

SELENIUM DEFICIENCY IN CHRONIC URAEMIA AND DIALYSIS

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Summary

Chronic uraemic and dialysis patients have significantly lower plasma selenium and plasma and erythrocyte glutathione peroxidase activities compared to normal healthy controls in the West of Scotland. Reduced dietary intake seems to be an important cause but other factors such as impaired gastrointestinal absorption and loss through dialysis membranes may also play a part. The possible clinical significance of these observations is discussed.

Introduction

Selenium, being present at the catalytic sites of the enzyme glutathione peroxidase (GSHPx), is an essential trace element in human metabolism and selenium deficiency has been implicated in cardiovascular diseases, myopathies, defective white blood cell function and neoplasia. Alteration in trace element metabolism may occur in uraemia and dialysis due to various factors such as dietary restriction, impaired gastrointestinal absorption and loss across dialysis membranes. In the present study, we investigate the effect of chronic uraemia and dialysis on plasma and tissue selenium.

Patients and methods

Thirty subjects each of the following four groups were studied; normal healthy controls, patients with end-stage chronic renal failure (CRF) with creatinine clearance <10ml per minute, patients on regular haemodialysis (HD) and patients on continuous ambulatory peritoneal dialysis (CAPD).

Blood samples were withdrawn through a plastic cannula pre-dialysis in HD patients and after a six hourly exchange in CAPD patients. Plasma selenium was measured by electrothermal atomic absorption spectrometry. Plasma and

GSHPx was measured by reaction rate spectrophotometry. A detailed dietary assessment was carried out in 18 patients and the average daily protein and selenium intake calculated.

Results

A significant reduction in plasma selenium and plasma and erythrocyte GSHPx were observed in all three patient groups compared with the normal controls. In over one-third of the patients, the plasma selenium and plasma and erythrocyte GSHPx were frankly subnormal. A strong correlation was found between the average daily protein and selenium intake (Table I).

TABLE I. Selenium status for uraemic and dialysis patients

	plasma selenium $\mu\text{mol/l}$	plasma GSHPx IU/l	Erythrocyte GSHPx IU/gm Hgb
Control	1.5 \pm 0.3*	214 \pm 55*	17 \pm 3*
CRF	1.0 \pm 0.3	109 \pm 36	13 \pm 4
HD	1.1 \pm 0.3	111 \pm 51	13 \pm 2
CAPD	1.0 \pm 0.3	87 \pm 34	13 \pm 4

* $p < 0.001$ by student's t test

CRF = chronic renal failure CCr $< 10\text{ml}$ per minute; HD = haemodialysis; CAPD = Continuous ambulatory peritoneal dialysis; GSHPx = glutathione peroxidase activity; Conversion $1 \mu\text{mol/L} = 79 \mu\text{g/l}$ from SI to traditional unit

Discussion

The essentiality of selenium in the nutrition of animals has been known for some time. However, its importance in human metabolism has only been recently established. Severe selenium depletion is now known to be associated with Keshan Cardiomyopathy in Northern China [1] and myopathy in patients on total parenteral nutrition [2]. In epidemiological studies done by Finnish workers, a moderately reduced serum selenium concentration was found to be correlated to increased risk of cardiovascular disease and cancer [3,4].

The biological role of selenium in man is attributed to the presence of seleno-cysteine at each of the four catalytic sites of the enzyme glutathione peroxidase. This selenium-dependent enzyme is present in many human tissue including erythrocytes, neutrophils and platelets. Its major function is the removal of hydrogen peroxide and other organic hydroperoxides generated during oxidative metabolism in cells and thus provides a major defence mechanism of the cells against oxidant damage [5]. GSHPx provides an indicator in tissue selenium status. Plasma selenium concentration and erythrocyte GSHPx are the most

sensitive index of short term and long term changes in selenium status respectively [6]. We used these two parameters to assess the selenium status in chronic uraemic and dialysis patients.

