Nutrición Hospitalaria

Nutr Hosp. 2014;30(4):952-959
ISSN 0212-1611 • CODEN NUHOEQ
S.V.R. 318

Original/*Otros*

Hypoalbuminemia and oxidative stress in patients on renal hemodialysis program

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Abstract

***Introduction*: Albumin is considered an important extracellular antioxidant molecule. hypoalbuminemia is a strong and independent predictor of mortality in patients on hemodialysis. The present study evaluated the relation between hypoalbuminemia and oxidative stress by comparing superoxide dismutase activity, lipid peroxidation and antioxidant micronutrient consumption in chronic renal failure patients.**

***Methods*: A case-control study was carried out with 64 patients of both sexes aged 18 to 59 years. The patients with hypoalbuminemia (ALB <3.5 g/dL) were defined as case (n = 26) and control (n = 38) those with ALB ≥ 3.5 g/dL. Determinations of activity superoxide dismutase (SOD) and nitric oxide production by the contraction of nitrite in erythrocytes, concentration of malondialdehyde (MDA) in plasma, lipid profile and micronutrient antioxidants intake were performed. For comparisons between groups, the Student t test was used. Possible associations between variables were tested using the chi-square test and Pearson correlation test.**

***Results*: Consumption of copper was significantly lower (p < 0.05) in the group with hypoalbuminemia. There was a positive correlation between the concentrations of albumin and intake copper (r = 0.280). Negative correlation was found between albumin and MDA concentrations.**

***Conclusion*: Hypoalbuminemia is associated with increased lipid peroxidation, and can contribute to oxidative stress in chronic renal failure patients. Additionally, patients with chronic renal disease undergoing hemodialysis evaluated in this study had reduced consumption of cooper.**

(*Nutr Hosp*. 2014;30:952-959)

DOI:10.3305/nh.2014.30.4.7667

Key words: *Chronic kidney disease. Hypoalbuminemia. Micronutrients. Lipid peroxidation. Superoxide dismutase.*

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Recibido: 4-VI-2014.
Aceptado: 23-VII-2014.

HIPOALBUMINEMIA Y EL ESTRÉS OXIDATIVO EN PACIENTES EN PROGRAMA DE DIÁLISIS RENAL

Resumen

***Introducción*: La albúmina se considera una molécula antioxidante extracelular importante. La hipoalbuminemia es un predictor fuerte e independiente de mortalidad en pacientes en hemodiálisis. El presente estudio evaluó la relación entre hipoalbuminemia y el estrés oxidativo mediante la comparación de la actividad de la superóxido dismutasa, la peroxidación lipídica y el consumo de micronutrientes antioxidantes en pacientes con insuficiencia renal crónica.**

***Métodos*: Este estudio de casos y controles se llevó a cabo con 64 pacientes de ambos sexos de 18 a 59 años. Los pacientes con hipoalbuminemia (ALB < 3,5 g / dL) se definieron como los casos (n = 26) y el grupo control (n = 38) aquellos con ALB ≥ 3,5 g/dL. Fueran realizadas determinaciones de la actividad de la superóxido dismutasa en los eritrócitos, la producción de óxido nítrico por la contracción de nitrito e concentración de malondialdehído (MDA) en plasma, el perfil de lípidos en plasma, la ingesta de proteínas y micronutrientes antioxidantes se realizaron. Para las comparaciones entre grupos, se utilizó la prueba t de Student. Posibles asociaciones entre variables se analizaron mediante el test de correlación lineal y Pearson y en la prueba de chi-cuadrado.**

***Resultados:* El consumo de cobre fue significativamente menor (p < 0,05) para el grupo con hipoalbuminemia. Correlaciones entres las concentraciones de albúmina y el uso de cobre (r = 0,280). Se encontró correlación negativa entre las concentraciones de albúmina y MDA.**

***Conclusión*: La hipoalbuminemia se asocia con aumento de la peroxidación lipídica, y puede contribuir al estrés oxidativo en pacientes con insuficiencia renal crónica. Además, los pacientes con enfermedad renal crónica sometidos a hemodiálisis evaluados en este estudio habían reducido el consumo de cobre.**

