

Research Article

Plasma Levels of Selenium (SE) and Glutathion Peroxydase (GSH-PX) and their Relationship to Supplementation of Selenium in Patients with Chronic Renal Failure (CRF) on Hemodialysis (HD)

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Abstract

Introduction: Plasma levels of Se and GSH-Px decrease with the progression of renal impairment and is particularly pronounced at the end stage of chronic kidney disease (CKD) as kidney proximal tubular cells are the main source of pGSH-Px activity. A number of authors found that Se supplementation increases its plasma levels in patients on HD, but publications about influence of Se supplementation on plasma GSH-Px are controversial-from a lack of any effect to a significant increase of the enzyme. The study aims to monitor levels of plasma selenium (pSe) and glutathione peroxidase (pGSH-Px) in patients on HD treatment with Se deficit, orally supplemented with Se for 3 months, and to evaluate the supplementation on pSe and pGSH-Px.

Material and Methods: 61 patients on regular hemodialysis, divided into two groups (1st group-33 pts. with pSe deficit and, 2nd group-28 with normal pSe levels) were tested at the beginning of dialysis sessions for serum hemoglobin, total protein, albumin, creatinine, urea, uric acid, C-reactive protein (CRP), phosphorus, potassium plasma Se and pGSH-Px activity. The same parameters were re-examined at the end of the study. The patients of the 1st group were supplemented with oral Se for 3 months and the results in the two groups were compared.

Results: All parameters (except pSe and pGSH-Px in the 1st group) showed no significant differences in the beginning and the end of the follow-up period in both patients groups. The levels of pSe and pGSH-Px in the 2nd

group also showed no significant change, but in the 1st group both parameters increased significantly at the end of the 3-months period. We found a significant correlation between pSe/pGSH-Px ($p < 0.01$), and between pGSH-Px/Creatinine ($p < 0.01$) at the start and the end of the study.

Conclusion: Our study suggests that supplementation of oral Se in patients with CKD on regular HD, significantly increases not only pSe, but pGSH-Px as well, despite a proved presence of bilateral nephrosclerosis in all patients of both groups. As a positive effect, at least one of the members of anti-oxidant system in this patients contingent is enhanced, namely pGSH-Px.

Keywords: Chronic kidney disease; Chronic renal failure; Hemodialysis; Selenium; Glutathione peroxidase

1. Introduction

Numerous studies have shown that the compounds containing trace elements (mainly enzymes), but not trace elements “per se”, are critical for biological activities in the human body [1-5]. Compounds with (Se), cuprum (Cu), and zinc (Zn) play a major role in the antioxidant protective system. They perform their antioxidant functions through the proteins in which they are included [1-3]. Se is a component of about 25 enzymes, including glutathione peroxidase family (GSH-Px), thioredoxin reductases and selenoprotein P. Selenium is a trace element that participates as a cofactor in a number of enzyme processes-regulating thyroid hormone metabolism, modulating immune processes, and enhancing antioxidant protection for the human body [4-7]. Although there are not too many studies of plasma selenium levels in patients with chronic kidney disease (CKD) on dialysis treatment, they prove a deficiency of this important element of vital human function, both in hemodialysis (HD) and in continuous ambulatory peritoneal dialysis (CAPD) patients [4-8]. Plasma levels of Se and GSH-Px decrease with the progression of renal impairment and is particularly pronounced at the end stage of chronic kidney disease (CKD), as the kidney proximal tubular cells are the main source of pGSH-Px activity [5, 7, 9]. A number of authors found that Se supplementation increases its plasma levels in patients on HD, but publications about influence of Se supplementation on plasma GSH-Px are controversial-from a lack of any effect to a significant increase of the enzyme [4, 5, 9].

1.1 Aim of the study

To monitor levels of plasma selenium (pSe) and glutathione peroxidase (pGSH-Px) in patients with Se deficit on HD, orally supplemented for 3 months with Se, and to evaluate its effect on pSe and pGSH-Px.

