56.9 ± 7.6	58.1 ± 7.7	.050	51.8 ± 11.2	53.1 ± 10.8	.090
BMI (kg/m^2)	24.2 ± 3.2*	24.8 ± 3.6	**.038**	21.0 ± 2.9*	21.5 ± 2.6	.092
MUAC (mm^2)	19.9 ± 3.3	20.8 ± 3.2	.06	18.2 ± 1.1	18.6 ± 0.9	.065
Reactance (Ω)	36 ± 12.6	42.5 ± 9.0	.06	32.0 ± 2.6	37.3 ± 1.5	.289
Phase angle (°)	3.7 ± 0.9	4.5 ± 0.9	.06	3.5 ± 0.5	3.8 ± 0.3	.120
Body cell mass (%)	37.8 ± 8.3	46.4 ± 7.7	.06	34.9 ± 2.1	37.6 ± 2.5	.108
Total body water (%)	55.7 ± 2.7	54.4 ± 4.0	.06	58.4 ± 8.4	55.1 ± 9.12	.179
Extracellular water (%)	60.5 ± 7.8	54.6 ± 6.3	.06	59.7 ± 4.9	55.8 ± 2.1	.108
Intracellular water (%)	39.4 ± 7.8	45.4 ± 6.3	.06	40.3 ± 4.9	44.3 ± 2.1	.108
Muscle mass (%)	36.6 ± 5.3	40.4 ± 7.8	.06	34.8 ± 5.1	37.4 ± 4.6	.108
Body cellular mass index	6.0 ± 0.8	7.2 ± 0.9	.06	5.3 ± 0.6	6.0 ± 1.0	.317

BMI, body mass index; ClCr, creatinine clearance; CRP, C-reactive protein; MAMC, mid-arm muscle circumference; nPNA, normalized protein nitrogen appearance.

Values are presented as mean ± standard error of the mean. *P* was calculated by Wilcoxon test. Significant differences are highlighted in bold.

*Differences at baseline between women who reverse and not reverse at baseline, *P* was calculated by Student's t-test.

In another study[10] involving 11 patients with creatinine clearance below 25 mL/minute/m^2 under 6 months of nutritional intervention, the number of malnourished patients dropped from 3 to 1 using the subjective global assessment scale.

Despite the PEW criteria having been widely used in studies on dialysis patients, we found only one study assessing the efficacy of nutritional education compared with oral supplementation. In that series, malnutrition was diagnosed by albumin values <3.5 g/dL and found that the number of malnourished patients fell significantly from 57.4% to 31.3% ($P < .05$) in the nutritional education group. Although it does not assess the PEW state, our study concurs regarding the improvement in albumin levels.[15]

Even if part of the results in our study may be effect of the oral supplementation, we consider that the function of an NEP is not only detecting malnutrition and patients with high risk for malnutrition but also explains how to take supplementation.

As indicated in the literature, differences in sex have an important influence on CKD outcomes.[16] Our study has found that after the intervention, male patients improved their nutritional status significantly, whereas women failed to improve and their nutritional status even worsened. This finding is contrary to the data of Campbell et al.,[4] which showed better results in women because of better adherence to dietary guidelines; nevertheless, our data on adherence have not yielded differences by sex. We believe, in agreement with Westland et al.,[13] that female sex is a risk factor associated with PEW.

In the PEW analysis of improvement, with the exception of the BMI <23 kg/m^2, it is remarkable that only 4 of 32 patients who started in a situation of wasting actually maintained it, therefore suggesting a low BMI as a chronicity of PEW status, indicating a requirement for earlier nutritional intervention. BMI can be influenced by several factors, such as water overload, age, inflammation, and others[17]; we believe, however, that these factors did not influence our affected population group because a normal hydration state and no age influence were detected. One of the common characteristics of the 10 women who completed the study and who remained in a PEW situation was the lower BMI they showed at the start of the study, a fact that highlights the importance of the starting point in any nutritional intervention. The 3 women whose nutritional status worsened also presented a low BMI for their age[18] and low levels of muscle and fat mass, with adequate intake and normal biochemical levels. Consequently, although not includable in the PEW criteria, they showed caloric malnutrition criteria[19] and were examples of the difference between malnutrition and PEW.[20,21]

On the other hand, the 4 men who completed the NEP in a state of PEW presented significantly lower levels of albumin, BMI, and body cellular mass index at the outset than the patients whose nutritional status improved. Defining features of elderly related frailty[22] were observed in these patients, coexisting with wasting, which represents an additional difficulty in improving nutritional status.[23] As a result, we consider that women with caloric malnutrition and men with elderly frailty characteristics are, as have been identified by other authors, groups at risk of PEW,[13] which strongly supports the recommendation of personalization and adaptation of any nutritional support.[2,7]

The literature has endorsed the use of restricted protein diets as a renoprotective measure, ensuring that this will not entail negative effects on nutritional status.[24,25]

We participate in the current open debate on this issue and consider that renal function and nutritional status are determining factors in its use.

One of the limitations of the study is the length of the intervention period. We have observed an improvement in most of the parameters analyzed—many of which at the limit of significance—suggesting that a longer intervention period would have had a greater influence on nutritional status. In addition, an increase in sample size would have enabled us to perform a multivariate analysis.

In conclusion, our study demonstrates the efficacy and safety of a PEN in patients with CKD-NDD by improving the nutritional status measured by PEW parameters and indicates the need to pay special attention to maintaining kidney function, female sex, and low BMI for personalizing more effective nutrition interventions.

Practical Application

The application of individualized nutrition education programs in nondialysis-dependent chronic kidney disease might decrease the levels of malnutrition and the complications from nutritional status on subsequent dialysis.

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