Original Research Article

Evaluation of Plasma Selenium Level and its Association with Malnutrition in Hemodialysis Patients in Golestan Province, Iran

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ABSTRACT

Introduction: Selenium (Se) is a rare element with well-demonstrated anti-oxidative effects that acts as an enzyme co-factor in physiological interactions. Low plasma Se level and malnutrition in hemodialysis (HD) patients could increase the risk of morbidity and mortality among these patients. Moreover, Se deficiency leads to oxidative stress and inflammatory response. Therefore, this study aimed to determine the association of plasma Se levels with malnutrition and inflammatory markers in HD patients. **Materials and Methods:** This cross-sectional study included 88 patients undergoing routine HD at dialysis unit of 5th Azar Hospital in Gorgan, northeastern Iran. In addition, 88 healthy individuals were selected from the patients' families as controls. Level of Se, C-reactive protein (CRP), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG) and albumin were measured in the patients and controls by the atomic absorption method. Se levels were categorized into two groups of "over half-normalized" and "under half-normalized" for further analysis. **Results:** Hyposeleniemia was found in two patients (2.3%). The mean level of Se in HD patients was lower than in the healthy controls (P< 0.001). Among all HD subjects, 30.3% had under half-normalized Se level. In addition, 79.5% of HD patients were well nourished and 20.5% were moderately malnourished. There was no statistically significant difference between the mean level of Se in the malnourished and well-nourished subjects. Total mean level of HDL, LDL, TG and CRP had not significant correlation with plasma Se levels. There was a significant positive correlation between the mean plasma albumin and Se levels in the HD patients (P<0.05). **Conclusions:** The mean plasma Se level of HD patients in this area is in the normal range. There is no association between plasma Se level and malnutrition. Based on our findings, hyposelenemia is not a problem in HD patients in the Golestan Province.
KEYWORDS: Selenium, Malnutrition, Inflammatory markers

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INTRODUCTION

Selenium (Se) is a rare element and an enzyme co-factor that plays an important role in physiological interactions such as thyroid hormones metabolism, immune response and anti-oxidative activity [1]. Previous studies have shown that Se treatment may improve immune system regulation and decrease oxidative stress. Low selenium level increases the risk of atherosclerosis and infection, and could lead to mortality [2].

Low plasma Se level in hemodialysis (HD) patients and its significant association with age, serum albumin, C-reactive protein (CRP), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels have been suggested [3]. Other studies showed a negative correlation between plasma Se and uric acid levels [4]. The reduction of plasma Se level may cause immune dysfunction, increased risk of infectious disease and mortality in these patients [2,5]. Malnutrition is a common problem in HD patients, which is often associated with increased risk of morbidity and mortality. Se deficiency leads to oxidative stress, inflammatory response and high oxidative stress, which can subsequently induce malnutrition [6,7]. The aim of this

study was to investigate the association of plasma Se levels with malnutrition and inflammatory markers in HD patients.

MATERIALS AND METHODS

In this cross-sectional study, 88 patients (mean age: 56.21 ± 15.11 years) undergoing routine HD at the dialysis unit of 5th Azar Hospital in Gorgan (northeastern Iran) were enrolled after obtaining written consent. In addition, 88 healthy controls (mean age: 42.05 ± 12.6 years) were selected from patients' families to determine the mean Se level in healthy individuals. The healthy controls were selected from the patients' families to match confounding factors related to diet, economy and lifestyle. Exclusion criteria included pregnancy, presence of active infection, consumption of vitamin E or C, lipoic acid, omega 3 fatty acids and immunosuppressive drugs. Blood samples were taken from each subject in the morning before the dialysis session. EDTA (1 mg/ml) was used as anticoagulant. Plasma was separated and stored at -80 °C until analysis. Plasma concentrations of CRP, HDL, LDL, triglycerides (TG) and albumin were measured via routine procedures using automatic analyzers. Dialysis dose and adequacy for HD patients were measured using the Kt/V values. Body mass index (BMI) was calculated as weight divided by squared height (kg/m^2). Plasma Se levels were measured by atomic absorption method. Se levels were categorized into two groups of "over half-normalized" and "under half-normalized" for further analysis.

