CPE Replacing Phosphorus-Containing Food Additives With Foods Without Additives Reduces Phosphatemia in End-Stage Renal Disease Patients: A Randomized Clinical Trial

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Objective: The purpose of the study was to verify the effects of replacing phosphorus-containing food additives with foods without additives on phosphatemia in end-stage renal disease (ESRD) patients.

Design: Randomized clinical trial.

Setting: Adult patients on hemodialysis for ≥6 months at a single center.

Subjects: A total of 134 patients with phosphorus levels of >5.5 mg/dL were included and were randomized into an intervention group (n = 67) and a control group (n = 67).

Intervention: The IG received individual orientation to replace processed foods that have phosphorus additives with foods of similar nutritional value without these additives. The CG received only the nutritional orientation given before the study. Clinical laboratory data, nutritional status, energy and protein intake, and normalized protein nitrogen appearance (nPNA) were evaluated at the beginning of the study and after 90 days.

Results: There was no initial difference between the groups in terms of serum phosphorus levels, nutritional status, and energy intake. After 3 months, there was a decline in phosphorus levels in the IG (from 7.2 ± 1.4 to 5.0 ± 1.3 mg/dL, $P < .001$), but there was no significant difference in the CG (from 7.1 ± 1.2 to 6.7 ± 1.2 mg/dL, $P = .65$). In the IG, 69.7% of the patients reached the serum phosphorus target of ≤5.5 mg/dL; however, only 18.5% of the CG subjects reached this level ($P < .001$).

Conclusion: At the end, there was no difference between the two groups in terms of nutritional status, energy intake, protein intake, and nPNA. The replacing phosphorus-containing food additives with foods without additives reduced serum phosphorus without interfering in the nutritional status of ESRD patients.

This article has an online CPE activity available at www.kidney.org/professionals/CRN/ceuMain.cfm

Introduction

HYPERPHOSPHATEMIA IS FREQUENT in patients who have chronic renal disease (CRD) and are on hemodialysis, and it is associated with increased risk for cardiovascular diseases, atherosclerotic events, secondary hyperparathyroidism, and bone disease.[1,2] It is also an independent risk factor for increased mortality in patients with end-stage renal disease (ESRD).[3,4] Epidemiologic studies suggest that higher serum phosphate levels, even levels that are well within the normal range, are associated with an increased risk for cardiovascular disease.[5,6] The treatment and prevention of hyperphosphatemia is one of the main objectives in the treatment of patients with ESRD. Phosphorus-binding agents and phosphorus-intake restriction are used to achieve this objective.[7,8] However, phosphorus-intake restriction is associated with protein-intake restriction and a risk of malnutrition.[4–8]

A phosphorus-restricted diet is based on the reduction of foods containing large quantities of the mineral, such as meats, dairy products, whole grain cereals, legumes, and nuts. Furthermore, studies show that the phosphorus in foods is available in both organic and inorganic forms.[9] Organic phosphorus, which is naturally present in foods, has a 60% absorption rate,[10] whereas inorganic phosphorus, which is added to industrialized foods, is absorbed at an estimated rate of 90%.[11] The additives (i.e., phosphorus salt or phosphoric acid) present in industrialized products preserve these foods colors, maintain their moisture, improve their flavor, homogenize their ingredients, and stabilize their proteins.[12,13] The consumption of foods with phosphorus additives has increased in recent decades due to their easy accessibility, which makes nutritional counseling on the reduction of phosphorus intake even more difficult for dialysis patients.[14] In the United States, the average phosphorus intake of men and women in 2009-2010, as measured by the National Health and Nutrition

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Examination Survey, exceeded the recommended daily allowance by up to 2 times.[15] In many countries, the phosphorus intake of the general population and of patients with kidney disease is not well known.

