Original Article

Effect of Selenium on Triglyceride and Total Cholesterol, Weight Gain, and Physical Activity on Hemodialysis Patients: A Randomized Double-Blinded Controlled Trial

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Abstract

Background: End-stage renal disease is one of the most important chronic diseases. Selenium is one of the so-called rare elements which are essential for our body functions. Here, we aimed to investigate and the effects of selenium supplement therapy on weight gain, physical activity, and triglyceride (TG) and total cholesterol in patients under hemodialysis. **Methods:** The current study is a double-blinded clinical trial performed on patients with ESRD under hemodialysis in 2019. In the beginning, serum selenium levels were assessed. All patients were randomly divided into two groups. The first group was under treatments with tablets of selenium 400 μg. Patients received selenium tablets three times after each hemodialysis session (3 times a week) and the other group received placebo tablets. 3 months after the beginning of the study, blood selenium levels, TG and total cholesterol, and weight and physical activities of patients were evaluated again and compared with the beginning. **Results:** A total of 78 patients were included. Serum selenium levels at the beginning of our study were 40.06 ± 8.50 in the intervention group and 45.00 ± 8.16 in control groups. Selenium levels and physical activities of patients were increased significantly in intervention group compared to baseline ($P < 0.001$ for both). Weight, physical activity, total cholesterol, and TG in both intervention and control groups did not change significantly after interventions ($P > 0.05$). **Conclusions:** We showed that selenium supplement therapies have beneficial effects in patients under hemodialysis. Furthermore, we showed that selenium supplement therapies have positive effects on serum selenium levels but no effects on total cholesterol and TG.

Keywords: *Lipid, physical activity, renal dialysis, selenium*

Introduction

End-stage renal disease (ESRD) is one of the most important chronic diseases worldwide which is also one of the leading causes of mortality and morbidity.[1] The prevalence of ESRD has increased in recent years in both developing and developed countries due to an increase in prevalence of other chronic diseases including diabetes mellitus (DM).[2-4] Hemodialysis is the most important and also prevalent treatment method for patients with ESRD performed by different techniques.[5,6] Different complications and issues have been reported in patients with hemodialysis during past decades.[7,8] Malnutrition is known to play a pivotal role in mortality of patients under hemodialysis.[9] Different studies indicated that almost 61% of hemodialysis patients have malnutrition which is mostly caused by increased oxidative stress and disturbance in anti-oxidant protection.[10,11] These studies have also shown that the levels of selenium is significantly affected and decreased in patients under hemodialysis.[12,13]

Selenium is one of the so-called rare elements which is essential for our body functions in low amounts.[14] Selenium is also known to have antioxidative roles and contribute in synthesis of selenoproteins and a cofactor for physiological interactions.[15] Different genes have been discovered in which their expression can lead to selenoproteins synthesis. Glutathione peroxidase, thioredoxin reductase, and deiodinases are some of the selenoproteins that prohibit collection of active oxygen and nitrogen.[16,17] Selenium has also functional roles in antioxidative stress, thyroid hormones metabolism, and immune responses. Lack of selenium is mostly caused due to malnutrition and nutritional

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problems.[18] Infections and biochemical stresses can also cause reduced selenium levels.[19] Decreased selenium levels in such patients have been shown in different studies. In a meta-analysis by Tonelli and Colleagues, 128 previous studies were reviewed and indicated that patients under hemodialysis have lower levels of selenium, zinc, and magnesium.[20] Some other studies have indicated lower selenium levels in patients under hemodialysis.

Patients with ESRD who are also under hemodialysis are vulnerable to increases C-reactive protein levels and other acute-phase reactants along with malnutrition, increased inflammation and mortalities.[21,22] Former studies also showed that age, serum albumin, low-density lipoprotein and high-density lipoprotein have significant correlations with levels of selenium.[23,24] Regarding the importance of selenium in metabolism and oxidative stress and its important roles in hemodialysis patients and also regarding insufficiency of selenium in patients under hemodialysis, selenium supplements might be beneficial. Here for the first time, we aimed to investigate and evaluate the effects of selenium supplement therapy on weight gain, physical activity, and triglyceride (TG) and total cholesterol in patients on hemodialysis in Iran.