(*Nutr Hosp*. 2014;30:952-959)

DOI:10.3305/nh.2014.30.4.7667

Palabras clave: *Enfermedad renal crónica. La hipoalbuminemia. Micronutrientes. La peroxidación lipídica. La superóxido dismutasa.*

Abbreviations

ALB: Albumin
apoA1: Apolipoproteins A1
apoA2: Apolipoproteins A2
BMI: Body mass index
CKD: Chronic kidney disease
Cu-Zn SOD: Copper-zinc superoxide dismutase
Kt/V: Dialysis quality index
DRI 's: *Dietary Reference Intakes*
EDTA: Ethylene diamine tetra acetic acid
HDL: High Density Lipoprotein
HD: Hemodialysis
Hb: Hemoglobin
LDL : Low Density Lipoproteins
MDA: Malondialdehyde
NO : Nitric Oxide
SPSS: Statistical Package for the Social Science
SOD: Superoxide dismutase
TBARS: Thiobarbituric acid reactive substances

Introduction

Chronic kidney disease (CKD) is a clinical syndrome characterized by slow, progressive and irreversible loss of renal functions, which results in accumulation of catabolites (uremic toxins), changes of water-electrolyte and acid-base balance, with deterioration of biochemical and physiological functions of all other organs, essentially[1]. The most used renal replacement therapy in the treatment of CKD is hemodialysis (HD), blood filtration process that removes excess fluid and metabolites, as well as amino acids, peptides and water soluble vitamins[2].

The incidence and prevalence of this disease is increasing in Brazil, and the prognosis is still bad, with high cost of treatment. In 2010, according to a census conducted by the Brazilian Society of Nephrology, the estimated number of patients on dialysis in Brazil was 92,091 individuals, and the estimated number of those who began treatment in that year was 18,972, from which 90.6 percent were HD[3].

Albumin is the biochemical marker of protein reserves most used in clinical practice for easy to measure and for being a powerful predictor of morbidity and mortality in CDK, regardless of the causes that lead to the reduction of its serum concentration[4]. In fact, particularly in the population of patients in dialysis, serum albumin values less than 2.5 g/dL are associated with risk of death 20 times higher when compared to the reference values of 4.0 to 4.5 g/dL; and even values within the normal range (3.5 and 4.0 g/dL) are associated with twice the risk[5].

Oxidative stress can be defined as the imbalance between levels of pro-oxidant compounds and antioxidants, with predominance of the first. The pro-oxidant state has been linked as a cause, and in some cases as a result of various illnesses, including kidney diseases[6]. Some clinical manifestations of CKD can be caused by overproduction of reactive oxygen species (ROS), favoring the manifestation of oxidative stress[7,8].

Quantification of free radicals produced *in vivo* is difficult because they have high reactivity and short half-life[7,9]. For this reason, compounds related to lipid and protein peroxidation has been used to evaluate the oxidative stress. Accordingly, increased oxidative stress in patients with CKD has been evidenced by increasing plasma concentration of malondialdehyde (MDA), as a marker of lipid peroxidation[7,9].

Antioxidants can be classified into non-enzymatic and enzyme. The main components of the antioxidant enzymatic system are the enzymes superoxide dismutase (SOD), catalase and glutathione peroxidase. Non-enzymatic antioxidants include compounds produced *in vivo*, such as reduced glutathione, ubiquinone, uric acid and the transport proteins of transition metals (transferrin and ceruloplasmin), besides the compounds obtained directly from the diet, such as vitamins (C, E and beta carotene) and antioxidant minerals (zinc, copper and selenium)[7,10].

Decrease in SOD activity was demonstrated in patients on hemodialysis, a change that seems to contribute to the occurrence of oxidative disorders[7]. The present study evaluated the relation between hypoalbuminemia and oxidative stress by comparing superoxide dismutase activity, lipid peroxidation, lipid profile and antioxidant micronutrient consumption in chronic renal failure patients on regular hemodialysis program.