Bell et al. conducted one of the main studies on the effects of phosphorus additives on phosphatemia in healthy subjects,[16] and it showed a significant increase in serum and urinary phosphorus levels. Sullivan et al. showed that the dietary restriction of phosphorus additives in patients who were on hemodialysis had a beneficial effect on phosphatemia, but the patients' protein intake, energy intake, and nutritional status were not considered in the study.[17]

Considering the lack of studies on the dietary restriction of phosphorus additives and the repercussions for nutritional status, we verified the hypothesis that replacing foods that have phosphorus additives with foods that do not have phosphorus additives reduces phosphatemia and maintains the nutritional status of ESRD patients.

Participants and Methods

Patients

This randomized trial was conducted with adult patients who had ESRD and were on hemodialysis at a single center. The Ethics Committee approved the study in November 2011 and the study was conducted in accordance with the guidelines in the Declaration of Helsinki. Written informed consent was obtained from all patients prior to their inclusion in the study. The study was registered at clinicaltrials.gov (NCT01965379). There was not an ongoing related trial.

The inclusion criteria were as follows: hemodialysis treatment for at least 6 months; both sexes; aged ≥18 years; persistent serum phosphorus levels of ≥5.5 mg/dL (at least 3 measurements) during the previous 3 months; absence of infection and neoplasia; preserved cognitive capacity; and reading and writing skills. The exclusion criteria were as follows: the use of enteral or parenteral therapy; the presence of physical limitations; cognitive limitations, or malabsorption diseases. Before the study began, the facility's registered dietitian provided all the participants with a nutritional orientation on the usual renal diet and the importance of restricting the intake of foods rich in phosphorus. The participants also received a nutritional booklet from the dietitian and the nutritional counseling was reinforced each month after the patients received their biochemical test results.

A total of 267 patients were evaluated for eligibility, and 140 patients were randomized into either the intervention group or the control group. According to the sample size calculation, 70 patients were necessary for the intervention group and for the control group (80% power). In the intervention group, three patients were lost (two patients received a transplant and one patient refused to participate); thus, a total of 67 patients were included for primary analysis. Three patients were also lost in the control group (two patients were moved to another facility, and one patient refused to participate). During the follow-up period, one patient was lost from the intervention group, and two patients were lost from the control group. Therefore, 66 intervention group patients and 65 control group patients completed the study. (A flow cart of the study is presented in Fig. 1).

The nutritional status, biochemical parameters, dietary intake of energy, protein, and phosphorus, and normalized protein nitrogen appearance (nPNA) were assessed in both groups at baseline and after 90 days (at the end of the study) by the study dietitian.

Baseline Assessment

The demographic, clinical, and laboratory characteristics of the intervention and control participants were obtained from medical records. The biochemical tests measuring serum creatinine, urea, hemoglobin, serum albumin, and phosphorus levels were performed using an automatic method; serum ionized calcium and intact parathyroid hormone levels were assessed using immunoassays and chemoluminometric assays (ADVIA Centaur, Siemens Healthcare Diagnostics, Erlanger, Germany), respectively. Ionized calcium was used in this study because it is recommended for CRD patients.[18,19] The mean values of the biochemical parameters (measured during the previous 3 months) were considered.

The patients underwent hemodialysis 3 times per week for 4 hours; a standard dialysis bath, a cellulose triacetate dialyzer (2.1 m^2), and a Nipro dialysis machine (Surdial model, Osaka, Japan) were used. The Kt/V was calculated using Dialsist 2.5 software.

Initially, the researcher (who was not blinded) performed individual nutritional interviews; the interview included a 24-hour dietary recall, a food frequency questionnaire,[20] and questions to assess the patient's knowledge about the renal diet.[21,22]

Anthropometric measurements were obtained postdialysis and included body mass index (BMI, kg/m^2), triceps skinfold thickness (TSF, mm), mid-arm muscle circumference (MAMC, cm), and mid-arm muscle area (AMA, cm^2). AMA was calculated from TSF and mid-arm circumference (MAC, cm) and corrected sex using the following formulas: AMA (corrected for males) = $[(\text{MAC (cm)} - \text{TSF (cm)}^2)/4 \times \pi] - 10$; and AMA (corrected for females) = $[(\text{MAC (cm)} - \text{TSF (cm)}^2)/4 \times \pi] - 6.5$.[21,23] The TSF was measured at the mid-point of the upper arm opposite the arteriovenous fistula with a Lange Skinfold Caliper (Beta Technology Incorporated, Cambridge, Maryland, USA). MAMC has been validated in hemodialysis patients and has been shown to be associated with a survival advantage.[24]

