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RESEARCH ARTICLE

Evaluation of the Impact of Nutritional Support on Quality of Life and Morbidity Indicators in Hemodialysis

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Abstract

Introduction: Protein-energy malnutrition is a predictor of morbidity and mortality in hemodialysis. Early nutritional intervention and appropriate clinical care are critical to reduce morbidity and improve quality of life in hemodialysis patients.

Purpose: Evaluate the impact of nutritional assistance in hemodialysis services with full nutritional assistance (group 1) and partial nutritional assistance (group 2).

Methods: A prospective cohort study of 56 patients (19 women and 37 men) followed-up for 12 months. There were 4 deaths, 4 kidney transplants, 6 transfers and 1 voluntary withdrawal, so that only 41 patients completed the study. Patients were assessed at the 3rd and 15th month of hemodialysis. *Main inclusion criteria:* Being on hemodialysis for at least 3 months and age ≥ 18 years. *Instruments:* Biochemical tests, SF-36, malnutrition-inflammation score, economic classification criteria of the Brazilian Association of Research Companies. *Statistics analysis:* were expressed as mean ± standard deviation, median, chi-square or Fisher's exact test, Mann-Whitney test, "t"-Student test, Pearson's correlation, ANOVA and Tukey's multiple comparisons. Level of significance: $p < 0.05$.

Results: Group 1 had a higher median age (p: 0.014). Group 2 and patients with indwelling catheter had higher median annual hospitalizations (5 and 6 days, p: 0.028 and 0.035, respectively). The malnutrition-inflammation score correlated negatively with albumin (r = -0.632, p: 0.000), and with SF-36 domains: physical functioning (r = -0.433, p: 0.001), physical aspects (r = -0.393, p: 0.003), general health (r = -0.412, p: 0.002), vitality (r = -0.338, p: 0.011), social functioning (r = -0.361, p: 0.006), emotional functioning (r = -0.278, p: 0.038), mental health (r = -0.313, p: 0.019), and positively with C-reactive protein (r = 0.479, p: 0.000).

Conclusion: Results suggest that full nutritional assistance can have a positive influence, reducing morbidity and controlling nutritional disorders in hemodialysis.

Keywords

Nutritional assessment, Quality of life, Morbidity, Renal replacement therapy, Observational studies

Introduction

The prevalence of malnutrition in hemodialysis (HD) is high, ranging from 40-80% [1,2]. The major nutritional problems are related to accumulation of metabolites between dialysis sessions and to nutrient loss during the procedure.

The micro-inflammatory state in uremia alone can lead to malnutrition by causing both anorexia and catabolism [3,4]. Blood contact with the dialyzer, which is not a fully biocompatible membrane, may also generate an inflammatory response. Proinflammatory cytokines, such as tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6), directly stimulate the ubiquitin-proteosome pathway as well as inflammatory response transcription factors NF-Kappa B pathways (NF-κB), contribu-

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ting to increased catabolism. Moreover, inflammation may have indirect effects on increased muscle degradation by promoting resistance to the action of anabolic hormones such as growth hormone (GH), insulin growth factor (IGF-1) and testosterone [5].

The dialysis procedure influences both energy and protein metabolism reducing plasma amino acids and intracellular muscle protein synthesis, leading to muscle proteolysis in an attempt to maintain the plasma amino acid concentration. Simultaneously, there is an increase in energy expenditure, which can last up to two hours after the dialysis session [6,7]. Other factors also contribute to the genesis of protein-energy malnutrition, such as: loss of amino acids during dialysis (4-8 grams per HD session on average, reaching up to 20 grams with high-flux dialyzers), metabolic acidosis and low food intake [8,9].

As previously noted, HD patients have a poorer quality of life (QoL) compared to the general population [10]. Thus, early nutritional intervention and appropriate clinical care become essential to welfare and QoL improvement. Therefore, the objective of this study was to evaluate the impact of nutritional counseling on QoL and morbidity indicators in HD.

