

Research Article

Effects of different types of protein supplementation on serum albumin levels in hemodialysis patients

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Abstract

Objectives: The objective of this study was to evaluate the nutritional status and protein intake of hemodialysis patients and to compare different supplementation strategies designed to recover the nutritional status and quality of life of these patients.

Methods: Fifteen patients undergoing hemodialysis at a clinic in a city of São Paulo state with serum albumin levels of less than 3.8 g/dL were evaluated. For the classification of nutritional status, the patients were submitted to anthropometric assessment for body mass index calculation and responded to the 7-point subjective global assessment scale. A 24-hour dietary recall was obtained for the evaluation of food intake and the nutritional composition of these foods was calculated using the Dietpro 5i software. The patients were divided into three intervention groups that received three different protein supplements: HDMax®, Albumax®, and 100% Whey®.

Results: The population studied had a mean age of 57.2 ± 16.79 years and a mean BMI of 27.9 ± 7.63 kg/m². Analysis of food intake showed a low intake of protein, which was positively correlated with low serum albumin levels ($p < 0.0159$). A significant increase in serum albumin concentration of the participants was observed after supplementation, irrespective of the supplement used ($p = 0.0075$).

Conclusion: The present study permits to conclude that protein supplementation increases serum albumin in hemodialysis patients and consequently improves the nutritional status of these patients.

Introduction

Chronic kidney disease (CKD) is a syndrome characterized by the progressive and irreversible loss of kidney function [1]. Deterioration of biochemical and physiological functions, catabolite accumulation, an altered electrolyte and acid-base balance, and metabolic acidosis are some of the consequences of insufficient glomerular filtration [2]. Progression of the disease can be identified by stages, in which stage 0 indicates the risk of developing CKD and stage 5 the need for renal replacement therapy [1].

Renal replacement therapy includes renal transplantation, peritoneal dialysis and hemodialysis, which are indicated when conservative treatment is no longer sufficient to maintain the quality of life of the patient. Hemodialysis is a dialysis modality that permits the intermittent removal of solutes and fluids [3]. During this process, blood is drawn from a vascular access (catheter or arteriovenous fistula) into an extracorporeal circulation system that contains a filter (dialyzer). In the filter, the blood comes in contact with the dialysate (dialysis solution) through a semipermeable membrane, removing toxins and returning clean blood to the patient [4,5].

Nutritional imbalances are common in patients with CKD undergoing hemodialysis, with 10 to 70% of hemodialysis patients showing some sign of malnutrition [6]. In this respect, protein-energy malnutrition has been shown to be one of the most important factors that influence morbidity and mortality in this population [7]. Careful medical and nutritional attention is therefore needed because of the increased risk of deteriorating nutritional status in these patients. One possible reason for the nutritional deficit is the loss of proteins (1 to 3 g per hemodialysis session) caused by the dialysis process, an inadequate

dietary pattern, and increased protein catabolism due to uremia, metabolic acidosis and hormonal disorders, among others [8].

Lowrie and Lew found serum albumin to be the nutrition-related biochemical parameter that most correlated with survival in dialysis patients. Concentrations of this protein between 3.51 and 4.0 g/dL were associated with a two-fold higher risk of death compared to serum albumin levels higher than 4.0 g/dL. This risk was five times higher in patients with serum concentrations of this protein between 3.01 and 3.5 g/dL [9]. Some authors suggested that reduced albumin concentrations are a consequence of deficient calorie and protein intake, which compromise the clinical state of the patient [1].

Studies evaluating the protein intake of dialysis patients reported a mean daily intake of 0.8 to 1.0 g/kg. Although a protein intake slightly below the recommended level is not harmful in some cases, dialysis patients should be advised to achieve the recommended intake of this nutrient [4]. The recommended dietary allowance for protein to promote a neutral or positive nitrogen balance is at least 1.2 g/kg/day for most stable patients and may be higher in the case of stress and increased metabolic requirements [1].

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For a complete representation of the nutritional status of the dialysis population, albumin should be combined with other nutritional indicators such as body composition, food intake and subjective assessment tools. This is necessary since albumin levels vary according to underlying complications and because of the long average lifespan of this protein and expected serum reduction with advancing age, with the observation of a decrease of 20% in individuals older than 70 years [8].

In view of the above considerations, the objective of the present study was to evaluate the nutritional status and protein intake of hemodialysis patients and to compare different supplementation strategies in order to contribute to the recovery of the nutritional status of these patients.

Methods

This study was conducted on patients treated at a hemodialysis clinic in a city of the state of São Paulo, Brazil. Criteria for inclusion in the study were age older than 18 years and serum albumin levels of less than 3.8 g/dL. Among the patients treated at the clinic, only 15 were eligible for participation in the study since exclusion criteria were active inflammation, liver disease, and peritoneal dialysis as modality. This was a longitudinal clinical study and the procedures were approved by the Ethics Committee of Universidade de Franca (UNIFRAN).

