

ORIGINAL ARTICLE

Nutrition

The effect of egg white diet on phosphorus control in dialysis patients

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Abstract

Introduction: Nutritional interventions have been envisaged to improve hyperphosphatemia and malnutrition, two important risk factors associated with mortality in dialysis patients. We evaluated the effects of egg white consumption on serum phosphate and malnutrition in dialysis patients.

Methods: In an open-label, per protocol clinical trial, conducted in Kerman dialysis centers, 150 hemodialysis patients aged ≥ 18 years with serum phosphorus ≥ 5.5 mg/dl were included in the study. All participants limited their intake of foods containing phosphorus for 4 weeks, and then they were divided into a control and an intervention group. The control group continued their ordinary diet and the participants in the intervention group consumed a Telavang egg white pack (containing six egg whites, 96 calories, 24 g protein) as a substitute for meat products 3 days a week for 8 weeks. Finally, changes in serum albumin, phosphorus, calcium, PTH, and cholesterol were measured.

Findings: At the baseline, there were no significant differences in the laboratory variables between the two groups. After 8 weeks, serum cholesterol (124.3 ± 38.1 , vs. 135.8 ± 28.8 , $p = 0.003$) and phosphorus levels (4.5 ± 1.03 , vs. 6.7 ± 1.5 , $p = 0.001$) were significantly lower in the intervention group compared with the control group. Also, serum albumin (4.5 ± 0.07 vs. 3.7 ± 0.4 , $p = 0.001$) was significantly higher in the intervention group. Moreover, phosphorus, PTH, and cholesterol levels in the intervention group were significantly lower than their baseline values ($p = 0.001$).

Conclusion: The results showed that the egg white could be a useful source of protein for dialysis patients, as it simultaneously reduces serum phosphorus and cholesterol, and increases serum albumin.

KEYWORDS

dialysis, egg white, end-stage renal disease, phosphorus, protein diet

INTRODUCTION

End-stage renal disease (ESRD) is a growing disease worldwide and in the Middle East, with an estimated 18% growth by 2030.^{1,2} The average prevalence of chronic kidney disease (CKD) in Iran is generally estimated at 15.14%.³ Despite advances in treatment and dialysis methods, the mortality rate of ESRD is 10 to 30 times higher than that of the general population.^{4,5} Two of the most important causes of death in ESRD patients are protein-energy malnutrition and cardiovascular disease.^{5,6} Hyperphosphatemia is one of the factors involved in vascular calcification and increased cardiovascular mortality in dialysis patients.⁷

Treatment of hyperphosphatemia and improving the nutritional status of dialysis patients is one of the main concerns of nephrologists, and achieving these two goals simultaneously is a major problem.^{8,9} One of the most basic treatments to reduce phosphorus concentration is to limit phosphorus in the diet.^{7,10} Diets with limited phosphorus are often associated with reduced dietary protein in dialysis patients, leading to malnutrition.^{7,11} It has been found that the high phosphorus-to-protein ratio in food is directly related to mortality in dialysis patients.¹¹ Therefore, in the diet of dialysis patients, foods with minimum organic phosphorus and a low phosphorus-to-protein ratio should be considered.^{12,13} Among protein food sources, egg white is a suitable source of protein with high biological value and a phosphorus-to-protein ratio lower than 2 mg/g.^{14,15} Therefore, in this study we decided to administer a package containing six egg whites three times a week for 8 weeks in hemodialysis patients and then evaluate the effect of this intervention on blood levels of phosphorus, albumin, and cholesterol in these patients.

MATERIALS AND METHODS

The present study is an open-label, parallel-group, per protocol clinical trial, conducted in Kerman dialysis centers between September 2020 and January 2021. This study was approved by the local Ethics Committee with the ethics approval code IR.KMU.REC.1398.027. The study was registered in the International Center for Clinical Trials registry of Iran with the registration number IRCT20190701044061N1.

The statistical population was the hemodialysis patients who referred to three dialysis centers of Shafa Hospital, Javad-al-Aemeh Clinic, and Samen Clinic in Kerman. The sample size was calculated to be 53 subjects for each group using G-power software and considering an effect size of 0.55, which was then increased to 75 to account for a 40% dropout.