Dietary Intake

The dietary recalls and food diaries were analyzed to calculate the energy and protein intake in both groups and to assist in the dietary counseling of the patients in

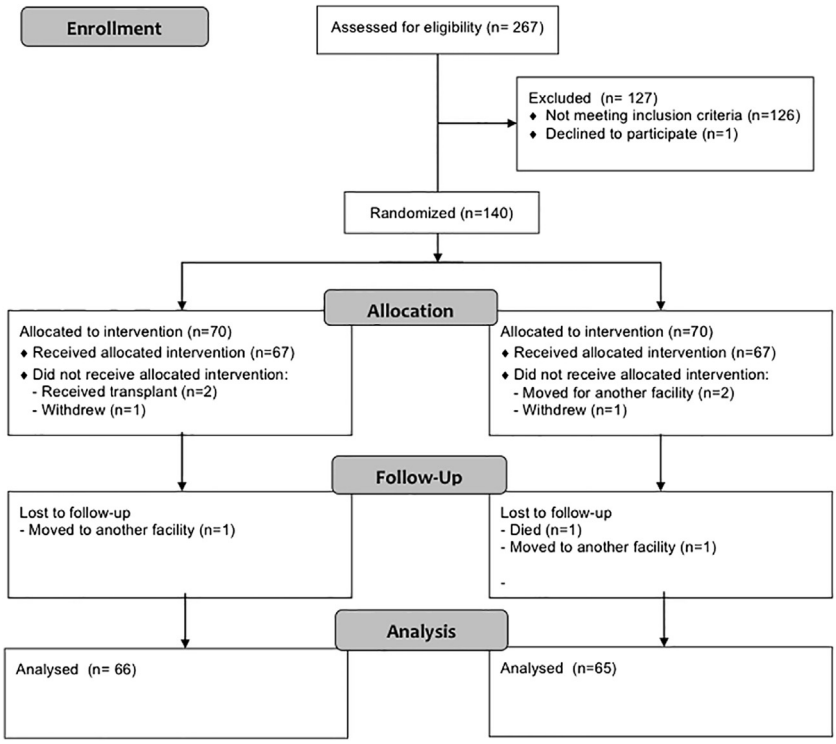

Figure 1. Flow diagram of the study.

the intervention group. The patients in both groups were asked to keep food diary after receiving instructions and a tool to estimate portion size, which were elaborate and presented by the study dietitian. The patients were asked to record their food and beverage intake during an assigned 3-day period, which included one dialysis day, one nondialysis day, and a weekend day. At the next dialysis session, the researcher questioned the patient about their intake, using the dietary record as a prompt and food models and measuring tools to accurately estimate portion sizes. The patients' dietary energy (kcal) and protein intake (g) were quantified using the Brazilian Food Composition Tables.[25,26] To calculate food consumption, household measurements and standard units were converted to grams and milliliters.[27]

Dietary protein intake was also estimated by calculating the nPNA from the patient's urea generation rate using the single-pool urea kinetic model.[21] The PNA was calculated during the first dialysis session of the week[28] and was normalized to the edema-free body weight (BW_{ef}) or to the ideal body weight when the patient was under 95% or over 115% of the ideal weight.[21,29]

Intervention Group

During the first 10 days of the study, the dietitian researcher analyzed the patients' nutritional statuses, energy intake, protein intake, and foods containing phosphorus additives according to the individual food diaries. To assess the participants' intake of foods containing phosphorus additives, the researcher identified the phosphorus additives on the food labels. Table 1 shows a list of the foods containing phosphorus additives that were regularly consumed by the patients.