Methods

The current study is a double-blinded clinical trial performed on patients with ESRD who have been under hemodialysis and referred to hemodialysis centers of Isfahan University of Medical Sciences in 2019. This study was approved by ethical committee of Isfahan University of Medical Sciences (ethical code: IR.MUI.MED.REC.1398.006) and all patients signed informed consent.

The number of the study population was considered using sample size determination formula. We included patients older than 18 years, patients with low serum selenium levels and also patients who had been under hemodialysis for more than 6 months.[25] Our exclusion criteria were: having hepatitis B or C, normal selenium levels, being under treatments with corticosteroids or nonsteroidal anti-inflammatory drugs 2 months prior to the study and having skeletal deformities which could affect the patient's ability to perform sit to stand test.[25]

At the beginning of the current study, serum selenium levels were assessed by extracting 3 ccs of fasting blood from patients before dialysis. Serum selenium was assessed using the atomic absorption method with unicam929-uk apparatus by Variant Company, USA. Patients with low selenium levels were entered into our study. Normal selenium levels of the Iranian population were reported to be 100.6 μg/l by Safaralizadeh and Colleagues.[26]

Weight of patients was also assessed using a calibrated scale after hemodialysis. Patient's lipid profiles (TG and total cholesterol) were also evaluated by blood tests. The physical activities of patients were measured using five times sit to stand test. In this test, the patient is seated on a chair and is asked to stand up completely and sit down five times as quickly as he/she can with the arms on the chest. The time of this ability is considered as the time of sit to stand test.[27,28]

All patients were randomly divided into two groups using random allocation software. The first group was on treatments with tablets of selenium 400 μg, Webber Naturals, Canada.[29] Patients received selenium tablets 3 times after each hemodialysis session (3 times a week) and the other group received placebo tablets containing glucose with the same characteristics of selenium tablets. Patients and nephrologists were unaware of patient's groups and tablets (double-blinded). Only the directors of the project --- that had nothing to do with patients and nephrologists --- had information about these items. The study duration was 3 months.

All patients were visited routinely during hemodialysis by nephrologists. 3 months after the beginning of the study, blood selenium levels, triglyceride and total cholesterol, and weight and physical activities of patients were evaluated again and compared with the results from the beginning of the study. Data were collected and analyzed using SPSS software version 21. Qualitative variables were analyzed using Chi-square test. Quantitative variables were analyzed by independent t-test and for evaluating and comparing variables before and after interventions, paired-samples t-test was used. Normality evaluations were performed using Kolmogorov--Smirnov test. Statistical analysis of these values was performed using $P < 0.05$ as a significance threshold.

Results

Here in this study, we included 88 patients based on our inclusion criteria but during the study, 10 patients were excluded. These patients include 4 patients in

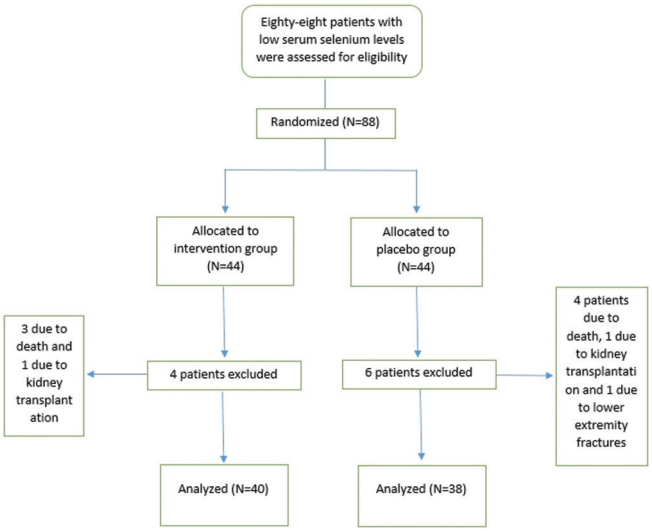

Figure 1: CONSORT diagram of patients.

the selenium group (3 patients due to death and 1 due to kidney transplantation) and 6 patients in the placebo group (4 patients due to death, 1 due to kidney transplantation and 1 due to lower extremity fractures). Our study population consisted of 48 males (61.5%) and 30 females (38.5%) with low selenium levels. The CONSORT flow diagram is indicated in Figure 1.