After they had received detailed information about the study, the 15 patients selected signed the free informed consent form and were submitted to nutritional assessment. Anthropometric evaluation consisted of the following measurements: weight, height, arm circumference, waist circumference, abdominal circumference, and biceps, triceps, subscapular and suprailiac skinfolds. Arm muscle circumference (AMC), arm muscle area and body fat percentage were also calculated. The measurements were obtained by trainees after the hemodialysis sessions so that the patients did not experience any water retention as recommended in the literature [4]. A Técnica® platform scale, Welmy® vertical stadiometer, inelastic tape measure and Prime Med Neo® adipometer were used for the measurements. Weight and height were used to calculate the body mass index (BMI) using the formula of Quetelet and the results were classified based on the cut-off points established by the World Health Organization and by Lipschitz according to age of the participants. Skinfolds were analyzed as described by Frisanchio (1990) [10,11].

For the analysis of food intake, the patients responded to 24-hour dietary recalls on 3 different days: one day of hemodialysis, one day without hemodialysis, and a weekend day [12]. The recalls were applied by trainees during the hemodialysis sessions. To estimate food intake on a weekend day, the participants undergoing hemodialysis on Tuesdays, Thursdays and Saturdays filled out a food diary on Sunday. The patients were instructed by the trainees on how to fill out the diary. The diary was filled out by an accompanying person if the patient was unable to do so. It was thus possible to estimate the energy-protein intake of each patient. The nutritional calculations were performed with the Dietpro 5i software. The results were compared to the Dietary Reference Intakes (DRIs), which are 10-35% of protein, or at least 1.2 g/kg/day; 45-65% of carbohydrates, and 20-35% of fat.

The patients were divided into three intervention groups of five subjects each. The first group received a protein energy supplement specific for hemodialysis patients (HDMax®, Prodiel), which is a ready-to-use, individually packaged drink. Its protein source is 50% calcium caseinate and 50% soy protein isolate. The second group consumed Albumax® powder from Max Titanium (vanilla flavor),

which is reconstituted in water. The third group received 100% Whey® protein supplement also from Max Titanium (chocolate flavor), which is reconstituted in water. The supplements were provided by the kitchen staff on the day of the hemodialysis session over a period of 37 days. The amount per portion and the nutritional composition of the supplements are shown in (Table 1).

The 100% Whey® and Albumax® supplements were portioned into sterile 300-mL plastic bottles using a specific measurement cup with a funnel. Each bottle had a label with instructions for the patient of how to dilute and consume the supplement, as well as the dialysis period (morning or afternoon), date, and name of each patient. The trainees provided the supplements and the kitchen staff delivered the bottles to the patients together with the dialysis snack. The HDMax® supplement was also provided by the kitchen staff and was identified by the trainees with a label that contained the patient's name and period of dialysis.

Serum albumin levels were collected by the trainees from the records provided by the Nephrology Clinic with the help of the responsible nutritionist for evaluation of the outcomes of the intervention and for comparison between the different types of supplement. Since serum albumin levels are obtained quarterly at the clinic, the values from January and April were used.

For statistical analysis, the quantitative variables are reported as arithmetic mean, standard deviation, median, and coefficient of variation. Since the normality test showed no normal distribution of the data according to Siegel and Castellan [13], correlations were analyzed using Spearman's correlation coefficient. The significance of differences between initial and final albumin concentrations in the total sample, irrespective of the type of supplement administered, was verified using the Wilcoxon test. The Kruskal-Wallis test, complemented by Dunn's test, was used for comparison of the three groups. A level of significance of $p < 0.05$ was adopted.

Results

One of the 15 participants selected withdrew from the study in the first week of intervention and was replaced with another patient. The sample consisted of five (33.3%) women and 10 (66.7%) men with a mean age of 57.2 ± 16.79 years.

With respect to the main reason for CKD in the population studied, 53.3% simultaneously had systemic arterial hypertension and diabetes mellitus, 40% only had systemic arterial hypertension, and 6.7% had nephrotic syndrome.

Anthropometric evaluation showed a mean height of the patients of 1.66 ± 0.09 m and a mean body weight of 78.3 ± 28.0 kg, resulting in a mean BMI of 27.9 ± 7.63 kg/m². The mean arm, waist and abdominal circumferences were 29.3 ± 4.93 , 91.6 ± 20.89 and 92.8 ± 21.88 cm, respectively. Skinfold measurements for the determination of body composition showed mean values of 8.69 ± 3.06 mm (biceps), 11.4 ± 3.38 mm (triceps), 12.08 ± 3.17 mm (subscapular), and 12.25 ± 3.93 mm (suprailiac). The calculation of AMC classified five (33.3%) patients as having mild malnutrition.