Based on these data, from the 10th day to 30th day, the patients received verbal and customized written counseling on substituting foods that contain phosphorus additives with foods of similar nutritional value that do not contain additives and on maintaining the same frequency of consumption. The researcher also instructed the patients to verify and to avoid purchasing items with ingredient lists included phosphorus-containing additives.

On the 45th day of the study, the researcher reinforced the instructions and asked the participants questions about foods containing phosphorus additives and verified their serum biochemical results, including their serum phosphorus levels. The researcher also provided each participant with an updated list of foods that could be substituted for foods containing phosphorus additives and hints about the preparation of foods without additives, including recipes.

Control Group

The patients maintained the nutritional regimen (the renal diet) that they received from the facility's registered dietitian and nephrologists before the start of the study. The patients continued to receive regular care from their dietitians.

Table 1. Foods Containing Phosphorus Additives That Are Often Consumed by Patients in the Intervention Group and Their Food Substitutions

Food	Category	Phosphorus Additives	Substitution
Milk	Whole milk in cartons "shelf stable"	Trisodium phosphate and disodium phosphate	Refrigerated whole milk
	Low-fat milk in cartons	Trisodium phosphate	Refrigerated low-fat milk
	Evaporated milk	Disodium phosphate	Refrigerated milk
	Milk based beverages	Disodium phosphate	Blended milk with fresh fruit
Yogurt	Plain yogurt	Tricalcium phosphate	Plain yogurt without additive
	With cereal	Tricalcium phosphate	Plain yogurt with oatmeal
	Bottled yogurt	Tricalcium phosphate	Blended yogurt with fresh fruit
Cheese	Requeijão cream cheese	Sodium polyphosphate	Spreadable Brazilian white cheese (Minas cream cheese)
	Processed cheese	Tricalcium phosphate	White Minas cheese
	Cheddar slices	Trisodium phosphate	Matured Minas cheese
Cold cuts	Bologna	Sodium tripolyphosphate	Homemade sliced meat*
	Ham	Tetrasodium pyrophosphate and sodium tripolyphosphate	Homemade sliced pork with sauce*
	Turkey breast	Sodium polyphosphate	Homemade chicken breast with sauce*
	Salami	Disodium pyrophosphate, Sodium tripolyphosphate	Homemade beef with red wine*
	Sausage (hot dog)	Sodium tripolyphosphate	Homemade sliced beef*
	Chicken breast fillets	Tetrasodium pyrophosphate	Homemade chicken breast fillet*
Breads, cakes, and biscuits	Toast	Monocalcium phosphate	French bread toast; Pitta toast
	White bread	Tricalcium phosphate	French bread
	Processed cakes	Monocalcium phosphate	Homemade cakes with fruits juice*
	Whole-wheat bread	Monocalcium phosphate	French wholemeal bread
	Cream crackers	Sodium acid pyrophosphate	French bread toast
	Water crackers	Sodium acid pyrophosphate	French bread toast
	Whole-wheat toast	Sodium acid pyrophosphate	French whole-wheat toast
	Cornstarch sugar cookies	Sodium acid pyrophosphate	Homemade cornstarch cookies*
	Marie® biscuits	Sodium acid pyrophosphate	Homemade sweet biscuits*
	Milk biscuits	Sodium acid pyrophosphate	Homemade cookies*
	Brazilian cheese roll mix	Tricalcium phosphate and sodium acid pyrophosphate	Homemade cheese rolls*
Instant noodles	Chicken	Sodium tripolyphosphate	Capellini with meat or chicken béchamel sauce (homemade)
	Beef	Sodium tripolyphosphate	
Powdered juices	Various flavors	Tricalcium phosphate	Lemonade, passion fruit, grape juices*
Beverages	Dark cola	Phosphoric acid	Homemade ice tea*
	Tubaína soda	Phosphoric acid	Homemade apple juice*
	Soy	Tricalcium phosphate	Homemade soy beverage with soy extract*
	Mate tea	Phosphoric acid	Homemade ice tea*
	Black tea	Phosphoric acid	Homemade herbal tea
	Soluble cappuccino mix	Dipotassium phosphate	Homemade cappuccino*
Various	Mayonnaise	Phosphoric acid	Homemade milk mayonnaise*
	Whipped cream	Sodium triphosphate and monophosphate	Plain yogurt without whey*
	Soup mix	Disodium pyrophosphate	Homemade soup*
	Salad dressing	Tricalcium phosphate	Homemade salad dressing*
	Rice seasoning	Tricalcium phosphate	Homemade natural seasoning blend*
	Frozen fried potato	Disodium pyrophosphate	Homemade fried potatoes

*All the recipes were prepared and tested before they were provided to the patients.