Methods

A prospective cohort study was conducted including 56 patients (19 women and 37 men) followed-up for 12 months, at three hemodialysis centers: Center of Nephrology and Dialysis at the Sírio-Libanês Hospital, Tatuapé Clinic of Nephrology and Renal Transplantation and Pro-Nefron Nephrological Center. The study was accomplished from June 2009 to September 2011. The study was duly approved by the Research Ethics Committee of Federal University of São Paulo-UNIFESP and by the Research Ethics Committee of the Sírio-Libanês Hospital. The patients were divided into group 01 (full nutritional assistance) and group 02 (partial nutritional assistance). Full nutritional assistance was defined as the presence of a Nutritionist during hemodialysis at the sessions dialysis center, actively searching for the patient. Partial nutritional assistance was characterized by the need to schedule an appointment, the Nutritionist not being present during HD sessions. Patients were evaluated on their 3rd and 15th consecutive month of HD. Patient recruitment occurred through consecutive sampling, provided that met the criteria for inclusion and exclusion established. Inclusion criteria: being on HD for at least three months and age ≥ 18 years. Patients having one of the following criteria were excluded from the sample: neoplastic diseases, mental illness, temporary catheter for hemodialysis access, acquired immunodeficiency syndrome, unsuccessful renal transplant in the last six months, advanced liver disease and liver transplantation, alcohol and (or) drug users, patients who migrated from HD to peritoneal dialysis after being on HD for a period longer than three months, and those who did not agree to sign the free informed consent. Instruments used: biochemical parameters (urea-pre and post-HD session, phosphorus, total calcium, calcium × phosphorus product, intact parathyroid hormone molecule , C-reactive protein (CRP), LDL-c, HDL-c, triglycerides (TG), albumin), SF-36 quality of life questionnaire (Medical Outcomes Study Questionnaire 36-Item Short Form Health Survey) translated into Portuguese and culturally validated by Ciconelli [11], malnutrition-inflammation score-MIS [12], classification criteria of the Brazilian Association of Research Companies (ANEP) [13]. Demographic and clinical data were obtained by checking the medical records. All biochemical parameters were collected pre-HD sessions, with the exception of urea, which was also dosed post-HD sessions. Creatinine and urea clearances were measured at the beginning, and it was also necessary to measure urea clearance at trial termination for adjustment of blood urea nitrogen pre-HD in order to estimate protein intake. Venous blood samples were collected pre-dialysis of the second HD session of the week in the Center of Nephrology and Dialysis at the Sírio-Libanês Hospital and at the Tatuapé Clinic of Nephrology and Renal Transplantation. At Pro-Nefron Nephrological Center the serum dosages were collected on the first HD session of the week. Biochemical parameters were analyzed by three different laboratories. Each laboratory's reference value was used for data interpretation. Normalization of serum levels measured was only applied to CRP, according to the laboratory's normality range upper limit (upper normal limit-UNL) due to varying methodologies and normality values between the different laboratories. Thus, it worked with the magnitude of variation in relation to the upper reference value, i.e., the number of times the dosed amount was increased or decreased relative to the laboratory's upper normal reference.

The percentage of interdialytic weight gain (%IDWG) was estimated in relation to the difference between post-dialysis weight and the following session's pre-dialysis weight; the monthly median was subsequently estimated from the number of dialysis sessions in that period.

Protein intake was assessed by estimating the protein equivalent of total normalized protein nitrogen appearance (nPNA) calculated through urea kinetics [14] and then normalized by total body water volume, using the Watson's formula [15]. According to the K/DOQI, 2000, the cutoff value adopted was ≥ 1.2 g/kg for stable patients on HD [14]. The following equations proposed by the NKF-DOQI [14] were adopted to calculate PNA in this study:

PNA: First dialysis of the week (g/day) =

$$\frac{\text{Pre-dialysis serum urea nitrogen (SUN)}}{\left[36.3+(5.48)\times(\text{Kt/V})+53.5/\text{Kt/V}\right]+0.168}$$

PNA: Second dialysis of the week (g/day) =

$$\frac{\text{Pre-dialysis serum urea nitrogen (SUN)}}{\left[25.8+(1.15/\text{Kt}/\text{V})+(56.4/\text{Kt}/\text{V})+0.168\right]}$$

For patients with significant residual diuresis, the pre-dialysis SUN was adjusted: SUNa = SUN {1 + [0.79 + (3.08/Kt/V)] × Kr/V}.

Hemodialysis efficacy was determined by Kt/Vurea, based on the kinetics of urea model. Second generation Daugirdas equation [16], standardized by the National Kidney Foundation (NKF-USA) guidelines was used. A Minimum Kt/Vurea of 1.2 per dialysis session [17] was the objective.

Statistical analysis was performed using the Minitab software version 16.1. Statistical results were expressed as mean ± standard deviation, median, chi-square or Fisher's exact test, Mann-Whitney test, "t"-Student test, Pearson's correlation, analysis of variance ANOVA with two factors of variation: group and time, and Tukey's multiple comparisons. Statistically significant level was established for values of $p < 0.05$.

Results

Forty-one (41) patients completed the study; the drop-outs were due to: 4 deaths, 4 kidney transplants, 6 clinic transfers and 1 voluntary withdrawal.