Hemodialysis patients aged 18 years and older undergoing maintenance hemodialysis for at least 3 months who had serum phosphorus ≥ 5.5 mg/dl and provided informed consent were included in the study. Exclusion criteria were allergy to eggs, liver, cardiopulmonary, or uncontrolled psychiatric disease, or a history of Parathyroidectomy.

After recording the patients' information, the participants were divided into a control group and an intervention group using the random allocation rules technique. Thus, 150 envelopes containing the type of treatment (75 for the egg white diet group and 75 for the control group) were randomly allocated to the patients in the order they referred to the centers. Initially, the study was designed as a crossover study. However, due to the onset of the COVID-19 pandemic, at the end of the first 8 weeks, the project was terminated after consultation with an expert statistician. The power of 88% was calculated with the patients who completed the study in both groups. Twenty-two patients (intervention: 4, control: 18) were excluded from the study due to death, kidney transplantation, or refusing to continue. In the end, 128 subjects (intervention: 71, control: 57) completed the study (Figure 1).

This study was performed in two phases: the initial phase (4 weeks) and the intervention phase (8 weeks). In the initial phase, all participants were asked to limit their intake of foods containing phosphorus; height, weight, serum albumin level, phosphorus, calcium, PTH, cholesterol, dialysis adequacy, type of dialysis, duration of dialysis, type, and amount of phosphorus-reducing drugs were recorded. Phosphorus-restricted diets were planned by a nutrition consultant and adherence to the diet was assessed weekly by a nurse.

In the intervention phase, the intervention group consumed a total of 24 packs of Telavang egg whites, one pack per day 3 days a week, (in one serving as a substitute for meat products). Each pack of Telavang egg whites contained six egg whites with a total of 96 calories and 24 grams of protein. The control group continued their regular diet. At the end of the eighth weeks, serum albumin, phosphorus, calcium, PTH, cholesterol, dialysis adequacy, rate of change in medication, and duration of dialysis were measured and recorded again. During the intervention, participants were asked to limit their dietary phosphorus intake. The participants' adherence to the diet determined by the dietician was followed by the nurse, and if a participant in either groups consumed more than three high-phosphorus meals a week, he/she was excluded from the study. All laboratory tests were performed using the same laboratory kits and by the same technician at Madar Laboratory, Kerman, Iran. The primary outcome was changes in serum levels of