Phosphate Binders

The prescribed phosphate binders and the prescription of Vitamin D for the patients in both groups were not modified and there was not any patient receiving cinacalcet or calcium during the study period.

Follow-Up

Patients were recruited from January to May 2012 and were followed for 90 days. At the end of the study, the patients in both groups kept a continuous 3-day food diary (dialysis day, a weekend day, and nondialysis day).

Anthropometric measurements (BMI, TSF, MAMC, and AMA), laboratory examinations (serum albumin, phosphorus, ionized calcium, hemoglobin, urea, creatinine, and parathyroid hormone levels), and Kt/V were also re-evaluated.

Outcome Measurement

The primary outcome was the prevalence of serum phosphorus levels of <5.5 mg/dL at the end of the study. The secondary outcome was the patients' poststudy nutritional statuses, as indicated by their protein and energy intake, which were evaluated using BMI, TSF, and AMA.

Randomization

Eligible participants were randomly assigned to one of two groups: the intervention group or the control group. A simple randomization list was generated by a computer and was kept concealed. Administrative staff personnel opened numbered and sealed envelopes in numerical order. It was necessary that the researcher not be blinded to the assigned dietary counseling groups.

Statistical Analysis

We used descriptive statistics to assess the clinical and laboratory data. The results are given as mean ± SD, when Student two-tailed *t* test was used to compare the results between the two groups. The chi-squared test, with Yates' correction when applicable, was used to compare the proportions of categorical variables. Either the paired *t* test or Wilcoxon signed-rank test was used for intra-group comparisons (initial minus final). We calculated and compared prestudy and poststudy changes in energy and protein intake from the patients' dietary records and in estimated nPNA (by calculation) both within and between the two groups. The Statistical Package for the Social Sciences, version 13.0 (SPSS Inc., Chicago, IL) was used for all the calculations. $P < .05$ was considered to be statistically significant.

Results

The baseline characteristics of the two groups are listed in Table 2. The control group had more males, longer times on dialysis, more phosphate binder users, and higher levels of serum albumin, hemoglobin, protein intake, and nPNA. The nutritional parameters were similar in both groups, the BMI showed that both groups were overweight; however, their energy and protein intake was below the levels recommended by the K/DOQI.[21]

During the study, serum phosphorus levels were analyzed in both groups; the level was significantly lower in the intervention group than in control group (serum phosphorus values at 45 days, 6.1 ± 1.5 mg/dL in the intervention group versus 7.3 ± 1.9 mg/dL in the control group, $P < .001$).

At the end of the study, the intervention group showed a significant reduction in the level of serum phosphorus and an increase in the level of serum albumin; however, there were no differences in the nutritional parameters compared with those at baseline (Table 3). In contrast, a significant reduction in the level of serum phosphorus was not observed in the control group, but there was a significant reduction in the level of serum albumin over the 90-day follow-up period.

Additionally, no differences existed between the groups in term of energy intake, protein intake, and nPNA (Table 4).

Compared with the control group patients, most of the intervention group patients n = 46 (69.7%) versus n = 12 (18.5%), $P < 0.001$ reached the recommended serum phosphorus level ≤ 5.5 mg/dL by the end of the study.