Table 1 shows socio-demographic and clinical characteristics of patients participating in the study. The patients were divided into two groups - full time nutritional assistance (group 1: 31 patients) and part time nutritional assistance (group 2: 25 patients), statistically significant differences were found in age (p: 0.014). Group 1 was markedly older, with a median age of 69 years (range: 23-83 years). In group 2, the median age was 53 years (range: 24-75 years). Regarding gender, 71% and 60% of patients were male in groups 1 and 2, respectively. There was no statistically significant difference regarding race in the population studied. The patients were considered white and nonwhite, which included yellow, mixed-race and black. The white race predominated in both groups, being 87.1% in group 1 and 76% in group 2. In terms of social class, they were divided into class A and B, and class C, D and E. Comparing the two groups, the difference was not statistically significant (p: 0.179). Social classes A and B were predominant in group 1 (58.1%), while 60% of the patients in group 2 were in social classes C, D and E. The study included patients with arteriovenous fistula (AVF) and indwelling catheters. AVF was prevalent in both groups, both at the beginning and end of the trial. In group 2, the percentage of patients with AVF was higher than in group 1 both at the beginning and end of the study (76 and 81.3% respectively). When analyzing the type of access for HD, patients with indwelling catheters had a higher median of annual hospitalizations compared to patients with AVF (6 days, p: 0.035). The main causes etiologies CKD in group 1 (with full nutritional support) were: Hypertensive nephrosclerosis (22.6%), diabetic nephropathy (6.4%), simultaneous presence of diabetes mellitus (DM) and systemic arterial hypertension (SAH) (9.7%), other causes (25.8%), and unknown etiology (35.5%). In group 2 (partial nutritional support), the percentage distribution for the main causes of CKD was the following: hypertensive nephrosclerosis (12%), diabetic nephropathy (20%), simultaneous presence of diabetes mellitus (DM) and systemic arterial hypertension (SAH) (20%), other causes (28%), and unknown etiology (20%).

Table 1: Socio-demographic and clinical characteristics of hemodialysis patients on at 3rd and 15th month follow-ups.

Variables N (%)	G1 31 (55.4)	G2 25 (44.6)	p
Age			0.014*
Mean ± SD	62.9 ± 16.7	52.8 ± 13.0	
Median	69	53	
Variation	23-83	24-75	
Gender			0.389
Female	9 (29.0)	10 (40.0)	
Male	22 (71.0)	15 (60.0)	
Race			0.315
White	27 (87.1)	19 (76.0)	
Non White	4 (12.9)	6 (24.0)	
Social Class			0.179
A + B	18 (58.1)	10 (40.0)	
C + D + E	13 (41.9)	15 (60.0)	
Type of Initial Access			0.241
AVF	19 (61.3)	19 (76.0)	
Indwelling catheter	12 (38.7)	6 (24.0)	
Type of Final Access[a]			0.478
AVF	17 (68.0)	13 (81.3)	
Indwelling catheter	8 (32.0)	3 (18.7)	
CKD Ethiology			
Hypertensive Nephrosclerosis	7 (22.6)	3 (12.0)	
Diabetic Nephropathy	2 (6.4)	5 (20.0)	
DM + SAH	3 (9.7)	5 (20.0)	
Other Causes	8 (25.8)	7 (28.0)	
Unknown Etiology	11 (35.5)	5 (20.0)	
Comorbidities			
Absence of Comorbidities	0 (0.0)	2 (8.0)	
Hypertension	12 (38.7)	5 (20.0)	
Diabetes	0 (0.0)	1 (4.0)	
Cardiovascular Diseases	1 (3.3)	0 (0.0)	
DM + SAH	5 (16.1)	3 (12.0)	
DM + SAH + CVDs	4 (12.9)	8 (32.0)	
SAH + CVDs	9 (29.0)	6 (24.00)	
N° of Comorbidities			
0 + 1	12 (38.7)	8 (32.0)	0.602
2 or +	19 (61.3)	17 (68.0)	
N° of Hospitalizations (days)			0.028*
Mean ± SD	5.23 ± 11	14.3 ± 22.21	
Median	0	5.0	
Variation	0-43	0-100	

Symbols and abbreviations: *: Statistically significant p value; [a]: 41 patients completed the study; G1: Group with full nutritional assistance; G2: Group with partial nutritional assistance; N: Number of patients; AVF: Arteriovenous fistula; DM: Diabetes mellitus; SAH: Systemic arterial hypertension; CVD (s): Cardiovascular disease (s); Tests used: Age ("t"-Student test), Gender, Social Class, Type of initial access, N° of comorbidities (chi-square), Race, Type of final access (Fisher's exact test), N° of days of hospitalization (Mann-Whitney).