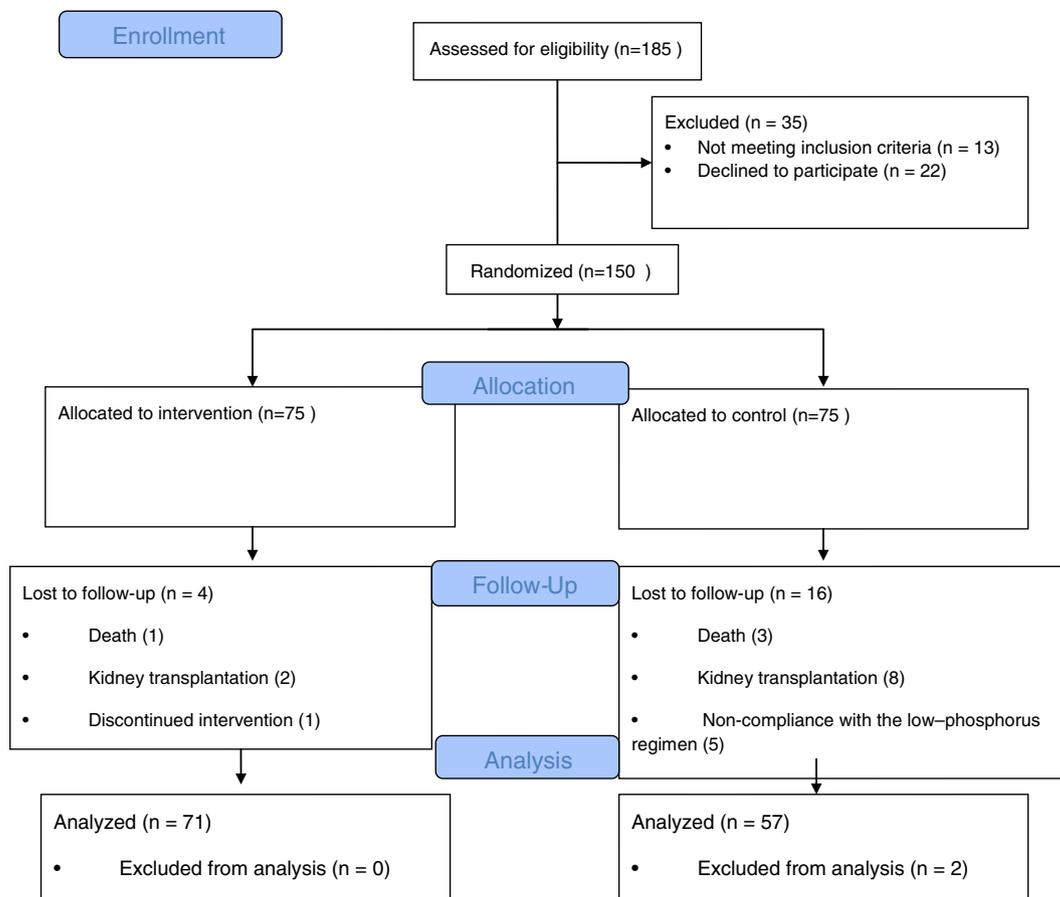


FIGURE 1 Flow chart of the study [Color figure can be viewed at wileyonlinelibrary.com]

phosphorus, albumin, calcium, PTH, and cholesterol. Ethical considerations were observed in all stages of the research.

The collected data were reported descriptively by mean (\pm standard deviation) and frequency (percentage). Data analysis was performed by SPSS software version 22 (SPSS Inc., Chicago, IL). *t*-test or its nonparametric equivalent was used to compare the means of the quantitative variables between the two groups. Paired *t*-test or its nonparametric equivalent, the Mann–Whitney test, was used for comparison of before and after values.

RESULTS

Out of 310 dialysis patients in the centers, based on eligibility criteria, 185 patients with phosphorus ≥ 5.5 mg/dl were selected. After reviewing the inclusion and exclusion criteria, 150 patients were finally selected and randomly allocated to either the intervention or the control group (Figure 1).

The mean age was 48.5 ± 6.2 years the intervention group and 54.3 ± 15.9 years in the control group ($p = 0.05$), and 63.4% of the intervention group and

61.4% of the control group were male. Table 1 shows that there was no statistically significant difference between the two groups based on age and gender. There was no significant difference in the mean quality of hemodialysis urea reduction ratio (URR) ($p = 0.62$) and KT.V ($p = 0.62$) between the two groups (Table 1).

Table 2 shows the results of biochemical measurements before and after the intervention. At the baseline, there was no significant difference in any of the biochemical variables between the two groups. After the study, PTH levels significantly decreased in both the intervention and control groups ($p = 0.001$, for both). Also, the differences were significant between the two groups ($p = 0.001$). After the intervention, albumin levels decreased significantly in the control group ($p = 0.001$); there was no significant difference in the intervention group ($p = 0.189$), while the difference was significant between the two groups ($p = 0.001$). The mean serum cholesterol level in the intervention group decreased significantly ($p = 0.001$) while it increased in the control group, but the increase was not significant ($p = 0.27$).

The mean serum calcium level increased in the intervention group nonsignificantly ($p = 0.317$), while in the control group, the reduction was significant ($p = 0.001$).

TABLE 1 Baseline characteristics

Variable	Intervention group (n = 71)	Control group (n = 57)	p value
Age (Year)	48.49 ± 16.19	54.26 ± 15.89	0.05
Gender (percentage)			
Male	63.4	61.4	0.856
Female	36.6	38.6	
URR	0.71 ± 0.09	0.70 ± 0.07	0.62
KT/V	1.35 ± 0.21	1.31 ± 0.18	0.35

Note: Data presented as mean ± SD.

Abbreviation: URR, urea reduction ratio.