The nutritional status of HD patients was evaluated and categorized as normal, mild to moderate or severe malnutrition using the subjective global assessment [8]. All patients were dialyzed using the same method and were matched for time, frequency and type of dialyzer (low flux).

Statistical analysis
Statistical analysis was performed using SPSS software (version 16, Chicago, IL, USA). Results were expressed as mean ± standard deviation (SD). Depending on the normality of data and type of variables, parametric or non-parametric tests were used. P-values less than 0.05 were considered statistically significant..

RESULTS

Plasma Se levels were determined for 88 HD patients and 88 healthy controls. Mean Se level in HD patients (101.60 ± 34.08 μg/L) was significantly lower than in the controls (111.42 ± 30.84 μg/L) (P< 0.001). Nevertheless, the mean level of Se in both HD patients and healthy subjects were in the normal range (60-120 μg/L) [9]. Only two HD patients (2.3%) had hyposeleniemia (Se level < 60 μg/L). The mean HDL, LDL and TG levels in HD patients were 39.8, 78.38 and 97 mg/dl, respectively. Based on results of the Spearman's correlation test, there was no significant correlation between HDL, LDL and TG levels and the plasma Se level (Figure 1). Moreover, the mean plasma level of albumin in HD patients was 4.28 g/L, which had a statistically significant correlation with Se level (Figure 2). Plasma CRP was negative in 52 HD patients (59.1%). However, 16 (18.2%), 15(17%) and 5(5.7%) HD patients had 1+, 2+ and 3+ CRP-positive tests, respectively. There was no significant correlation between CRP and plasma Se level in the Kruskal-Wallis test (P=0.846). While 79.5% of HD patients had normal nutritional status, moderate malnutrition was found in 18 patients (20.5%). There was no significant correlation between nutritional status and plasma Se level in the Fisher's exact test (P=0.631).
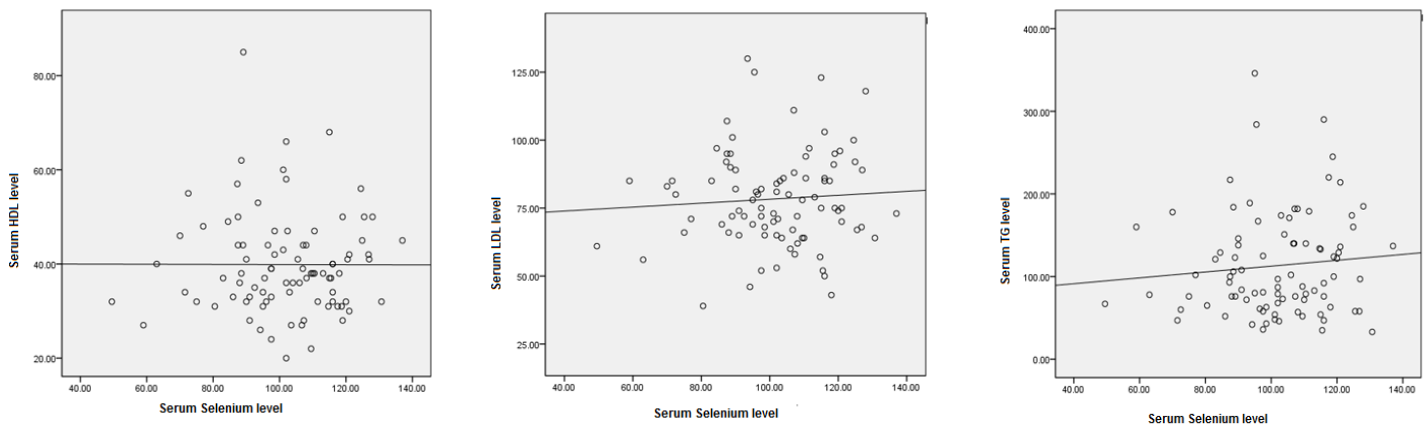
Figure 1. Correlation of Se level with HDL, LDL and TG concentrations in HD patients (n=88)
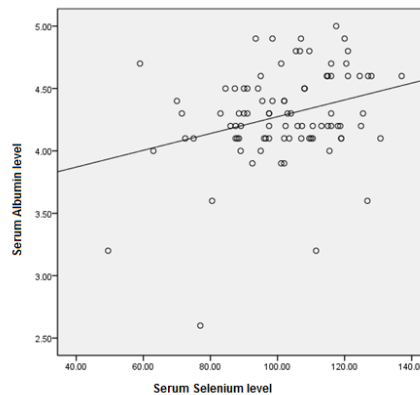