The following were among other causes for both groups: polycystic kidneys, systemic erythematosus lupus, membranoproliferative glomerulonephritis (MPGN), nephrolithiasis, renal tuberculosis and interstitial nephritis. As for the number of comorbidities, patients were classified as: 0-1 comorbidity or with 2 or more comorbidities, with no statistically significant difference between groups. The most common comorbidities were SAH, DM, cardiovascular disease(s) and associations between these. Group 2 had a higher number of days of hospitalization per year,

Table 2: Comparison of biochemical and clinical parameters between groups were evaluated on the 3rd and 15th month of hemodialysis by analysis of variance with two factors of variation: group and time.

Variables	**G1-M3**	**G1-M15**	**G2-M3**	**G2-M15**	**p**
N (%)	31 (55.4)	25 (44.6)	25 (61.0)	16 (39.0)	
Phosphorus (mg/dL)					
Mean	5.2	4.5	5.1	5.1	
Period					0.4
Group*Period					0.329
Total Calcium (mg/dL)					
Mean	9.6	9.1	10.3	10.2	
Period					0.075
Group*Period					0.313
PTHi (pg/mL)					
Mean	527.1	358.7	570.8	506.3	
Period					0.151
Group*Period					0.517
Ca × P Product (g^2/dL^2)					
Mean	50.6	41.1	51.4	53.4	
Period					0.333
Group*Period					0.140
Albumin (g/dL)					
Mean	3.7	3.7	3.6	3.7	
Period					0.384
Group*Period					0.483
CRP (× UNL)					
Mean	5.0	2.3	7.4	5.8	
Period					0.009*
Group*Period					0.504
LDL-c (mg/dL)					
Mean	116.4	82.6	82.6	90.3	
Period					0.297
Group*Period					0.101
Triglycerides (mg/dL)					
Mean	185.1	178.7	155.3	153.0	
Period					0.728
Group*Period					0.870
IDWG (%)					
Mean	2.7	2.9	2.8	3.1	
Period					0.186
Group*Period					0.772
Kt/V_{urea}					
Mean	1.3	1.4	1.3	1.2	
Period					0.507
Group*Period					0.191
nPNA (g/kg/day)					
Mean	1.3	1.1	1.4	1.3	
Period					0.097
Group*Period					0.803

Symbols and abbreviations: *: Statistically significant p value; G1: Group with full nutritional assistance; G2: Group with partial nutritional assistance; N: Number of patients; M3: 3rd month-beginning of monitoring; M15: 15th month-end of monitoring; iPTH: Intact parathyroid hormone; Ca × P: Calcium × phosphorus product; CRP: C-reactive protein × UNL-upper normal limit); LDL-c: Low density lipoprotein cholesterol; %IDWG: Percentage of interdialytic weight gain; Kt/Vurea: Volume of plasma cleared of urea; nPNA: Equivalent of total normalized protein nitrogen appearance.

Table 3: Comparison between groups 1 and 2 for some drugs used by patients on a regular hemodialysis program.

Variables	Group	Yes N (%)	No N (%)	p
D Vitamin**	G1	12 (38.7)	19 (61.3)	0.400
	G2	7 (28)	18 (72)	
Carbonate/Calcium Acetate**	G1	9 (29)	22 (71)	0.438
	G2	5 (20)	20 (80)	
Sevelamer Hydrochloride**	G1	15 (48.4)	16 (51.6)	0.002*
	G2	22 (88)	3 (12)	
Statins**	G1	12 (38.7)	19 (61.3)	0.320
	G2	13 (52)	12 (48)	
Fibrates***	G1	0 (0)	31 (100)	0.005*
	G2	6 (24)	19 (76)	

Symbols and abbreviations: *: Statistically significant p value; G1: Group with full nutritional assistance; G2: Group with partial nutritional assistance; Yes-N (%): Number and percentage of patients using the medication; Non-N (%): Number and percentage of patients who did not use medication; Tests applied: Chi-square**; ***Fisher's exact test.

with a median of 5 (range, 0-100 days ± 22) versus 0 day (range, 0-43 days ± 11) when compared to group 1, showing statistical significance (p: 0.028).

According to Table 2, group 1 showed significant reductions in clinical parameters such as: phosphorus, total calcium, parathyroid hormone and calcium × phosphorus product, but without statistical significance. There was a trend toward a lower percentage of interdialytic weight gain in group 1, although not statistically significant.