2. Material and Methods

61 patients on regular hemodialysis (34 men and 27 women, aged 19 to 67 years), divided into two groups (1st group-33 pts. with pSe deficit and, 2nd group-28 with normal pSe levels) were tested at the beginning of dialysis sessions for serum hemoglobin, total protein, albumin, creatinine, urea, uric acid, C-reactive protein (CRP), phosphorus, potassium and calcium by routine procedures with automatic analyzer. Plasma Se was determined by

atomic absorption spectrometry (AAS), using a HITACHI® Z-500 spectrometer and pGSH-Px activity-with a CX7 Synchron system (Beckman Instruments, CA, USA, kit Ransel; Randox, Ireland). The same parameters were re-examined at the end of the study in the both groups of patients. The patients of the 1st group were supplemented with 200 µg/day oral Se for 3 months and the results in the two groups were compared. The statistical analyses were performed using SPSS19.0 software (Chicago, IL, USA). Statistical accepted significance is $p < 0.05$.

The study protocol was reviewed and approved by the Ethics Committees of the all participating University Hospitals and all the patients gave a written informed consent.

3. Results

Hemoglobin, total protein, albumin, creatinine, urea, uric acid, C-reactive protein (CRP), phosphorus, potassium and calcium showed no significant differences in the beginning and the end of the follow-up period in both patient groups. The levels of pSe and pGSH-Px in the 2nd group also showed no significant change, but in the 1st group both parameters increased significantly at the end of the 3-months period, despite plasma total proteins and albumins were unchanged: pSe-1 rises from: 497.5 +/- 132.6; to pSe-2: 1012.4 +/- 269.8 mcg / l; pGSH-Px-1 rises from: 7.8 +/- 1.6; to pGSH-Px-2: 24.8 ± 6.8 U/gHb (Table 1).

Laboratory parameters	1 st Group Supplementd by Se /Start/	1 st Group /Study's end /	P<	2 nd Group Unsupplementd by Se /Start/	2 nd Group /Study's end/
pSe (µg/L)	497.5 ± 132	1012.4 ± 269	0.01	814.2 ± 254	832.4 ± 198
pGSH-Px (U/gHb)	7.8+/-1.6	24.8+/-6.8	0.01	20.9+/-8.8	19.7+/-9.2
T-protein (g/L)	65.5 ± 3.3	64.3 ± 3.1	N.S.	65.5 ± 3.3	66.1 ± 2.3
Albumin (g/L)	36.5 ± 2.1	37.2 ± 3.3	N.S.	37.5 ± 2.1	36.9 ± 2.7

Table 1: Plasma Se, GSH-Px and proteins in Se supplemented and un-supplemented HD patients at the start and end of the study.

The rise of plasma Se due to the Se supplementation is well visualized in the next Figure 1.

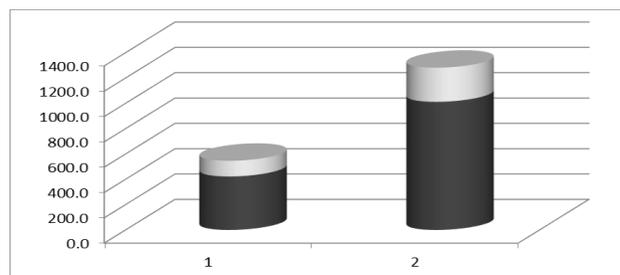


Figure 1: pSe (µg/L) (MD+/-SD) in 1st group before (1) and after (2) Se supplementation.

The improvement of plasma enzyme activity of GSH-Px in Se-supplemented patients is shown on the next Figure 2.

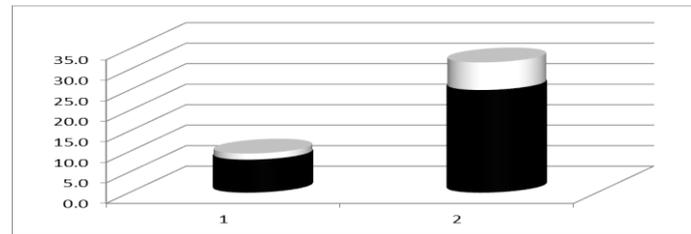


Figure 2: pGSH-Px (MD+/-SD) in 1st group before (1) and after (2) Se supplementation.