TABLE 2 Biochemical variables at baseline and after 8 weeks

Items	Groups	Baseline	After 8 week	p value ¹
P (mg/dl)	Intervention	7.20 ± 1.06	4.5 ± 1.03	0.001
	Control	6.79 ± 1.12	6.7 ± 1.5	0.701
<i>p</i> value ²		0.52	0.001	
Ca (mg/dl)	Intervention	9.25 ± 1.5	10.54 ± 1.01	0.317
	Control	9.62 ± 1.16	9.0 ± 1.04	0.001
<i>p</i> value ²		0.14	0.07	
PTH	Intervention	437.8 ± 262.5	189.47 ± 159.66	0.001
	Control	540.7 ± 396.7	440.08 ± 3.7.98	0.001
<i>p</i> value ²		0.35	0.001	
Alb (g/dl)	Intervention	3.8 ± 0.46	4.5 ± 0.07	0.189
	Control	4.01 ± 0.30	3.7 ± 0.4	0.001
<i>p</i> value ²		0.10	0.001	
TG (mg/dl)	Intervention	140.19 ± 38.25	124.28 ± 38.07	0.001
	Control	131.77 ± 33.64	135.77 ± 28.77	0.27
<i>p</i> value ²		0.23	0.003	

Note: Data presented as mean ± SD; *p* value¹ for before and after the study. *p* value² for between the groups.

Abbreviations: Alb, albumin; Ca, calcium; P, phosphorus; PTH, parathyroid hormone; TC, total cholesterol.

The mean serum phosphorus level decreased significantly in the intervention group ($p = 0.001$), while it showed no significant changes in the control group ($p = 0.701$).

As shown in Table 3, the difference in mean dose of drugs (calcium carbonate 500 mg tablets, sevelamer 800 mg capsules, calcitriol 0.25 mcg pearls, and cinacalcet 30 mg tablets) in the two groups was not statistically significant before the intervention. The mean dose of drugs was significantly lower after the intervention in the intervention group compared with the control group. The Wilcoxon Signed Ranks test showed that in the intervention group, the average dose of drugs decreased after the intervention. This reduction was significant in all drugs except for cinacalcet. In the control group, the mean dose of the drugs either increased or showed nonsignificant changes after the intervention.

Participant in either groups who consumed more than three high-phosphorus meals a week were excluded from the study. The nonadherence to phosphorus-restricted diets was more common in the control group (five patients in control group vs. one patient in intervention group).

The egg white packages were well tolerated and no side effects were reported by the patients. Only one patient complained of the unpleasant smell of this food and she finally left the study after 3 weeks.

DISCUSSION

In this study, we examined the effects of an egg white diet for 8 weeks to control phosphorus in dialysis

TABLE 3 Drugs used by the two groups at baseline and after 8 weeks

Items	Groups	Baseline	After 8 weeks	<i>p</i> value ¹
Calcium carbonate (mg/day)	Intervention	626.76 ± 88.42	401.41 ± 66.99	0.002
	Control	354.55 ± 65.74	609.09 ± 71.88	0.0001
<i>p</i> value ²		0.06	0.05	
Sevelamer (mg/day)	Intervention	1915.49 ± 145.74	349.30 ± 107.33	0.0001
	Control	1454.55 ± 149.83	1934.55 ± 134.04	0.0001
<i>p</i> value ²		0.05	0.0001	
Calcitriol (mcg/day)	Intervention	0.211 ± 0.023	0.081 ± 0.022	0.0001
	Control	0.213 ± 0.030	0.213 ± 0.035	0.890
<i>p</i> value ²		0.912	0.001	
Cinacalcet (mg/day)	Intervention	5.49 ± 1.73	2.54 ± 1.31	0.07
	Control	14.18 ± 3.72	13.64 ± 3.46	0.763
<i>p</i> value ²		0.076	0.001	

Note: Data presented as Mean ± SD, *p* value¹ for before and after the study (Wilcoxon Signed Ranks test), *p* value² for between the groups (Mann-Whitney test).

TABLE 4 The design features and sample size in studies about the effect of egg white-based nutritional intervention in dialysis patients.

