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The Effect of Zinc Sulfate on Malnutrition in Hemodialysis Patients

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Abstract

Background: Malnutrition is common in hemodialysis patients and it must be controlled quickly. This study aimed to investigate the effect of zinc sulfate on malnutrition in dialysis patients.

Methods: This study was a randomized controlled trial on 84 hemodialysis patients referred to Imam Hossain hospital in Shahroud (northeastern of Iran). Patients were randomly divided into two case and control groups. For the intervention group, one tablet of zinc sulfate 220 mg was administered daily for 8 weeks. Both groups were subjected to standard dialysis three times in the week and all patients were assessed for malnutrition using a standard questionnaire, lab tests, and necessary examinations in the first stage, one month and two months after the treatment.

Results: Of 84 patients, 39 cases (46.4%) were female and rest was male. The mean age of the patients was 59.1±27.2 years. The mean total duration of dialysis was 2.9±2.3 years. The severity and extent of malnutrition at the beginning and one month after the study did not differ between the two groups, but after the second month, there was a significant decrease of malnutrition in the intervention group (Pvalue=0.015). Also, malnutrition variables were significantly associated with BMI less than 18 kg/m2 (Pvalue<0.039), and serum creatinine less than 3 mg/dl (Pvalue<0.011) and hemoglobin less than 11 g/dl (Pvalue<0.001),

Conclusions: The results of this study showed that zinc sulfate consumption for at least 2 months could significantly reduce the severity of malnutrition in hemodialysis patients.

Keywords: Malnutrition, Zinc sulfate, Hemodialysis.

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Introduction

End=stage renal disease (ESRD) is one of the causes of mortality and disability worldwide.[1] Hemodialysis is considered as the dominant treatment in many of these patients.[2] Hemodialysis has a profound effect on individual and family life for various reasons[3] and despite this method of treatment, it is a healthier and more patient's survival, but, it did not change the progressive of the disease and completely did not replace the function of the kidneys.[4] In addition to observing the hemodialysis diet, limitation of fluids and medications are considered to be essential actions for the treatment of renal failure.[5,6] One of the complex, multi-factorial and prevalent complications of hemodialysis in renal patients is energy–protein malnutrition which has a direct correlation with the mortality rate of these patients. Inappropriate food intake,

anorexia, metabolic disorders, diseases and loss of protein, amino acids, and vitamins during dialysis and also the high rate of catabolism due to increased production of inflammatory cytokines, it can easily threaten the nutritional health of these patients.[6] This will eventually intensify the loss of muscle tissue and fat stores that increases the vulnerability to various types of infections and diseases and increases disability and mortality.[6,7]

According to studies in the United States, the number of patients with kidney failure is doubled every 7 years. The statistics in our country also show a dramatic increase in chronic renal failure, so that the total number of patients with dialysis in Iran during the first two months of the year of 1992 was 3670, this figure was 8500 in 2002 and reached 28000 in 2020.[8] According to studies conducted in developing countries, 42% of hemodialysis patients are malnourished. Anthropometric, biochemical and dietary indicators are among the nutritional indicators used in assessing the nutritional status of these patients which are more sensitive to intra-arm muscle (MAMC) and serum albumin levels.[8-10] Zinc and iron deficiency is common in dialysis patients and is seen in most patients. Patients who undergo long-term dialysis are at increased risk for zinc deficiency.[9] Zinc has an antioxidant that has anti-inflammatory properties and regulates immune response.[4] Zinc deficiency in chronic kidney disease may be due to decreased bowel movements and absorption impairment.[10] Zinc deficiency may be associated with symptoms of uremia, such as anorexia, loss of taste, sexual dysfunction, and reduced immune function.[11] Better zinc levels are associated with reduced levels of inflammation, oxidative stress, dyslipidemia, and malnutrition in dialysis patients.[12] Adjusting the diet to meet nutritional needs and preventing and delaying undesirable side effects can greatly improve the quality and longevity of these patients.[11-12] Regarding the high prevalence of dialysis patients in the community and the frequency of malnutrition rates in dialysis patients, this study aimed to investigate the effect of zinc sulfate on reducing malnutrition in patients undergoing dialysis in Shahroud.

Materials and Methods

This prospective triple-blind clinical trial was performed on 84 patients with hemodialysis referred to Imam Hossain hospital, Shahroud, Iran from November 2017 to November 2018 that randomly divided into two equal groups.

Inclusion criteria were having a hemodialysis history over 6 months; age over 15 years and under 65 years; no use of

supplemental medication in the last 4 weeks and no addiction to alcohol, smoking or drugs; satisfaction in research.

Exclusion criteria were the presence of any uncontrolled malignancy; suffering too severe diseases such as heart, liver and gastrointestinal disease; chemotherapy; severe burns and dissatisfaction in research.