Regarding drugs routinely prescribed in HD, it was observed that in group 2 about 88% of the patients used sevelamer hydrochloride to chelate phosphorus from foods, compared to 48.4% in group 1, with statistical significance (p: 0.002). Approximately 44.6% (n: 25) of study patients had to use statins to control dyslipidemia, and 10.7% (n: 6) used fibrates to reduce TG. There was a tendency for clinical improvement serum levels of LDL-c and TG in group 1, which used less statins to control LDL-c and no fibrates to reduce TG. In group 2, 24% of patients were taking fibrates to control TG versus 0% in group 1, which was statistically significant (p: 0.005) (Table 3).

Table 4 shows that malnutrition-inflammation score (MIS) was negatively correlated with albumin (r = -0.632, p: 0.000) and positively with CRP (r = 0.479, p: 0.000). There was negative correlation between MIS and the following of SF-36 quality of life domains: functional ability (r = -0.433, p: 0.001), physical functioning (r = -0.393, p: 0.003), general health (r = -0.412, p: 0.002), vitality (r = -0.338, p: 0.011), social functioning (r = -0.361, p: 0.006), emotional aspects (r = -0.278, p: 0.038), mental health (r = -0.313, p: 0.019), summarized physical component (r = -0.364, p: 0.006), summarized mental component (r = -0.314, p: 0.019). The summarized mental component was positively correlated with albumin (r = 0.387, p: 0.003) and CRP (r = 0.295, p: 0.029). The number hospitalization days per year was positively correlated with MIS (r = 0.292, p: 0.029), and negatively with albumin (r = -0.290, p: 0.030).

Table 4: Pearson's correlation between malnutrition-inflammation score (MIS), biochemical and clinical variables, and SF-36 domains of 56 patients on hemodialysis.

MIS	**Albumin**	r = -0.632
		p = 0.000*
	CRP	r = 0.479
		p = 0.000*
	Functional Ability	r = -0.433
		p = 0.001*
	Limitations due to Physical Aspects	r = -0.393
		p = 0.003*
	Pain	r = -0.063
		p = 0.643
	General Health	r = -0.412
		p = 0.002*
	Vitality	r = -0.338
		p = 0.011*
	Social Functioning	r = -0.361
		p = 0.006*
	Limitations due to Emotional Aspects	r = -0.278
		p = 0.038*
	Mental Health	r = -0.313
		p = 0.019*
	Summarized Physical Component	r = -0.364
		p = 0.006*
	Summarized Mental Component	r = -0.314
		p = 0.019*
	No. of Hospitalization Days per Year	r = 0.292
		p = 0.029*

Symbols and abbreviations: *: Statistically significant p value; r: Pearson's coefficient; CRP: C-reactive protein.

Discussion

Nutritional follow up in dialysis treatment is an advantage for the adequacy of fluid intake, dietary intake of sodium, potassium, calcium and phosphorus, leading to major interventions in the water and mineral metabolism with long-term implications, particularly in renal osteodystrophy and cardiovascular events. Uremia and

diabetes alone cause significant nutritional changes in these patients if not adequately monitored, and so does aging.

There was a statistically significant difference in age between groups, and although group 2 was younger, 68% of patients in group 2 had two or more comorbidities, with a median of 5 days of annual hospitalization against 0 day when compared to group 1. This finding suggests involvement of socioeconomic factors, such as a more difficult access to health, and lower lifelong quality of life, since patients in group 1 were predominantly in social classes A and B, whilst in group 2 they were in classes C, D and E (Table 1). In Brazil, data regarding the socioeconomic status of patients with CKD on dialysis are scarce. However, the profile of renal disease in Brazil seems to reflect the economic reality. According to the ANEP, 70.4% of the population belong to social classes C, D and E [13].

It is well grounded in the literature that the catheter as access for HD, is associated with increased infections, and higher morbidity and mortality [18,19]. A study by Taylor, et al. found that the relative risk of bacteremia in those using catheter for HD was estimated to be ten times greater than in patients with AVF. It was also observed that 18.5% of all deaths in dialysis patients were related bacteremia [20]. In this study, of the 56 patients on HD, 18 (32%) had permanent catheters and of these, 7 (38.9%) were hospitalized during the follow-up due to infection of the access, representing a high rate of catheter infection. AVF was the predominant type of access for HD in the studied population (68%). This is an important factor in reducing morbidity and mortality, considering that 55.4% of the patients were elderly, a condition that often hinders the construction of AVF as access for HD. These findings corroborate the literature, since patients with indwelling catheters had a higher median number of days of annual hospitalization when compared to patients with AVF (6 vs. 0 days, respectively; p: 0.035) (Table 1).