We found a significant correlation between pSe/pGSH-Px (at the start-p<0.01) and (at the end-p<0.01) and between pGSH-Px/Creatinine (at the start-p<0.01) and (at the end-p<0.05), but not between pSe/CRP and between pGSH-Px/CRP at the start and the end of the study.

4. Discussion

The likely mechanisms for the emergence and augmentation of pSe deficit in hemodialysis patients are reduced dietary intake, impaired intestinal absorption of selenium, decreased serum levels of selenium-binding protein, increased oxidative stress and loss of selenium by urine or in dialysis procedure [1-7]. Low Se intake and low Se soil concentration are also an important cause of this deficiency [8-10]. Bioavailability of Se in soils varies greatly in different regions. Fish and mammal organs, such as kidney and liver, are known to accumulate significant levels of Se and are, potentially, good dietary sources of this essential element for humans. In general, fruits and vegetables contain low Se levels, however, depending on Se bioavailability cereals may constitute an important source of Se [11-12]. It is well-known that Brazil nuts are very rich in selenium and only a few nuts a day would provide the necessary amount of selenium in deficiency, but they also contain too much phosphate, which makes them unsuitable for dialysis patients [12-14]. However, it has been indicated that Se deficiency might occur in HD patients in nonspecific areas where environmental Se is sufficient. Deficiency of selenium causes pathological abnormalities in a number of organs and systems in the human body presented in the following points [1, 8, 15-17]:

1. Grought retardation
2. Reproductive disturbances
3. Muscle degeneration
4. Hepatocyte necrosis
5. Pancreas degeneration
6. Cardiomyopathy
7. Disturbed cell membrane

The presence of oxidative stress, which is manifested by an excess of oxidative radicals and decreased levels of antioxidants, has been demonstrated in dialysis patients [3, 8, 15, 17]. In our study, oxidative stress is confirmed by

abnormally reduced levels of plasma levels of glutathione peroxidase (P-GSH-Px) and Se. Plasma glutathione peroxidase (pGSH-Px) is also decreased due to the fact that selenium is required for its synthesis and activation, and the localization of the enzyme formation process is in proximal renal tubules that are significantly damaged by CRF [4, 5]. Our finding of a positive correlation between increase of pSe and pGSH-Px suggests a rise of synthesis of pGSH-Px due to Se supplementation, but the publications about this issue in the medical journals are very heterogeneous [4, 5, 14, 17]. The undisputed rise to normalizing levels of pSe and the beneficial effect of selenium supplementation on one of the important antioxidant enzymes as well as maybe of the other beneficial activities of Se “per se” is encouraging. The lack of correlation between pSe/CRP and pGSH-Px/CRP suggests that the acute inflammation “per se” could not be an important factor on the Se turnover in the human body. For us it was especially interesting to find out whether, despite the irreversibly reduced renal parenchyma in terminal CRF of hemodialysis patients, the body of these patients has compensatory mechanisms to restore the enzyme activity of this antioxidant enzyme (GSH-Px), when supplementing selenium, and the answer was positive. At the other hand, our study presented several limitations. The sample sizes were small, we did not have a control with healthy subjects, and we did not have meaning data from the diet of patients, because the foods have different concentrations of Se and there is no accurate software to calculate the diets and, the major problem in dietary assessment was inaccuracy in patients recordings of dietary intake.

5. Conclusion

Our study suggests that supplementation of oral Se in patients with CKD on regular HD, significantly increases not only pSe, but pGSH-Px as well, despite the patients on regular HD have proved bilateral nephrosclerosis. The phenomenon is probably due to the activation of small islets of renal parenchyma and, to a greater extent, the presence of outbreaks of GSH-Px synthesis (upon import of Se) into non-renal body tissues. As a positive effect, at least one of the members of anti-oxidant system of this patient’s contingent is enhanced-plasma GSH-Px.

Conflict of Interest

We declare that we are not in conflict of interests in this study.

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