Blinding description: In this study, patients, and the person responsible for drug distribution and analyzer it is blinded. All patients were examined for malnutrition before splitting into the intervention.

The division of patients into two groups of intervention and control is done by a qualified nurse who does not know the actions performed in the two groups. Do malnutrition examination, drug therapy prescribing and results recorder will be done by a qualified nurse without any knowledge of the type of intervention and patients. In this study, eligible patients were selected by a simple census method to complete the sample size. Eligible patients were randomly divided into intervention and control groups with using quadric randomized blocks.

For all patients suspected of malnutrition in both groups, a valid nutritional status questionnaire was used, that validity and reliability of which have been confirmed by various researchers, including Sosiototati, Ebrahim and Tirmantajin-Jankovic.[13-15]

This questionnaire includes demographic and clinical information (age, sex, duration of dialysis and place of residence, blood tests (serum albumin, cholesterol, creatinine, hemoglobin, and dialysis adequacy) and specialized assessment of nutritional status. Nutrition status assessment (NSA) has 9 items that was included personal information, underlying diseases, history of drug and food allergies, history of medication and nutritional supplements, nonmetric information (height, weight, BMI, arm circumference, normal weight, weight loss or weight gain, weight change time, digestive and eating problems (diarrhea, vomiting, nausea, constipation, swallowing, and chewing disorders), clinical condition (edema, ascites, muscle wasting, and skin and nail changes) and related laboratory tests. Each of these items had a score of one (minimum score) to 4 (maximum score). Therefore, the score of each person varied from 9 to 36 points. Therefore, based on the total scores of these 9 items, patients were divided into three groups: mild malnutrition (score 5 to 15), moderate malnutrition (score 16 to 25), and severe malnutrition (score 26 to 36).

Patients in the intervention group received zinc sulfate (one tablet of zinc sulfate 220 mg daily for 8 weeks). However, patients in the control group were treated with a placebo like intervention group. Both groups were subjected to standard hemodialysis three times in the week, according to standard and identical conditions.

Measured patient-related variables were including age, sex, smoking, substance abuse and the duration of the hemodialysis and the variables associated with it was including the cause of dialysis, duration of dialysis, background diseases and malnutrition status and severity. Also was done required tests include: hemoglobin, creatinine, and BUN, URR rate, BMI, and arm circumference at the beginning of the study, 4 weeks and 8 weeks after treatment, and the malnutrition status was measured using an NSA questionnaire. All treatments were performed for patients in both groups for eight weeks. The flow diagram of the study is shown in figure 1.
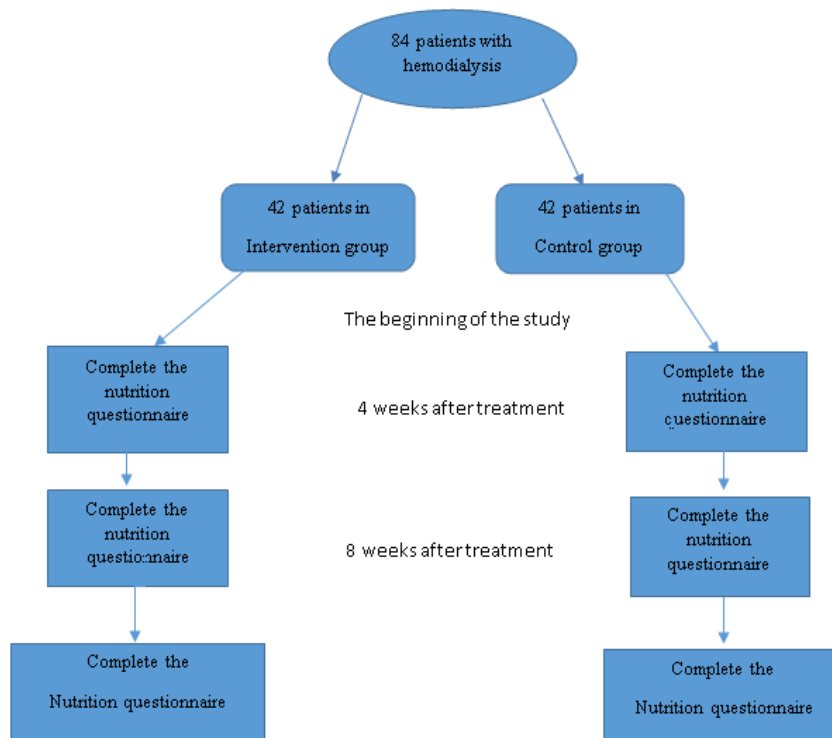

Figure 1. The flow diagram of the study

Data analysis was performed based on intention to treat analysis by statistical software SPSS version 16. Sample size using Epi info 7.2 at a significant level of 5% and a power of 80%, equal to 42 people in each group and a total of 84 people. For describing the findings, descriptive statistics such as mean±standard deviation and frequency were used. Due to the quantitative and qualitative variables, independent T and Chi-square tests were used in the significance level of 0.05.