Patients and methods

This was a case-control study, involving 64 patients, of both genders, aged between 18 and 59 years and who were divided into two groups. The patients with hypoalbuminemia (ALB < 3.5 g/dL) were defined as case or G1 (n = 26) and control or G2 (n = 38) those with ALB ≥ 3.5 g/dL. Patients were recruited from a dialysis clinic. The participants of groups were matched by age, body weight, height, body mass index (BMI) and dialysis quality index (Kt/V). The patients were included in this study according to the following criteria: age between 18 to 59 years, participation in regular program of dialysis in three weekly sessions for more than 6 months, and the absence of clinical complications like fistula infection, hypotension, cardiac arrhythmia, hypoglycemia, dyspnea, fainting or heart attack.

Evaluation of nutritional status

Global nutritional state was classified according to body mass index (BMI), based on cutting points proposed by the World Health Organization (WHO) (2000)[11]. The measures of body weight were carried out before and after the session of hemodialysis by using a digital scale with capacity of 150 kg and precision of 100

grams, and study participants were barefoot and wearing light clothes. Height was measured using wall-mounted stadiometer, graduated in centimeters, with vertical plastic bar and fixed. Weight and height were measured three times for each participant, and for analysis was considered the average of these measures. The current weight considered was the weight measured after the hemodialysis session.

Collection of biological material for determination of biochemical parameters

Blood samples were obtained for assessment of antioxidant activity by determining the plasma concentration of nitrite and the activity of the enzyme superoxide dismutase (SOD) in erythrocytes. Lipid peroxidation was also evaluated by measuring the concentration of malondialdehyde (MDA) in plasma. Blood collection was performed immediately before sessions of each class of hemodialysis, according to days of the week and in the morning, afternoon and evening shifts. Samples were obtained from 10 mL of blood with participants according to the clinical routine for biochemical analysis of blood collection. The samples were transferred to tubes containing ethylenediamine tetraacetic acid (EDTA) as an anticoagulant. The plasma was separated by centrifugation at 1831 x g for 15 minutes at 4° C and stored in cryogenic tubes to -80° C until the time of the analyses of MDA and nitrite concentration.

For determination of SOD enzyme activity, the erythrocyte mass obtained from total blood was washed three times with 5 mL of 0.9 % saline solution, homogenized by inversion and centrifuged at 2493 x g for 10 minutes at 4° C. After the last centrifugation, the saline solution was aspirated, discarded, and erythrocyte mass stored in cryogenic tubes to -80° C until the time of analysis.

Determination of superoxide dismutase (SOD) activity in erythrocytes

Superoxide dismutase activity was determined by the amount of SOD able to inhibit in 50 % the formation of nitrite, in accordance with the method described by Das, Samanta and Chainy (2000)[12]. To express the results in terms of U SOD /mass of hemoglobin (U SOD /gHb), the erythrocyte lysed was measured according to the cyanmethaemoglobin method.

Determination of plasma levels of nitrite

The determination of nitric oxide production was accomplished by using colorimetric method of Griess that evaluates indirectly the nitric oxide through its metabolite, sodium nitrite[13]. Nitrite concentrations were calculated from the standard curve by the use of sodium nitrite ($NaNO_2$) at concentrations from 0 to 100 μM in PBS (pH 7.2).

Evaluation of plasma lipid peroxidation

Evaluation of lipid peroxidation was carried out by determination of malondialdehyde (MDA) in plasma. The concentrations of MDA were defined by production of thiobarbituric acid reactive substances (TBARS) according to the method described by Ohkawa, Ohishi and Yagi (1979)[14], with adaptations. An analytical calibration curve was prepared with MDA as standard at concentrations of 1, 5, 10, 25 and 50 μM. The measures were performed in duplicate by using a way of reaction containing acetic acid pH 3.5 and thiobarbituric acid (TBA) 0.5 %. Reading absorbance was done in the wavelengths of 532, 510 and 560 nm, for calculation of the corrected absorbance, proposal to minimize interference of heme and hemoglobin pigments[15]. The results were expressed in nmoL/mL of plasma MDA.

Evaluation of lipid profile

The lipid profile evaluation was carried out based on the classification of the values obtained for LDL cholesterol, HDL cholesterol and triglycerides, according to reference values of V Brazilian Guideline on Dyslipidemias and Atherosclerosis prevention (2013)[16]. The results of lipidogram were obtained from the database of the own clinic, directly from the electronic patient data file. Biochemical dosages were gotten in the clinical laboratory, which uses enzymatic colorimetric method.