Author (year, country)	Sample size	Design	Follow-up duration	Intervention (frequency)	Control	Results
Li et al. (2019, China) ²²	53	Single-center, controlled, open-label, prospective interventional study	6 months	200 ml of milk and two egg whites (thrice weekly for 3 months)	Nutritional counseling alone	A significant improvement in serum albumin in intervention group
Guida et al. (2018, Italy) ²³	23	Open-label, randomized controlled trial	3 months	Replacing one serving of meat (i.e. 120 g) with 5.5 egg whites or one serving of fish (i.e. 150 g) with 6 egg whites	Unchanged diet	A significant decrease in serum phosphate. No change in serum albumin
Weratean et al. (2017, Thailand) ²⁴	14	Randomized crossover study	28 weeks	Received HPLPS for 12 weeks, washout for 4 weeks and received RS for 12 weeks	Received RS for 12 weeks, washout for 4 weeks and received HPLPS for 12 weeks	An improvement in nutritional status. No increase in serum phosphorus
Taylor et al. (2011, USA) ¹⁵	13	Pilot study	6 weeks	Eight ounces (225 g) of pasteurized liquid egg whites, one meal per day for 6 weeks	–	Fall in serum phosphorus. An improvement in serum albumin
González-Espinoza et al. (2005, Mexico) ²⁵	28	Randomized, open-label, controlled clinical trial	6 months	15 g of egg-albumin-based protein supplement, two servings/day	Conventional nutritional counseling alone	A significant improvement in serum albumin in intervention group

Abbreviations: HPLPS, high-protein, low-phosphorous snack; RS, regular snack.

patients. After 8 weeks serum cholesterol and phosphorus levels were significantly lower in the intervention group compared with the control group. Also, serum

albumin was significantly higher in the intervention group. Moreover, in the intervention group, phosphorus, PTH, and cholesterol levels were significantly lower than

their baseline values. The need for phosphorus chelator drugs was significantly reduced in the intervention group. Patients who completed the study did not report any side effects during the intervention. The egg whites were only given thrice weekly, and therefore, this is a feasible supplementary regimen as it is low-cost, easy to administer, and well tolerated.

Due to the role of hyperphosphatemia in increasing the risk of cardiovascular mortality, prevention and correction of hyperphosphatemia using nutritional interventions are among the main components of dialysis patient management.^{7,16,17} Not all phosphorus-containing food sources have the same effect on hyperphosphatemia.^{13,18} Bioavailability is low in plant sources such as phytates, but it is about 60% in animal proteins such as casein.^{13,19} Therefore, animal protein sources are more suitable than plant protein sources for dietary phosphate interventions.¹⁰ Low-protein phosphorus-containing food sources with good bioavailability and low phosphorus-to-protein ratios are suitable for dialysis patients.²⁰ Egg white, which is a source of high biological value protein with a protein digestibility corrected amino acid score (PDCAAS) of 97%, has an ideal phosphorus-to-protein ratio (1.42 mg/g protein) with no cholesterol, so it is a healthy source of protein for dialysis patients.^{20,21}

Table 4 contains the design features and sample size of five studies that have examined the effect of egg-white-based nutritional interventions on dialysis patients.^{15,22–25} Although some of them had a crossover design, the maximum sample size was 53, which is still much lower than the sample size of the present study. In studies by González-Espinoza et al., Weratean et al., and Li et al., the focus was on the effects of nutritional interventions on the nutritional status of dialysis patients.^{22,24,25} As with the results of our study, they found that egg-white-based diets improve nutritional status in dialysis patients. In the studies of Guida et al. and Taylor et al., the focus of the studies was on phosphorus control of dialysis patients and they found that phosphorus levels decreased in the intervention group.^{15,23} However, contrary to our study, serum albumin level did not increase in Guida et al.'s trial. This may have been due to less egg white consumption in Guida et al.'s study.

One of the limitations of our study was the limited follow-up period and lack of crossover design. A crossover design could have increased the analytical power of the study. However because of the onset of the COVID-19 pandemic and also the dropout in the control group, we terminated the study at the end of the first 8 weeks' follow-up period. Other than more cases of death and kidney transplantation, the cause for higher dropout in the control group was more noncompliance with the low-phosphorus regimen. This shows that our egg white diet

regimen was well tolerated and led to a favorable change in laboratory tests. In spite of this, the power calculated with the final sample size was 88%, which is acceptable. It is suggested that future studies use a crossover design with a longer follow-up, examining more laboratory variables, such as magnesium, potassium, nPCR, normalized protein catabolic rate, and inflammatory variables such as CRP and IL-6 as well as sodium intake and interdialytic weight gain should also be considered.

CONCLUSION

The results of our study show that egg white, which simultaneously reduces serum phosphorus and cholesterol and increases serum albumin, can be a useful source of protein for dialysis patients.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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