This study has an ethics code number (IR.SHMU.REC.1396.63) from the ethics committee of Shahroud University of Medical Sciences and with code, IRCT2017102136703N2 on 8-11-2017 has been registered in Iranian clinical trials system. The essential information and the objectives of the study were explained to the patients, and written consent was obtained for participation in the plan.

Results

In this study, 45 (53.6%) of the participants were male and the rest were female. The mean age of all patients was 59.3±27.9 years that was no significant difference between the two groups. The mean BMI of all patients was 24.1±3.5 kg/m^2 that was no significant difference between the two groups. The demographic, clinical, and laboratory data of the two groups are listed in table 1. Patients' severity of malnutrition showed that there was no significant difference between the two groups at the beginning of the study and one month after treatment with zinc sulfate, but in the second month of treatment, the severity of malnutrition was significantly lower in the intervention group (Pvalue<0.015). Table 2 shows the malnutrition status of patients in the two groups at different times. In this study, independent variables with malnutrition were investigated in the multivariate regression model. As was shown in table 3, malnutrition variables were significantly associated with BMI less than 18 kg/m^2 (Pvalue<0.039), and serum creatinine less than 3 mg/dl (Pvalue<0.011) and hemoglobin less than 11 g/dl (Pvalue<0.001), and there was no significant relationship with other variables. The results of the multivariate logistic regression model are presented in table 3.

Table 1. The demographic, clinical and lab information of patients in beginning of study

Demographic & clinical information	Intervention group Mean±SD/Number (%)	Control group Mean±SD/Number (%)	Total Mean±SD/Number (%)	Pvalue
Age (year)	59.3±27.9	58.9±27.3	59.1±27.3	0.088
Age category				
−<20 years	0(0.0)	0(0.0)	0(0.0)	
−20-40 years	8(19.1)	6(14.3)	14(16.7)	
−40-60 years	23(54.7)	24(57.1)	47(55.9)	0.125
−>60 years	11(26.2)	12(28.6)	23(27.4)	
Sex				
−Male	23(54.7)	22(52.4)	45(53.8)	0.059
−Female	19(45.3)	20(47.6)	39(46.2)	
BMI (kg/m^2)	24.3±3.5	23.9±3.4	24.1±3.5	0.213
Duration of dialysis (year)	3.1±2.4	2.8±2.3	2.9±2.4	0.109
Arm circumference (cm)	32.6±4.2	31.9±4.3	31.2±4.2	0.097
Serum creatinine (mg/dl)	2.7±3.8	2.4±3.5	2.5±3.6	0.103
BUN (mg/dl)	67.4±25.6	65.9±26.4	66.3±25.9	0.091
Hemoglobin (g/dl)	9.7±1.9	10.1±2.1	9.9±1.9	0.184
URR* (%)	59.5±3.5	58.6±4.3	58.9±3.9	0.089

Table 2. Frequency distribution of patients in two groups based on severity of malnutrition

Severity of malnutrition at different times	Intervention group Number (%)	Control group Number (%)	Total Number (%)	Pvalue
Beginning of study				
−Mild malnutrition	7(16.7)	9(21.4)	16(19.1)	
−Moderate malnutrition	24(57.1)	23(54.8)	47(55.9)	0.117
−Severe malnutrition	11(26.2)	10(23.8)	21(25.0)	
1 Mount after intervention				
−Mild malnutrition	12(28.6)	10(23.8)	22(26.2)	
−Moderate malnutrition	23(54.8)	24(57.1)	47(55.9)	0.055
−Severe malnutrition	7(16.7)	8(19.1)	15(17.9)	
2 Mount after intervention				
−Mild malnutrition	21(50.0)	10(23.8)	31(36.9)	
−Moderate malnutrition	17(40.5)	26(61.9)	43(51.2)	0.015
−Severe malnutrition	4(9.6)	6(14.3)	10(11.9)	

Table 3. Relationship between independent variables with malnutrition in multivariate logistic regression model