Evaluation of consumption of antioxidant micronutrients

The evaluation of the dietary intake of antioxidant micronutrients was carried out through the application of questionnaire to 24 hours Recall in three non-consecutive days. The daily intake of zinc, selenium, copper, and vitamins C and E were calculated using the software "*Avanutri online*", developed by Avanutri & Nutrition Services and Computing Ltda. The average percentage of adequacy of micronutrients intake was calculated based on the *Estimated Average Requirement* (EAR) of the nutrient present in the *Dietary Reference Intakes* (DRI 's)[17].

Statistical analysis

Data obtained were processed in Excel for Windows and Statistical Package for the Social Science (SPSS) version 18.0. It was performed an exploratory and descriptive analysis in the variables. For continuous variables, data were presented as mean and standard de-

viation, and for categorical variables with measures of absolute and relative frequencies. For the comparisons in relation to quantitative variables between the groups, it has been used the parametric, since such variables followed the normal distribution, according assessment through the Kolmogorov-Smirnov test. The associations between variables were tested by applying the chi-square test. In addition, Pearson's correlation analysis was applied to find out the correlation. A significance level of $p < 0.05$ was used in all analyses.

Ethical aspects

This study was approved by the Ethics on Research Committee of Federal University of Piauí (CAAE 12356513.6.0000.5214). The study was conducted in compliance with the recommendations of Resolution 466/2012 of the National Health Council on studies involving humans[18] and the Declaration of Helsinki[19]. All the participants enrolled in this study signed an informed consent after explanations about the objectives and possible benefits and risks of the study.

RESULTS

The comparison between the groups studied allowed to be shown that the serum concentration of albumin was significantly smaller ($p < 0.01$) in G1 (3.33 ± 0.16 g/dL) compared to G2 (3.74 ± 0.14 g/dL). For all of the others parameters evaluated the groups had similar averages (Table I). It was observed that the majority of patients in both groups were male, with 76.9% and 71.1% of men, respectively in G1 and G2.

In relation to antioxidant activity, there were no statistically significant differences between patients with or without hypoalbuminemia for SOD enzyme activity in erythrocytes or NO production in plasma, determined by measuring the concentration of nitrite (Table II).

As for the analysis of plasma MDA concentration, a lipid peroxidation marker analyzed (Table III), the mean found in G1 (3.87 ± 1.02 nmol/mL) was significantly greater ($p < 0.05$) when compared with G2 (3.31 ± 1.13 nmol/mL). The table III also shows the lipid profile of patients studied. There was no statistically significant difference between groups was observed in the lipid parameters investigated. However, almost two-thirds of the participants had low levels of HDL-c (G1 = 61.5%; G2 = 65.8%) and almost a third also presented high levels of triglycerides (G1 = 30.8%; G2 = 31.6%), lipid profile considered atherogenic.

The mean values, standard deviations and percentages of suitable average for the consumption of micronutrients antioxidant by renal patients are presented in table IV. The comparison between groups revealed mean of copper intake significantly smaller ($p < 0.05$) in G1. The average percentage of adequacy was below the recommendations for all nutrients analyzed in both

Table I
Mean values and standard deviations of age, weight, height, body mass index (BMI), index of dialysis (Kt/V) and serum albumin in chronic renal failure patients with (G1) or without (G2) hypoalbuminemia

Parameters	*G1 (n = 26)*	*G2 (n = 38)*	*p**
	Mean ± SD	*Mean ± SD*	
Age (years)	39.38 ± 10.13	43.97 ± 11.45	0.104
Post-dialysis weight (Kg	62.84 ± 16.65	64.69 ± 12.48	0.639
Height (m)	1.63 ± 0.10	1.65 ± 0.06	0.816
BMI (Kg/m^2)	24.09 ± 5.24	24.17 ± 4.85	0.947
Serum albumin (g/dL)	3.33 ± 0.16*	3.74 ± 0.14	0.000
Kt/V	1.32 ± 0.26	1.37 ± 0.27	0.501

*Statistically significant difference with regard to G2; Student's t-test.