Discussion

Over the course of the study, the replacement of foods that contained phosphorus additives with foods of at similar nutritional value that did not contain additives reduced the serum phosphorus level of the ESRD patients. Notably, the nutritional status of the subjects did not appear to change during the 3-month study although reducing phosphorus intake in clinical practice without compromising protein intake is difficult.[30] Renal care professionals who work with hemodialysis patients face an important challenge in counseling patients with hyperphosphatemia. Furthermore, low patient adherence to dietary recommendations has been demonstrated in a comparative study on European and American hemodialysis patients.[31] The present study shows that individualized nutritional interventions, follow-ups and personalized diets were effective in reducing the serum phosphorus levels of the intervention patients. Sullivan et al. demonstrated that achieving a small but clinically significant reduction in the serum phosphorus levels of hemodialysis patients is possible through nutritional education about reading processed food labels.[17] In a study conducted in four European countries, Fouque et al. demonstrated an increase in patients' awareness of the phosphorus content in food; however, our patients have not yet developed a similar awareness.[32]

In the United States, researchers used direct chemical analysis to calculate the phosphorus content of foods and concluded that it was significantly underestimated on the food label or in nutritional software in 15%-25%, especially in individuals consuming more highly processed foods.[6,33] Other studies also have shown that the phosphorus-protein ratio (mg/g) obtained from chemical analysis is greater than that obtained from food labels and nutritional software.[34-36] In the present study, the phosphorus-protein ratio was not controlled, because the phosphorus content of processed foods is not declared on food labels. In 1996, in the United States, researchers estimated that additives were responsible for over 30% of adults' dietary phosphorus intake, and this proportion has been increasing.[37] Recently, the same

Table 2. Baseline Characteristics of the Intervention and Control Groups

Characteristics	Intervention (n = 67)	Control (n = 67)	*P* Value
Age (y)	56.4 ± 13.2	56.3 ± 14.6	.97
Sex, n (%)			
Male	35 (52.2)	47 (70.1)	.03
Female	32 (47.8)	20 (29.9)	
Race, n (%)			
White	39 (58.2)	44 (65.7)	.37
Mixed/Black	28 (41.9)	23 (34.4)	
Cause of renal failure, n (%)			
Hypertension	31 (46.3)	28 (41.8)	.03
Diabetes	25 (37.3)	16 (23.9)	
Glomerulonephritis	4 (6.0)	16 (23.9)	
Other	7 (10.4)	7 (10.4)	
Time on hemodialysis (mo)	35.5 ± 36.3	52 ± 49	.01
Kt/V	1.3 ± 0.2	1.4 ± 0.3	.06
Serum phosphorus (mg/dL)	7.2 ± 1.4	7.1 ± 1.2	.79
Serum iCalcium (mmol/L)	1.2 ± 0.1	1.2 ± 0.2	.24
Serum albumin (g/dL)	3.9 ± 0.3	4.3 ± 0.5	.001
Serum PTH (pg/mL)	835.5 ± 509.2	878.6 ± 727.8	.91
Hemoglobin (g/dL)	11.1 ± 1.5	11.7 ± 1.5	.03
Serum creatinine (mg/dL)	9.7 ± 3.3	10.3 ± 3.5	.33
Taking phosphate binders, n (%)	47 (70)	63 (94)	.001
BMI (kg/m^2)	25.7 ± 4.8	26.2 ± 5.6	.67
TSF (mm)	18.5 ± 11	15.6 ± 8.4	.10
AMA (cm^2)	35.5 ± 11.5	37.7 ± 11.2	.27
Energy intake (kcal/kg/d)	26.7 ± 8.2	28.7 ± 7.7	.15
Protein intake (g/kg/d)	0.9 ± 0.4	1.1 ± 0.4	.02
nPNA (g/kg/d)	1.1 ± 0.2	1.2 ± 0.2	.01

iCalcium, ionized calcium; BMI, body mass index; TSF, triceps skinfold thickness; AMA, arm muscle area; nPNA, normalized protein nitrogen appearance.

Unless otherwise noted, the values are presented as mean ± SD.