The European guidelines recommend that the percentage of interdialytic weight gain (IDWG) should be between 4 and 4.5% of body weight at most [9], while the K/DOQI, 2000 has set a 5% limit [14], because complications such as cardiac dysfunction and pulmonary congestion arise from excessive IDWG, particularly in patients with reduced diuresis. Adherence to adequate fluid intake is commonly measured by IDWG [21]. In the present study IDWG was found to be adequate in groups 1 and 2, both in the initial and final periods of the trial. However, group 2 showed a tendency to have a higher IDWG percentage when compared to group 1, suggesting that a full-time Nutritionist can positively impact patients' awareness and adherence to treatment (Table 2).

Inasmuch as chronic renal patients are considered chronically inflamed, CRP was used as an inflammatory marker. Group 1 showed a greater reduction in CRP levels during follow-up, which may or may not be related to improvement of the nutritional state. Given the CRP (× UNL-upper normal limit) values found, it can be said that both groups had persistent inflammation during the trial (Table 2).

Evidence suggests that albumin synthesis is suppressed when CRP is increased. In this study, both groups virtually kept serum albumin levels below 4.0 g/dL during the follow-up period (Table 2). This may mean that these patients have a doubled susceptibility to risk death, mainly from cardiovascular events, as albumin is a strong predictor of cardiovascular mortality [22].

K/DOQI guidelines, 2003 [23] on the management of dyslipidemia in CKD recommend statins as first choice for adequacy of lipid profile, driven primarily by LDL-c. It was observed in this study that group 1, which had full time nutritional assistance, showed reduction of serum TG and LDL-c, with serum dosage decreasing from suboptimal to optimal values (Table 2), without requiring the use of fibrates or statins. Group 2, which had partial nutritional assistance, 52% made use of statins and 24% of patients used fibrates to reduce LDL-c and TG, respectively (Table 3), starting the trial with optimal serum LDL-c and maintaining it throughout the period. As for TG in the same group, serum levels were slightly increased, but close to borderline values. Although not statistically significant, there was a trend for clinical improvement in group 1 (Table 2) without the use of medication, suggesting once more that the role of the nutritionist can positively influence morbidity reduction in HD.

Changes in bone and mineral metabolism trigger laboratory abnormalities in serum levels of calcium, phosphorus, PTH and active vitamin D (calcitriol). The ability of phosphorus clearance of a 4-hour HD session is approximately 900 mg of phosphorus [24]. In contrast, the daily amount of ingested phosphorus to meet the recommended 1.2 g protein/kg/day intake is about 1000 mg/day, exceeding the clearance capacity of the hemodialysis session [25]. Thus, there is a paradox between the recommendation of hyperproteic diets and dietary restriction of phosphorus intake. Food sources of phosphorus have a relationship between the amount of phosphorus and protein content. The best strategy is to select foods with lower phosphorus/protein ratio, which is hardly achieved without nutritional guidance to clarify this to the patient. As to phosphorus, both groups began and ended the study with values within the range recommended by K/DOQI, 2003 [25] (i.e., 3.5-5.5 mg/dL). However, there was a more significant reduction in phosphorus between the initial and final periods for group 1 (Table 2). Both in the beginning and the end of the trial the two groups had serum PTH above 300 pg/mL, which is above K/DOQI, 2003 [25] recommendation (i.e., 150-300 pg/mL), but

still within the maximum value suggested by KDIGO, 2009 [26] (two to nine fold above maximum laboratory reference value). Group 1 showed a more representative decrease in serum PTH levels from a clinical standpoint. Calcium × phosphorus product was in accordance with K/DOQI, 2003 [25] guideline recommendation (< 55 mg^2/dL^2) in both groups (Table 2). Furthermore, in group 1 wherein the reduction of phosphorus levels was higher, the amount of chelant (sevelamer hydrochloride) used among patients was lower (48.4%), suggesting even drug savings (Table 3). In group 2, 88% were using sevelamer hydrochloride and although it was not statistically significant in the evaluation period, group 1 benefited with full-time nutritional assistance, showed significant reduction, from a clinical point of view, in total calcium, phosphorus, calcium × phosphorus product and PTH levels (Table 2), as well as a lower percentage of patients using phosphate chelant (sevelamer hydrochloride) (Table 3). This highlights the importance of the nutritionist as an education and transformation agent when awareness-building can cause behavioral changes that may influence improvement of QoL and survival on dialysis, due to a better control of risk factors that have cardiovascular implications. Studies show that less than 25% of dialysis patients adhere to diet and prescription drugs [27]. To increase adherence to treatment it is necessary to promote integrated, continuous actions, with the participation of a multidisciplinary team and involvement of family members and caregivers to achieve treatment effectiveness for these patients [28].