Table II
Antioxidant profile in chronic renal failure patients with (G1) or without (G2) hypoalbuminemia

Indicators	*G1 (n = 26)*	*G2 (n = 38)*	*p**
	Mean ± SD	*Mean ± SD*	
SOD (U/g Hb)	2,502.03 ± 1,294.30	2,535.54 ± 1,561.85	0.928
Nitric oxide (μm)	1.15 ± 0.08	1.17 ± 0.10	0.447

*Statistically significant difference with regard to G2;Student's t-test; (p = 0.05).

groups studied except for the selenium whose consumption was above the recommended.

Table V presents the correlation coefficients for the serum concentrations of albumin and superoxide dismutase activity, lipid peroxidation, lipid profile and antioxidant micronutrient consumption in chronic renal failure patients on regular hemodialysis program. The serum concentrations of albumin showed weak positive correlation with BMI and dietary intake of copper. On the other hand, it was demonstrated negative correlation between serum albumin and plasma MDA.

Discussion

The serum albumin concentrations of patients were below that considered ideal for chronic renal patients in dialysis treatment (≥ 4.0 g/dL), even in the control group. Serum albumin is a marker used in clinical practice important in assessing the conditions of patients on dialysis because hypoalbuminemia is a strong, independent predictor of mortality[5]. However, its interpretation must take into account that low levels may reflect malnutrition, loss of albumin in the dialysate, systemic diseases, hyperhydratation, advanced age, and especially the presence of inflammation[20]. A limitation of this study is that no marker of inflammation was evaluated, which could have contributed to a better interpretation of the situation found of hypoalbuminemia.

It´s important to point out that albumin is considered an important extracellular antioxidant molecule for its ability to connect to different types of substances, limiting its harmful effects on cells[21]. The oxidative stress and inflammation are characteristic of advanced kidney disease that play an important role in the progressive deterioration of kidney structure and function, and are associated with some cardiovascular risk factors and numerous other complications of CKD[22]. Inflammation and malnutrition may also contribute to increased levels of oxidants in renal patients[23].

In this study, no difference was found between the groups of patients in HD with or without hypoalbuminemia in relation to enzyme activity SOD in erythrocytes or the production of NO in plasma. No studies were found evaluating the oxidative stress in renal patients in HD that take into account the activity of SOD by the method used here or evaluating the enzime activity in renal patients with hypoalbuminemia. Nevertheless in some studies that investigated the activity of SOD by *Randox* method in renal patients in HD this enzyme activity was reduced in relation to the values found in healthy individuals[7,8,24].

When comparing the results of NO production as measured by nitrite concentration obtained in this study with those demonstrated by Bianchi et al.

Table III
Plasmatic concentration (mean ± standard deviation) LDL, HDL, triglycerides and MDA in chronic renal failure patients with (G1) or without (G2) hypoalbuminemia

Parameters	*G1 (n = 26)*	*G2 (n = 38)*	*p**
	Mean ± SD	*Mean ± SD*	
Plasma LDL-c (mg/dL)	91.35 ± 43.72	88.37 ± 31.63	0.767
Plasma HDL-c (mg/dL)	36.12 ± 11.93	34.66 ± 11.19	0.625
Plasma Triglycerides (mg/dL)	159.42 ± 98.94	175.24 ± 104.27	0.542
Plasma MDA (nmol/mL)	3.87 ± 1.02*	3.31 ± 1.13	0.046

*Statistically significant difference with regard to G2; Student's t-test.

Table IV
Mean values, standard deviations and percentage of adequacy of antioxidant micronutrients intake in chronic renal failure patients with (G1) or without (G2) hypoalbuminemia

Nutrients	*G1 (n = 26)*	*G2 (n = 38)*	*% adequacy medium*[a]	*p**
	Mean ± SD	*Mean ± SD*	*Mean ± SD*	
Zinc intake (mg)	5.79 ± 2.52	6.22 ± 3.95	54.98 ± 31.14	0.592
Copper intake (mg)	0.66 ± 0.28*	0.81 ± 0.36	77.21 ± 33.99	0.024
Selenium intake (mcg)	59.44 ± 32.78	71.95 ± 57.07	117.32 ± 80.53	0.320
Vitamin C intake (mg)	46.52 ± 32.62	64.69 ± 66.99	59.89 ± 55.41	0.154
Vitamin E intake (mg)	9.32 ± 4.40	9.96 ± 9.72	63.89 ± 46.99	0.726

[a]% Adequacy medium = percentage of adequacy medium. *Statistically significant difference with regard to G2; Student's t-test.