P values are based on the chi-squared test, *t* test, or Mann–Whitney *U* test.

authors observed that additives contributed the highest percentile of intake of phosphorus, approaching the tolerable upper intake levels (UL, 2005-2006 NHANES).[6]

In the present study, the energy and protein intake of the patients in the two groups (Table 2) were initially below the level recommended by the KDOQI, as has also been observed in other studies.[38,39]

Data from observational studies have shown that the prescription of phosphate binders is associated with a survival benefit.[40,41] Although most of the patients in the present study were under the phosphate binder prescription, serum phosphorus levels were above the recommended ranges. These high levels might be the result of patients' low-prescription adherence due to the number and size

Table 3. Comparison of Initial and Final Laboratory and Nutritional Parameters of the Two Study Groups

	Intervention			Control		
Characteristics	Initial (n = 67)	Final (n = 66)	*P* Value	Initial (n = 67)	Final (n = 65)	*P* Value
Phosphorus (mg/dL)	7.2 ± 1.4	5.0 ± 1.3	<.001	7.1 ± 1.2	6.7 ± 1.2	.65
iCalcium (mmol/L)	1.2 ± 0.1	1.2 ± 0.1	.79	1.2 ± 0.2	1.1 ± 0.1	.88
Hemoglobin (g/dL)	11.1 ± 1.5	10.8 ± 1.4	.10	11.7 ± 1.5	11.2 ± 1.5	.06
PTH (pg/mL)	832 ± 512	748 ± 498	.07	877 ± 739	953 ± 742	.08
Kt/V	1.3 ± 0.2	1.3 ± 0.2	.87	1.4 ± 0.3	1.3 ± 0.2	.06
Albumin (g/dL)	3.9 ± 0.3	4.1 ± 0.5	.004	4.3 ± 0.5	4.1 ± 0.3	.006
Creatinine (mg/dL)	9.7 ± 3.3	8.8 ± 2.8	.001	10.3 ± 3.6	9.1 ± 2.5	.001
nPNA (g/kg/d)	1.1 ± 0.2	1.1 ± 0.2	.74	1.2 ± 0.2	1.2 ± 0.2	.42
BMI (kg/m^2)	25.7 ± 4.8	25.4 ± 4.7	.72	26.2 ± 5.6	26.2 ± 5.7	1.00
TSF (mm)	18.5 ± 11	17.8 ± 9.7	.70	15.6 ± 8.4	15.3 ± 7.3	.29
AMA (cm^2)	35.5 ± 11	32.5 ± 9.3	.10	37.7 ± 11	39.6 ± 13	.39

PTH, parathyroid hormone; nPNA, normalized protein nitrogen appearance; BMI, body mass index; TSF, triceps skinfold thickness; AMA, arm muscle area.

The values are presented as mean ± SD.

P values are based on either the paired *t* test or Mann–Whitney *U* test.

Table 4. Comparison of Dietary Changes (Final Minus Initial Values) Comparison Between the Intervention and Control Groups

Parameters	Intervention (n = 66)	Control (n = 65)	*P* Value
Energy intake difference (kcal/kg/d)	−2.28 ± 7.3	−0.22 ± 5.4	.07
Protein intake difference (g/kg/d)	−0.09 ± 0.3	−0.04 ± 0.3	.31
nPNA difference (g/kg/d)	−0.01 ± 0.2	−0.02 ± 0.3	.84

nPNA, normalized protein nitrogen appearance.
The values are presented as mean ± SD.
P values are based on *t* test or the Mann–Whitney *U* test.

of the pills that are required to achieve the desirable effect. Karamanidou et al. demonstrated an adherence rate of approximately 50% in ESRD patients, and Ketteler et al. suggested a reduction in the number of pills per day to boost adherence in CRD patients, despite the reduced effect, which could be compensated for by restricting patients' daily intake of phosphorus additives.[42,43]

The initial statistical comparison of the randomized intervention and control groups showed that the control group had more male patients and higher serum albumin, protein intake, and nPNA rates. Nevertheless, there were no significant differences between the groups in terms of BMI, TSF, AMA, and energy intake. Thus, we compared the initial and final results within each group.