Patients were divided randomly into two groups of intervention and control. Serum selenium levels at the beginning of our study were 40.06 ± 8.50 in intervention group and 45.00 ± 8.16 in control groups. There were no significant differences between two groups regarding baseline selenium levels ($P > 0.05$). Comparing the demographic data, there were also no significant differences between two groups regarding age ($P = 0.236$) and sex ($P = 0.137$) and causes of ESRD ($P = 0.358$). Evaluating hemodialysis duration in patients showed no significant difference between two groups ($P = 0.586$). The demographic data of patients are summarized in Table 1.

Both intervention and control groups were assessed for their selenium levels, weight, sit to stand test, total cholesterol, and TG before and after treatments. Results of comparisons between these items indicated that selenium levels and physical activities of patients were increased significantly in intervention group compared to baseline ($P < 0.001$ for both). Other variables in both intervention and control groups did not change significantly ($P > 0.05$). These data are summarized in Table 2.

We also analyzed data that were related to selenium levels, weight, sit to stand test, total cholesterol, and TG before and after interventions among intervention and control groups. These data showed no significant difference between levels of selenium, weight, sit to stand test, total cholesterol, and TG before interventions among patients ($P > 0.05$). Further analysis showed that selenium levels and physical activities of patients were increased significantly in intervention group compared to control group ($P < 0.001$ for selenium and $P < 0.001$ for Physical activities). Weight, physical activity, total cholesterol, and TG in both intervention and control groups did not change significantly after interventions ($P > 0.05$).

Table 1: Demographic data of patients

Variable	Intervention (*n*=40)	Control (*n*=38)	*P*
Sex			
Male	28 (70%)	20 (52.6%)	0.137
Female	12 (30%)	18 (47.4%)	
Age (mean±SD)	57.20±11.9	57.42±13.7	0.236
Cause of ESRD			
HTN	8 (20%)	4 (10.5%)	0.358
DM	18 (45%)	23 (60.5%)	
Other	14 (35%)	11 (29%)	

HTN: Hypertension, DM: Diabetes mellitus

Discussion

Here, we showed that selenium supplement therapies had significant beneficial results on increasing both selenium levels and also physical activities in intervention group compared to controls. We also showed that these therapies had no significant effects on items, such as weight and triglyceride and total cholesterol in patients. Positive effects of antioxidant therapies especially selenium therapy have been evaluated among patients under hemodialysis in different literature. In a study by Nasri performed in 2016 in Iran, effects of antioxidant therapies including vitamin C and flavonoids were assessed. It was reported that selenium therapies are associated with reduced oxidative and inflammatory stress among patients under hemodialysis (Nasri). In a systematic review by Coombes and Colleagues in 2012, they declared that antioxidant therapies have positive effects and are efficient in decreasing oxidative stress in patients under hemodialysis.[30] These data emphasize on the critical roles of selenium therapies. In another study by Koenig and Colleagues in 1997, they indicated that intravenous administration of selenium was associated with increased selenium levels after 2 weeks. They administered 400 μg three times a week in 12 patients.[29] They concluded that selenium should be considered for micronutrient supplementation in these patients. Another study by Richard and Colleagues in 1990 also showed increased selenium levels in patients with ESRD after intravenous administration of selenium.[31] These data showed that intravenous selenium therapy is an effective method of increasing selenium levels in a short time. These results are in line with the results of our study.