(2009)[7], who evaluated the effect of hemodialysis on systemic oxidative stress in patients with terminal CKD, using this parameter and measured by the same method, it was observed that patients from Teresina had higher means (1.15 ± 0.08 mM) to those found by these authors for patients with renal hypoalbuminemia (0.10 ± 0.01 mM).

In relation to lipid peroxidation in renal patients, several studies have shown increased peroxidation in patients with CKD due to an imbalance between antioxidant activity and the production of free radicals, especially in patients on hemodialysis, although hypoalbuminemia have not been investigated[7,25,26]. In the present study, highest average plasma concentrations of MDA were found in patients with hypoalbuminemia. Moreover, negative correlation was observed between the concentrations of serum albumin with the MDA, demonstrating inverse relation between these parameters, in which high levels of MDA relate with hypoalbuminemia.

The relation between kidney disease and lipids has been documented for more than three decades, being postulated the hypothesis that changes in the lipid profile may cause renal mesangial cells proliferation by promoting the progression of kidney disease[27]. Initially, it was believed that hyperlipidemia would be resulting from compensatory hepatic synthesis of lipoproteins in response to urinary loss of albumin, wich could precipitate or aggravate glomerular and interstitial tubules disease. In a cascade of events, the condition that triggered albuminuria could therefore coexist with (or be replaced by) lipid-mediated damage. Persistent albuminuria, as resulting from increased glomerular basement membrane permeability, stimulates excess hepatic lipoprotein synthesis, thus continuing a lipid-mediated injury cycle[28].

Table V
Correlation between the concentrations of serum albumin, and body mass index, lipid profile, dietary intake of antioxidant micronutrients, antioxidant profile and lipid peroxidation in chronic renal failure patients

Parameters	*Serum albumin (g/dL)*	
	r	*p*
Body mass index (Post-HD) (Kg/m^2)	0.451	0.000*
Plasma LDL (mg/dL)	-0.065	0.609
Plasma HDL (mg/dL)	-0.147	0.247
Plasma TG (mg/dL)	0.149	0.240
Erythrocyte SOD activity (U/g Hb)	-0.027	0.834
Plasma NO (μm)	-0.010	0.939
Plasma MDA (nmol/mL)	-0.314	0.012*
Vitamin C intake (mg)	-0.050	0.631
Vitamin E intake (mg)	-0.026	0.840
Zinc intake (mg)	-0.098	0.442
Selenium intake (mcg)	0.108	0.395
Copper intake (mg)	0.280	0.025*

*Pearson Correlation test.

The analysis of the levels of LDL-c and HDL-c of the groups studied showed that although the majority of patients presented levels of LDL-c classified as great or borderline, almost two-thirds of the participants had low levels of HDL-c, lipid profile regarded as atherogenic. It is worth mentioning that associations haven't been found between hypoalbuminemia and lipid profile parameters analyzed. The lipid profile of patients studied in Teresina was similar to that described in other studies that evaluated lipid profile in renal patients in HD[29].

Patients with CKD have important changes in lipid metabolism; the most typical manifestation is the mixed dyslipidemia with predominance of hypertriglyceridemia associated with low HDL-c. Although LDL-c is not usually elevated, LDL particles may to assume pro-atherogenic characteristics: small, dense and suffer a higher degree of lipid peroxidation[30].

Among the reasons for this lipid profile are malnutrition and hypoalbuminemia present in many of these patients. The hypoalbuminemia determines pathophysiological changes in lipid metabolism, by decreasing the oncotic pressure, which stimulates the hepatic synthesis of albumin and other proteins, including the apolipoproteins, determining also increased of total cholesterol, triglycerides and LDL, and of HDL decrease[28].