In the intervention group, a reduced serum phosphorus level was observed without changes in calcium, hemoglobin, or PTH levels; a significant increase in the serum albumin level was also observed (Table 3). In contrast, there were no changes in these parameters in the control group, with exception of a statistically significant reduction in serum albumin level. Isakowa et al. randomized stage 3-4 CRD patients to assess whether the use of phosphate binders or the combination of phosphate binders and dietary phosphate restriction would decrease FGF-23 levels.[44] They also measured serum calcium, phosphate, and PTH levels, and they concluded that there was a reduction in FGF-23 in the intervention group; however, no change in serum calcium and PTH levels. Compared with PTH, FGF-23 is a more sensitive marker for phosphorus homeostasis. Another study on stage 3-4 CRD patients compared the effects of a meat-based diet to the effects of a vegetarian diet on phosphorus homeostasis, and it showed a decrease in serum phosphorus levels but no changes in calcium and PTH levels.[30] In the present study, compared with the control group, the intervention group showed a tendency toward PTH reduction when compared to the control group. This may have resulted from the short study period, which may not have allowed for the desirable effect on PTH. There was a significant decrease of serum creatinine during the period of intervention in both groups, without differences in muscle mass and in the dialysis dose, which could not be explained.

There were no changes in the nutritional parameters—BMI, lean mass, and fatty mass—during the study period: the maintenance of similar energy intake and protein intake over the course of the study may explain this finding. The average BMI in the study groups remained within the range recommended by the KDOQI; the patients' remained in the upper 50th percentile for normal individuals, which translates to BMIs for men and women that are no higher than 23.6-24.0 kg/m^2).[21] In the intervention group, the TSF remained within the recommended limits, and there were no variations in AMA throughout the study. The HEMO study demonstrated the importance of maintaining the recommended levels of these nutritional parameters and showed that changes in skin thickness and muscle mass were related to all-cause mortality, poor cardiac outcomes, and infection-related deaths.[45]

Although a 2-kcal per kg/d reduction occurred in the intervention group (Table 4), this reduction is less than 5% of the recommended energy consumption (30-35 kcal, K/DOQI), and it had no effect on the patients' final nutritional status. It is important to consider that patients who are treated with hemodialysis have sedentary lifestyles and are less active than healthy sedentary individuals.[46]

Initially, the average protein intake in the intervention group was below the recommended level, which remained constant throughout the study. However, the nPNA was within the recommended level throughout the duration of the study. The nPNA is a better reflection of protein intake than those calculated in Tables. A study showed that patient

Table 5. Percentage of Patients in the Two Groups Who Reached the Target Level for Serum Phosphorus (≤5.5 mg/dL) at the End of the Study

Group	P ≤ 5.5 mg/dL, n (%)	P > 5.5 mg/dL, n (%)	*P* Value
Intervention (n = 66)	46 (69.7)	20 (30.3)	<.001
Control (n = 65)	12 (18.5)	53 (81.5)	

P, serum phosphorus.
Chi-square test.

survival decreases when protein intake measured by nPNA is below 0.9 g/kg/d in dry weight/day.[47]

The nutritional intervention strategy used in this study showed that the most of the patients in the intervention group reached the recommended serum phosphorus level (Table 5).[48] A recent meta-analysis has shown that nutritional education interventions are effective in reducing serum phosphorus levels in HD patients.[49]

Some limitations of this study should be considered. First, the study was conducted in a sample of prevalent hemodialysis patients at a single center. Second, it was not a double-blind study. Third, the patients' actual phosphorus intake could not be quantified because it would require the biochemical analysis of all the foods that they consumed. Fourth, this short-term study lasted only 3 months. Further research is needed to confirm these results with larger sample and longer duration.

Conclusion

The intervention group of ESRD patients on hemodialysis showed reduced serum phosphorus concentrations after nutritional counseling on restricting the intake of foods containing phosphorus additives and substituting these foods with those with similar nutritional value that do not contain these additives; these results were observed without changes in the patients' nutritional status over the 3-month study period.

Practical Application

This low-cost and simple intervention can be easily implemented by a renal dietitian. This study shows the importance of using individualized nutritional counseling among ESRD patients in combination with phosphate binders to reduce serum phosphorus levels.

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