Figure 2. Correlation of Se level with albumin concentration in HD patients (n=88)

In this study, HD patients with normal plasma Se level (n=86) were divided into two groups. Group A included 60 patients (69.7%) with upper limit half-normalized Se levels (>111μgr/dl) and group B included 26 patients (30.3%) with lower limit limit half-normalized Se level (<111μgr/dl).

DISCUSSION

The results of this study show the low prevalence of hyposelenemia (2.3%) in HD patients in Gorgan, Iran. In addition, the plasma Se levels in HD patients were lower than the control group, but not in the hyposelenemia range. Mean plasma Se level in HD patients was 101.6 μg/L, which is significantly lower than the healthy controls (111.42 μg/L). However, studies of Zacharias et al. (8 μg/L) [10] and Guoas et al. (56.76 μg/L) [11] have reported lower mean plasma Se levels for HD patients. A

meta-analysis of 128 studies on level of trace elements in HD patients showed that Se level is significantly lower in HD patients compared with healthy controls [12]. Se deficiency in HD patients could be due to oxidative stress since they have increased pro-oxidant activity (diabetes, chronic inflammatory state, uremia, bio-incompatibility of dialysis membranes) and or reduced antioxidant capacity (vitamins C and E levels, glutathione system and Se)[13-14]. Low Se dietary intake and low Se concentration in soil could also be important causes of Se deficiency. Moreover,

bioavailability of Se in soil varies in different regions. Fish and mammals' organs such as kidney and liver, are known to have high Se content. Cereals may also act as important sources of Se [15].

In the present study, the mean level of Se in HD patients was in the normal range. Only 2.3% of HD patients had hyposeleniemia. Inconsistent with our findings, a study in Brazil found that all HD patients have Se deficiency [16]. The difference between the two studies may be related to differences in dietary intake of Se and Se concentration in soil. A previous study in the Golestan Province has reported high Se content in soil samples of this area (mean: 3.7±1.61 mg/kg) [17]. Furthermore, consumption of mammal organs especially lamb liver is common in this area.

In this study, 20.5% of HD patients had malnutrition, which indicates the low prevalence of malnutrition in this area compared to other areas in Iran [18,19]. Moreover, there was no significant relationship between malnutrition and plasma Se level.

The results of this study indicated a positive correlation between plasma albumin level and Se level in HD patients. HD adequacy, CRP, lipid profile and malnutrition had no significant association with plasma Se levels. However, study of Gue et al. reported that T-cell function and inflammation (CRP) have a negative correlation with Se deficiency [11].

CONCLUSION

Although the mean plasma level of Se in HD patients is lower than in healthy individuals, it is in the normal range. According to the results of our study, hyposelenemia is not a problem in HD patients in the Golestan Province.

REFERENCES

1. Mehdi Y1, Hornick JL, Istasse L, Dufrasne I. Selenium in the environment, metabolism and involvement in body functions. Molecules. 2013 Mar 13;18(3):3292-311. doi: 10.3390/molecules18033292.

2. Iglesias P, Selgas R, Romero S, DiezJJ. Selenium and kidney disease. JNephrol. 2013 Mar-Apr;26(2):266-72.

3. Fujishima Y OM, Itai K, Kato K, Tanno K, Turin TC, Onoda T, Endo S, Okayama A, Fujioka T. Serum selenium levels in hemodialysis patients are significantly lower than those in healthy controls. Blood Purification. 2011;32(1):43-7.

4. Martí del Moral L AA, Navarro-Alarcón M, López-Ga de la Serrana H, Palomares-Bayo M, Oliveras-LópezMJ. Altered serum selenium and uric acid levels and dyslipidemia in hemodialysis patients could be associated with enhanced cardiovascular risk. Biol Trace Element Research. 2011 Dec;144(1-3):496-503.