The decrease in the lipolytic enzymes activity involved in lipid metabolism appears to be the main mechanism responsible for decreased HDL in patients on kidney dialysis treatment, as well as reduction of apoA1 and apoA2[31]. In relation to the increase in LDL levels in nephropathic patients, the main mechanism may involve reduction in its catabolism, whereas levels of apolipoprotein B, main apolipoprotein of LDL, in kidney patients are increased[27].

As mentioned previously, kidney patients in HD are susceptible to disorders in the metabolism of lipids and thus an atherogenic lipid profile. The development of atherosclerosis has been related to increased lipid peroxidation in CDK, by susceptibility to oxidative modification of LDL, with formation of conjugated dienes and final products of this oxidation[25]. Oxidative changes, resultant of reduction in the formation of HDL, and an increase of LDL, facilitate entry and LDL accumulation in arterial walls, causing renal and vascular damage due to pro-oxidant activity of these particles[27]. Moreover, the LDL is susceptible to damage induced by ROS and, when oxidized, it seems to be an important factor for the development of atherosclerotic lesions by promoting direct damage and destruction of endothelial cell[26].

There are evidence that the diet has a direct effect on antioxidant status in the body through the action

of nutrients as beta carotenoids, alpha tocopherols, ascorbic acid, zinc, selenium and copper, helping to protect cells from the toxic effects of oxidative stress and prevent to against disease. Hemodialysis patients live in a pro-oxidative state, so it is also important to assess the presence of antioxidants into their diets[32]. The majority of patients studied presented low daily intake of vitamins E and C, and minerals zinc and copper. However, no correlation was observed between the daily intake of micronutrients antioxidant and oxidative stress markers. Exception of copper, there was no association between low intake of these micronutrients and the presence of hypoalbuminemia.

Vitamin E is the most important lipophilic antioxidant and it acts protecting the polyunsaturated fatty acids of cell membranes[32]. The vitamin C is a hydrophilic antioxidant, and low serum levels of this vitamin reduce the activity of non-enzymatic antioxidant systems and can increase oxidative stress that occurs in chronic kidney disease[10].

Zinc and selenium are important cofactors of enzymatic antioxidant system composed especially by glutathione peroxidase, superoxide dismutase and catalase. Zinc, particularly has important role in the stability of cell membranes and in the protection of cells against lipid peroxidation[32]. Selenium is an essential trace element that contributes to an appropriate activity of glutathionine peroxidase, which protects cells from lipid peroxidation[33]. Low levels of selenium in serum and erythrocytes were found in chronic renal failure patients[24,33]. In the present study, most patients had inadequate dietary intake of zinc, while less than half of them had low intake of selenium.

Copper is an essential trace element for the maintenance of mechanisms of protection by copper-zinc superoxide dismutase (Cu-Zn SOD), ceruloplasmin and metallothionein activity[34]. In chronic renal failure patients low concentrations of copper has been observed in erythrocytes associated with lower activity of SOD[35].

There are few studies related to the consumption of micronutrients in patients with CKD. Low intakes of antioxidant micronutrients in the evaluable patients can be partially explained because of dietary restrictions with low phosphorus and potassium common in renal patients contribute to limiting the intake of foods like fruits, vegetables, dairy, meat and other foods rich in vitamins and minerals[23]. Additionally, diets with low biological value proteins or insufficient consumption of foods of animal origin have low amounts of zinc since the best sources of zinc are shellfish, red meat, liver, eggs and viscera.

Conclusions

The presence of hypoalbuminemia may increase lipid peroxidation and contribute to oxidative stress in these patients. This fact may be evidenced by the presence of negative correlation between serum concentrations of albumin and plasma concentrations of malondialdehyde. However, no evidence was found of relation between hypoalbuminemia with antioxidant activity evaluated by determining the activity of enzyme superoxide dismutase in erythrocytes and nitric oxide production in plasma. Additionally, patients with chronic renal disease undergoing hemodialysis evaluated in this study had reduced consumption of cooper, which may have influenced the activity of superoxide dismutase, since there was no adaptive and compensatory response of this enzyme to oxidative stress.

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