Both groups reached the minimum target Kt/Vurea recommended by K/DOQI, 2006 [17] (1.2 per HD session) at the beginning and at the end of the trial. Therefore, Kt/Vurea was not a parameter that contributed negatively to the evolution of nutritional status in this study (Table 2).

Regarding nPNA, group 1 (median age of 69 years) had lower initial values that decreased during the period when compared to group 2; it was also below the K/DOQI, 2000 [14] recommendation (1.2 g/kg/day for stable patients on HD) at trial termination (Table 2). These findings can perhaps be attributed to the occurrence of physiologic alterations in the elderly population: changes in body composition (decreased muscle mass and increased adipose tissue), lower sensory perception (taste and smell) and compromised teeth (edentulism). One of the limitations to nPNA use is that it only reflects recent nitrogen intake.

MIS is an instrument strongly related to morbidity and mortality according to a study by Rambod M, et al. [29], and the risk of death for patients in dialysis increases two-fold for every 2-point increase in the score. In this author's study patients with higher MIS scores had worse QoL in SF-36 domains. There was positive correlation of MIS with nPNA, CRP, interleukin-6 and the erythropoietin dose, and negative correlation with pre-albumin, serum iron, CMB and lean body mass. The present study's correlation analysis reinforces the findings of Rambod, et al. [29] and confirms the value of the malnutrition-inflammation score as a predictor of morbidity and mortality, since MIS showed moderate negative correlation with albumin, weak positive correlation with the number of days of annual hospitalization and moderate positive correlation with CRP (× UNL). Thus, patients who scored higher in MIS were those who had more nutritional problems, more inflammation and more hospitalizations during the year. MIS had moderate negative correlation with the following SF-36 domains: physical functioning, general health, vitality, social functioning, mental health, summarized physical component, and summarized mental component. This means that higher scores in MIS (worse nutritional status) reflected in lower SF-36 values, i.e., worse QoL. MIS showed weak negative correlation with the emotional aspects domain. SF-36 pain domain was the only one that did not show statistically significant correlation in Pearson's correlation analysis (Table 4). Clinically, reports of interference of this domain in QoL and dietary intake of patients, affecting their nutritional status were not seen.

Conclusion

Lower MIS values reflected better nutritional status and QoL by SF-36, lower levels of CRP and better albumin level values, which could reduce morbidity and mortality conditions. Patients with higher MIS scores and lower serum albumin levels were the ones who had worse clinical outcome. There was a significant clinical improvement in phosphorus, total calcium, PTH, and calcium x phosphorus product associated with the use of phosphorus chelant by group 1. The same group also had better TG levels without use of fibrates, and LDL-c with lower use of statins. In addition, the percentage IDWG was lower. The data suggest that the role of full time nutritionist during HD sessions positively influence nutritional status, improves MIS values, the QoL questionnaire, may reduce morbidity in HD and controls nutritional disorders.

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Support and Financial Disclosure Declaration

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Conflict of Interest Declaration

There is no conflict of interest.

Ethical Statement

Please find Ethical Statement.