Independent variables	Odds Ratio	95% Confidence	Pvalue
Age category (year)			
−>20	1.000		
−20 to 40	1.016	1.142-0.0852	0.093
−40 to 60	1.077	1.238-0.0881	0.075
−<60	1.161	1.351-0.0912	0.053
Sex			
−Male	1.000		
−Female	1.125	1.213-0.815	0.069
Body mass index (kg/m^2)			
−18-25	1.000		
−<18	1.723	1.985-1.456	0.039
−>25	0.881	1.105-0.612	0.085
Duration of dialysis (year)			
−<1	1.000		
−1-3	1.151	1.323-0.871	0.103
−>3	1.182	1.388-0.927	0.079
Arm circumference (cm)			
−>35	1.000		
−<35	1.296	1.542-1.109	0.052
Serum creatinine (mg/dl)			
−<3	1.000		
−>3	1.489	1.763-1.216	0.011
BUN (mg/dl)			
−<40	1.000		
−>40	1.028	1.282-0.857	0.079
Hemoglobin (g/dl)			
−<11	1.000		
−>11	1.551	1.854-1.256	0.001
URR (%)			
−>60	1.000		
−<60	1.081	1.218-0.855	0.068

Discussion

The results of this study showed that zinc sulfate consumption for at least 2 months could significantly reduce the severity of malnutrition in dialysis patients. It was also found that factors like BMI of less than 18kg/m^2, creatinine less than 3mg/dl and hemoglobin below 11g/dl could significantly increase the severity of malnutrition. Malnutrition is a common finding in hemodialysis patients and its symptoms are observed in more than 35% of these patients.[16] The severity of malnutrition in these patients varies from mild to very severe.[17] According to the results of several studies, there is no single method for assessing the nutritional status of hemodialysis patients and most scholars have emphasized with a combination of existing methods, including the study of the clinical history of weight loss, dietary evaluation and anthropometric indexes, biochemical parameters, evaluation of impedance analysis, and etc. In this study, a measure of malnutrition evaluation in hemodialysis patients was a combination of cases that were evaluated in the form of a questionnaire, clinical examinations, and laboratory tests.[18,19] The results of this study showed that all patients at the beginning of the study had a degree of malnutrition. This finding is similar to the results of El-Shazly, Roozbeh and Matson studies which states that the prevalence of malnutrition in dialysis patients is between 85% and 95%, consistency hip-and-thigh.[20-22] One of the reasons for inadequate intake and anorexia in these patients can be pointed out, is the presence of inflammation and infection, gastrointestinal upset, feeling weak and post-dialysis fatigue, nausea, depression, and medication.[23]

The results of this study showed that the use of zinc sulfate supplementation could significantly reduce the severity of malnutrition among hemodialysis patients. However, zinc sulfate should be continued for at least two months in these patients. This result is fully consistent with the results of Lok and Chevalier but is relatively consistent with Jerne's study, which found that one month of zinc sulfate treatment was sufficient to reduce malnutrition.[24-26]

The middle of the arm circumference (MAC) represents the skeletal, skeletal, and subcutaneous fat muscles, and is a rough estimate of the body's fat and protein reserves. It is also used as a rapid method to assess the status of long-term nutritional intervention.[27,28]

Middle arm muscle circumference (MAMC) is a quick way to calculate the estimated amount of muscle mass, and values below 5 percent or above 95 percent indicate some type of nutritional risk.[29] In this study, subcutaneous fat was used to measure malnutrition, assuming that in various studies, the index of adipose tissue in the area of the triceps muscle shows the total body fat reserves and the fat thickness at this location indicates the average thickness of the total subcutaneous reserves. The measurement of this part can be very accurate.[30]

In many studies, BMI has been used to assess malnutrition. In the present study, BMI was used but no significant difference was observed between the two groups regarding this criterion and the finding is similar to the Morais study but differs from the Ashabi study, perhaps the reason for this difference is related to the sample size and different sex

composition of the two studies or the difference in the duration of dialysis of patients in the two groups.[31,32]

In many studies, blood albumin levels have been identified as a common indicator in the nutritional assessment of patients, and a dose of less than 3.5 g/dl has been shown to indicate protein-energy malnutrition.[33,34] However, in the present study, for various reasons, such as technical problems in the laboratory of Imam Hossain hospital and the lack of cooperation of patients to collect urine albumin in 24 hours, this test was not used to assess malnutrition.

Creatinine is derived from the non-enzymatic metabolism of skeletal muscle. Low serum creatinine levels indicate nutritional disorders in these patients that will be associated with increased mortality.[35] In this study, about half of the patients had lower creatinine than normal at the start of the study, indicating severe malnutrition but, with use of zinc sulfate significantly increased the creatinine content of these patients, which indicated an improvement in their malnutrition, which is consistent with the results of Pupim and Kalantar-Zadeh studies.[36,37]

The results of this study showed that the use of zinc sulfate, reduces the severity of malnutrition in dialysis patients, but it needs to be used regularly for at least two months. But in order to fully confirm this, more research is needed with larger sample size. Therefore, all patients with malnutrition hemodialysis should be screened for vitamin deficiencies, especially zinc sulfate, and corrected as soon as possible if such defects are identified.

Acknowledgement

Conflict of Interest

The authors declare that they have no conflict of interest.

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