There are also some studies on oral selenium administrations. Omrani and Colleagues performed a study on 84 patients under hemodialysis and evaluated the effects of 3 months oral selenium supplement therapies on lipid profile in patients. They indicated that selenium therapies had no beneficial effects on lipid profiles in patients under hemodialysis.[32] These results are also in line with the results of our study. Furthermore, an important point of our study is that we evaluated weight and physical activities of patients along with selenium levels and lipid profile and showed that selenium supplement therapies have beneficial effects only on physical activity and selenium levels. Another study was performed by Salehi and Colleagues in 2013. They evaluated the effects of selenium supplement therapies in 80 patients under hemodialysis and showed that these therapies lead to reduced malnutrition through alleviating oxidative stress and inflammation.[33] Furthermore, they showed that selenium therapies have no significant effects on lipoproteins. These results are also in line with the results of our study. We also evaluated the effects of selenium therapies on physical activity and weight of patients and indicated positive effects on physical activities. We suggest that these results could be because of small study populations or also limited study duration. As a

Table 2: Comparison of different variables between two groups before and after interactions

Variable		Time	Mean±SD	*P*
Weight (Kg)	Intervention	Before interactions	69.47±16.24	0.089
		After interactions	70.55±16.10	
	Control	Before interactions	63.60±13.63	0.088
		After interactions	63.77±13.82	
Sit to stand test (seconds)	Intervention	Before interactions	14.22±6.61	0.001
		After interactions	16.11±7.24	
	Control	Before interactions	20.28±8.87	0.250
		After interactions	20.25±8.54	
Selenium (µg/l)	Intervention	Before interactions	40.06±8.50	0.000
		After interactions	66.65±10.93	
	Control	Before interactions	45.00±8.16	0.741
		After interactions	42.90±7.33	
Total cholesterol (g/dl)	Intervention	Before interactions	140.50±39.73	0.197
		After interactions	136.42±38.68	
	Control	Before interactions	143.97±29.40	0.194
		After interactions	147.36±34.12	
TG (g/dl)	Intervention	Before interactions	107.46±48.09	0.227
		After interactions	120.06±52.23	
	Control	Before interactions	124.84±63.03	0.323
		After interactions	134.37±59.94	

result, we can conclude that selenium supplement therapies have no significant effect on lipid profile on patients on hemodialysis in short term therapies. However, long-term studies on larger populations might indicate different results.

The effects of different agents on selenium levels in patients on hemodialysis have also been investigated in different studies. In a study by Kamińska-Galwas and Colleagues, the assessed levels of different micronutrients in 52 patients with ESRD who have been treated with erythropoietin and 21 healthy subjects. They concluded that levels of selenium were decreased during hemodialysis and no significant influence was observed by erythropoietin on its levels.[34] Stockler-Pinto and Colleagues also investigated the effects of Brazilian nut supplements on selenium levels on 81 patients on hemodialysis and showed that consumption of Brazilian nuts is associated with increased selenium levels and therefore, decreased oxidative stress.[35] These data could be used as nutritional suggestions in patients under hemodialysis or for patients who are not able to use selenium supplements. On the contrary, it has been shown that selenium supplement therapies are not associated with changes in thyroid function tests or acute phase reactants which could be some concerns among physicians.[36] All of these data along with our results put great emphasis on pivotal roles of selenium in patients on hemodialysis. We suggest that physicians especially nephrologists should consider selenium supplements for patients on hemodialysis. The limitations of our study were that we entered a limited number of patients and also could not evaluate their daily activity. We also did not consider their medical history which could indeed influence the measured factors.

Conclusions

Taken together, we showed that selenium supplement therapy has beneficial effects in patients on hemodialysis. Furthermore, we showed that selenium supplement therapies have positive effects on increasing serum selenium levels along with physical activities. On the contrary, these therapies had no significant effects on triglyceride and total cholesterol or weight of patients. We suggest that physicians should consider selenium supplement therapies as an effective way of reducing oxidative stress especially in patients on hemodialysis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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