Table 1. Nutritional information per portion of the supplements used in the study.

	HDMax® (200 mL)	Albumax® (20 g)	100% Whey® (20 g)
Energy (kcal)	300	64	80
Protein (g)	13.4	15	12.5
Carbohydrates (g)	40	1.06	5

The following mean values were obtained with the 24-hour dietary recalls: 1,202.23 ± 336.87 calories, which consisted of 158.16 ± 44.46 g carbohydrates, corresponding to 53.44 ± 5.04%; 37.77 ± 13.56 g lipids, corresponding to 30.06 ± 5.52%, and 52.35 ± 18.98 g protein, corresponding to 17.98 ± 3.51%. Mean cholesterol was 166.76 ± 62.83 mg; sodium 1,096.98 ± 543.57 mg; iron 6.84 ± 2.55 mg; calcium 324.58 ± 202.65 mg; phosphorus 638.69 ± 196.23 mg; vitamin C 59.38 ± 53.77 mg; potassium 1,469.90 ± 449.33 mg, and fiber 14.60 ± 6.15 g.

There was a positive correlation between serum albumin concentrations and the amount of protein consumed with the meals by the patients during the study ($p < 0.0159$). This relationship can be explained by the low protein intake in 93.33% of the participants, corresponding to a mean intake of 0.73 g protein/kg body weight per day. The mean initial serum albumin concentration found was 3.22 g/dL.

A statistically significant increase in serum albumin levels was observed after supplementation, irrespective of the product used ($p = 0.0075$). The mean serum albumin concentration after supplementation was 3.44 g/dL. A more expressive increase was observed in subjects of the group supplemented with 100% Whey® and Albumax® compared to patients receiving the HDMax® supplement. The comparison of the three different protein supplements is illustrated in (Table 2).

Discussion

According to the classification of nutritional status based on AMC, five (33.33%) subjects had mild malnutrition. These findings do not agree with the results reported by D'Amico *et al.* [14] who studied 63 hemodialysis patients from the town of Guarapuava, center-south region of Parana state, and identified no patient with malnutrition when this classification was made based on AMC.

The problems of methods for assessing food intake are related to factors that lead the patients to make mistakes such as misunderstanding the questions, erroneous estimation of the size of some portions by not knowing the correct quantity of daily food consumption, and difficulties in recalling. [15]

The daily protein intake values of the population studied differ from those reported by Cabral *et al.* [16] in a study involving 37 dialysis patients from the University Hospital of the Federal University of Pernambuco. The authors found a mean protein intake of 1.4 g/kg/day, a value higher than that observed in the present study (0.73 g protein/kg/day) and in other studies on patients undergoing hemodialysis [17]. The adequate protein intake in the study of Cabral *et al.* [16] may explain the observation of serum albumin levels of 3.5 g/dL in 49.5% of the sample, a value higher than the mean serum albumin concentration found in the present study (3.2 g/dL) before the intervention, corresponding to 66.67% of patients with levels of less than 3.5 g/dL.

The increase in serum albumin concentrations as a result of protein supplementation observed in the present study agrees with the results of Pupim *et al.* [18] reported for a sample of 10 subjects, five supplemented for 3 months with Nefrodial® and the remaining subjects serving as control. The authors demonstrated the importance

of routine supplementation of hemodialysis patients, associating it with a reduction in morbidity and mortality in this population, and stated that the longer the time of intervention, the better the effect on serum albumin concentrations.

Calegari *et al.* [19] submitted 18 patients from the Porto Alegre University Hospital to a 3-month intervention during which they received a non-processed supplement made from a combination of the following ingredients: milk, eggs, crystal sugar, sweetened condensed milk, corn starch, fruit gelatin, and sunflower oil. Although the authors observed significant improvement in the Subjective Global Assessment score and in the 6-minute walk test, there were no significant alterations in serum albumin levels. The authors highlighted the idea that supplementation of hemodialysis patients can positively interfere with the quality of life and life expectancy of this population.

Conclusion

The present study permits to conclude that protein supplementation increases serum albumin concentrations in hemodialysis patients and may contribute to improve the nutritional status of this population. In addition, the results of protein supplementation differ according to the product used and the supplements therefore need to be prescribed according to the individual necessities of the patients.

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Table 2. Comparison of the effect of the protein supplements on serum albumin concentrations of hemodialysis patients (Franca-SP, 2015).

Type of supplement	p value
HDMax® vs. 100% Whey® supplement	$p < 0.05$
HDMax® vs. Albumax® supplement	$p < 0.05$
100% Whey® vs. Albumax® supplement	$p > 0.05$

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