5. Fujishima Y OM, Itai K, Kato K, Tanno K, Turin TC, Onoda T, Endo S, Okayama A, Fujioka T. Serum selenium levels are inversely associated with death risk among hemodialysis patients. Nephrol Dial Transplant. 2011 Oct;26(10):3331-8.

6.Mehrotra R, Kopple JD.Protein and energy nutrition among adult patients treated with chronic peritoneal dialysis. Adv Ren Replace Ther. 2003 Jul;10(3):194-212. Review

7.Morais AA, Silva MA, Faintuch J, Vidigal EJ, Costa RA et al. Correlation of nutritional status and food intake in hemodialysis patients. Clinics (Sao Paulo). 2005 Jun;60(3):185-92.

8. Kalantar-zade K, Kleiner M, Dunne E, Lee GH, Luft FC. A modified quantitative subjective global assessment of nutrition for dialysis patients. Nephrol Dial Transplant. 1999Jul;14(7):1732-8.

9. Longo DL, Harrison TR. Harrison's principles of internal medicine. 18th ed. New York ; London: McGraw-Hill; 2012

10. Zachara BA GJ, Palus J, Zbrog Z, Swiech R, Twardowska E, Wasowicz W. The Effect of Selenium Supplementation in the Prevention of DNA Damage in White Blood Cells of Hemodialyzed Patients: A Pilot Study. Biol Trace Elem Res. 2011 Sep;142(3):274-83.

11. Guo CH WC, Chen PC, Yang TC. Linkage of some trace elements, peripheral blood lymphocytes, inflammation, and oxidative stress in patients undergoing either hemodialysis or peritoneal dialysis.Perit Dial Int. 2011 Sep-Oct;31(5):583-91.

12. Yang CY, Wu ML, Chou YY, Li SY, Deng JF, Yang WC, et al. Essential trace element status and clinical outcomes in long- -term dialysis patients: a two-year prospective observational cohort study. Clin Nutr 2012;31:630-6.

13. Tonelli M, Wiebe N, Hemmelgarn B, Klarenbach S, Field C, Manns B, et al. Trace elements in hemodialysis patients: a systematic review and meta-analysis. BMC Med 2009;19;7:25. PMID: 19454005

14. Hemmati. M, Kadkhodaee M, Zahmatkesh M, Mahdavi-Mazde M, Ghaznavi R, Mirershadi F. Blood antioxidant levels and alterations of serum calcium and pH in hemodialysis patients. Tehran University Medical Journal. 2008;66(1):12-17. [Persian]

15. Mehdi Y, Hornick JL, Istasse L, Dufrasne I. Selenium in the environment, metabolism and involvement in body functions. Molecules 2013;18:3292-311. 16.

16. Stockler-Pinto MB, Malm O, Azevedo SR, Farage NE, Dorneles PR, Cozzolino SM, Mafra D. Selenium plasma levels in hemodialysis pati ents: comparison between North and Southe ast of Brazil. J Bras Nefrol. 2014;36(4):490-5. [Article in English, Portuguese]

17. Semnani Sh, Roshandel Gh, Keshtkar AA , Zendehbad A, Rahimzadeh H, Besharat S , et al . Relationship between Soil Selenium level and esophageal cancer: An ecological study in Golestan province of Iran. J Gorgan Uni Med Sci. 2010; 12 (3) :51-56. [Persian]

18. Sohrabi Z, Eftekhari MH, Eskandari MH, Rezaeianzadeh A, Sagheb MM. Malnutrition-inflammation score and quality of life in hemodialysis patients: is there any correlation? Nephrourol Mon. 2015 ;23;7(3):e27445. doi: 10.5812/numonthly.7(3)2015.27445. eCollection 2015.

19. Amirkhanloo S, Maghsoudloonejad R, Eshghinia S. Nutritional status of hemodialysis patients using subjective global assessment (SGA). Journal of Gorgan University of Medical Sciences,Winter 2016; 17(4); 85-90.