References

1. Marcen R, Teruel JL, de la Cal MA, Gamez C (1997) The impact of malnutrition in morbidity and mortality in stable hemodialysis patients. Spanish Cooperative Study of Nutrition in Hemodialysis. Nephrol Dial Transplant 12: 2324-2331.
2. Cano NJ, Roth H, Aparicio M, Azar R, Canaud B, et al. (2002) Malnutrition in hemodialysis diabetic patients: Evaluation and prognostic influence. Kidney Int 62: 593-601.
3. Kalantar-Zadeh K, Kopple JD (2001) Relative contributions of nutrition and inflammation to clinical outcome in dialysis patients. Am J Kidney Dis 38: 1343-1350.
4. Kalantar-Zadeh K, Kopple JD (2003) Inflammation in renal failure. UpToDate. Inc., Boston, USA.
5. Stenvinkel P (2013) Can treating persistent inflammation limit protein energy wasting? Seminars in Dialysis 26: 16-19.
6. Ikisler TA, Pupim LB, Brouillette JR, Levenhagen DK, Farmer K, et al. (2002) Hemodialysis stimulates muscle and whole body protein loss and alters substrate oxidation. Am J Physiol Endocrinol Metab 282: E107-E116.
7. Pupim LB, Flakoll PJ, Brouillette JR, Levenhagen DK, Hakim RM, et al. (2002) Intradialytic parenteral nutrition improves protein and energy homeostasis in chronic hemodialysis patients. J Clin Invest 110: 483-492.
8. Raj DS, Zager P, Shah VO, Dominic EA, Adeniyi O, et al. (2004) Protein turnover and amino acid transport kinetics in end-stage renal disease. Am J Physiol Endocrinol Metab 286: E136-E143.
9. Fouque D, Vennegoor M, Wee PT, Wanner C, Basci A, et al. (2007) EBPG guideline on nutrition. Nephrol Dial Transplant 22: 45-87.
10. Evans RW, Manninen DL, Garrison LP Jr, Hart LG, Blagg CR, et al. (1985) The quality of life of patients with end-stage renal disease. N Engl J Med 312: 553-559.
11. Ciconelli RM (1997) Tradução para o português e validação do questionário genérico de avaliação de qualidade de vida. Medical Outcomes Study 36-Item Short-form Health Survey (SF-36). Federal University of São Paulo, Paulista School of Medicine, São Paulo, SP, Brazil.
12. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH (2001) A malnutrition-inflammation score is correlated with morbidity and mortality in maintenance hemodialysis patients. Am J Kidney Dis 38: 1251-1263.
13. (2013) ANEP-Associação Nacional de Empresas de Pesquisa. Data based on a Socio-economic Survey, 2000 - Instituto Brasileiro de Opinião Pública e Estatística (IBOPE).
14. (2000) Clinical practice guidelines for nutrition in chronic renal failure. K/DOQI, National Kidney Foundation. Am J Kidney Dis 35: S1-S140.
15. Watson PE, Watson ID, Batt RD (1980) Total body water volumes for adults males and females estimated from simple anthropometric measurements. Am J Clin Nutr 33: 27-39.
16. Daugirdas JT, Blake PG, Ing TS (2008) Manual of Dialysis. (4th edn), Guanabara Koogan, Rio de Janeiro.
17. (2006) National Kidney Foundation, K/DOQI: Clinical practice guidelines for hemodialysis adequacy, Update 2006. Am J Kidney Dis 48: S28-S32.
18. Stefan G, Stancu S, Capuşa C, Ailioaie OR, Mircescu G (2012) Catheter-related infections in chronic hemodialysis: A clinical and economic perspective. International Urology and Nephrology 45: 817-823.
19. Campos RP, Do Nascimento MM, Chula DC, Riella MC (2011) Minocycline-EDTA lock solution prevents catheter-related bacteremia in hemodialysis. J Am Soc Nephrol 22: 1939-1945.
20. Taylor G, Gravel D, Johnston L, Embil J, Holton D, et al. (2004) Incidence of bloodstream infection in multicenter inception cohorts of hemodialysis patients. Am J Infect Control 32: 155-160.
21. Ghaddar S, Shamsedden W, Elzein H (2009) Behavioral modeling to guide adherence to fluid control in hemodialysis patients. J Ren Nutr 19: 153-160.
22. Lowrie EG, Lew NL (1990) Death risk in hemodialysis patients: The predictive value of commonly measured variables and an evaluation of death rate differences between facilities. Am J Kidney Dis 15: 458-482.
23. Kidney Disease Outcomes Quality Initiative (K/DOQI) Group (2003) K/DOQI clinical practice guidelines for managing dyslipidemias in patients with kidney disease. Am J Kidney Dis 41.
24. Hou SH, Zhao J, Ellman CF, Hu J, Griffin Z, et al. (1991) Calcium and phosphorus fluxes during hemodialysis with low calcium dialysate. Am J Kidney Dis 18: 217-224.
25. National Kidney Foundation (2003) K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis 42: S1-S201.
26. (2009) KDIGO clinical practice guidelines for the diagnosis, evaluation, prevention and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int 76: S1-S113.
27. Hoover HH (1989) Compliance in hemodialysis patients: A review of the literature. J Am Diet Assoc 89: 957-959.
28. Nerbass FB, Morais JG, Santos RG, Krüger TS, Koene TT, et al. (2010) Adesão e conhecimento sobre o tratamento da hiperfosfatemia de pacientes hiperfosfatêmicos em hemodiálise. J Bras Nefrol 32: 149-155.
29. Rambod M, Bross R, Zitterkoph J, Benner D, Pithia J, et al. (2009) Association of malnutrition score with quality of life and mortality in hemodialysis patients: A 5-year prospective cohort study. Am J Kidney Dis 53: 298-309.