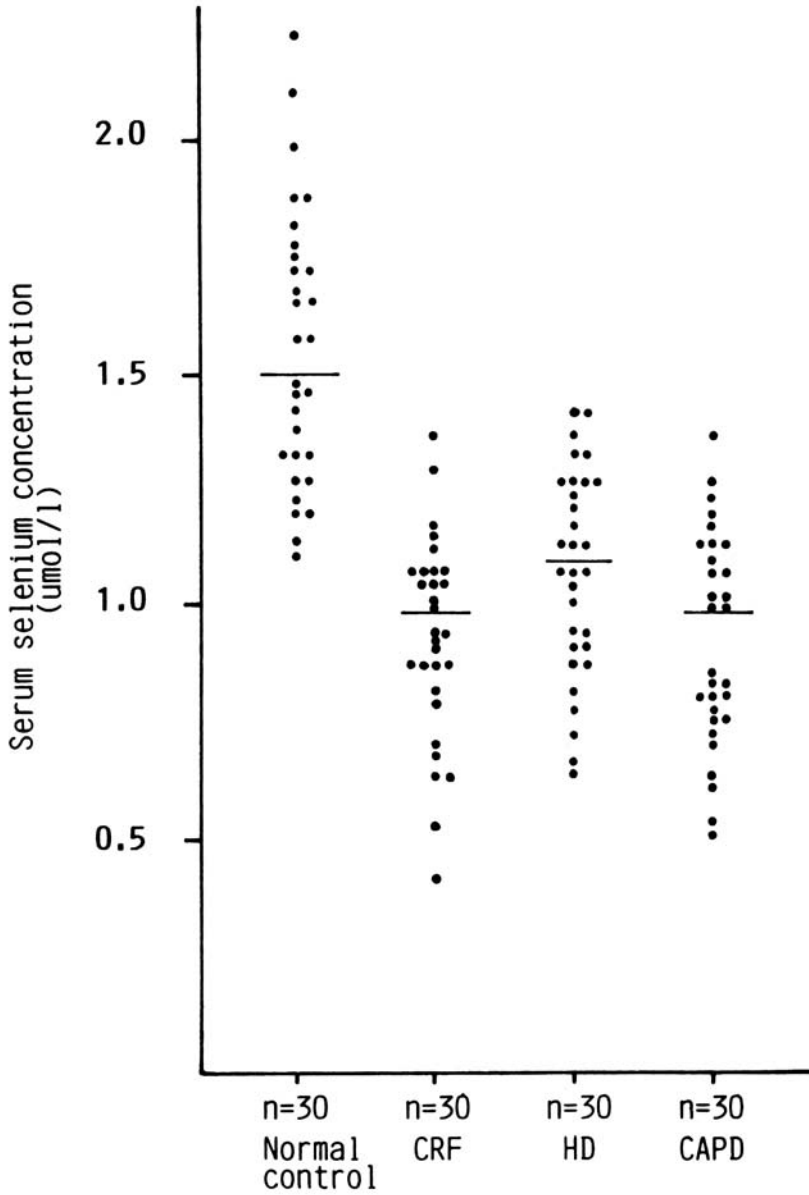


Figure 1. Distribution of plasma selenium and plasma and erythrocyte GSHPx

It is known that plasma selenium varies with selenium intake which in turn is dependent on the selenium content of the soil. Our result shows that in the normal healthy population in the West of Scotland the normal range of plasma selenium is between 1.1 to 2.2 $\mu\text{mol/l}$ (mean $1.5 \pm 0.3 \mu\text{mol/l}$). A highly significant reduction in plasma selenium concentration was observed in chronic uraemia and after commencement on haemodialysis or CAPD. The mean value ($1.0 \pm 0.3 \mu\text{mol/l}$) is, however, much higher than the extremely low level reported in patients with cardiomyopathy and myopathy [1,2]. Nevertheless, the pathogenesis of uraemic cardiomyopathy and myopathy is still not fully understood. Various mechanisms such as secondary hyperparathyroidism and cobalt toxicity have been postulated. It may be possible that a relative selenium deficient state with increased susceptibility to oxidant damage interacts with these factors in the pathogenesis of uraemic cardiomyopathy and myopathy.

Indirect but substantial evidence in epidemiological studies have shown that a relative dietary selenium deficiency is an independent risk factor for cardiovascular disease and cancer [3,4]. In a significant number of our uraemic and dialysis patients, the serum selenium levels are approaching the values reported in the Finnish studies. A more important observation is the corresponding fall in plasma and erythrocyte GSHPx, indicating tissue and long term selenium deficient state. Impaired GSHPx in the lipoxygenase pathway in the metabolism of arachidonic acid may increase platelet aggregability and hence cardiovascular risk [7]. Uraemic and dialysis patients have increased risk of cardiovascular disease but the causes are multifactorial. Further work, including assay of myocardial selenium content will be necessary before any definite conclusion could be drawn on the significance of these observations. Uraemic and dialysis patients have also been reported to have increased risk of cancer. Defective immunological surveillance is thought to be an important factor. It is well documented in animal studies that selenium is essential for the post-phagocytic cytotoxicity of neutrophils [8]. The Finnish epidemiological study has also suggested a synergistic effect of vitamin E and selenium in protection against cancer [4]. The few studies on vitamin E status in uraemia and dialysis have reported both normal and low values after haemodialysis [9]. Interaction between various micronutrients such as copper, zinc manganese, iron, vitamin E and selenium as regard to their antioxidant functions have been studied in animals [10]. Since uraemia and dialysis can result in disturbance of metabolism of many trace elements and micronutrients, these had to be taken into consideration before a direct correlation could be attributed to selenium deficiency and increased incidence of cancer in uraemia and dialysis. It is interesting that two of our thirty patients in the haemodialysis group, both with low plasma selenium and erythrocyte GSHPx, have developed cancer, carcinoma of colon in one and of breast in the other.

There are several causes of plasma and tissue selenium depletion in chronic uraemia and dialysis. Reduced dietary intake is one since fish and meat are important sources of dietary selenium and we have observed a strong correlation between the average daily protein and selenium intake. Decreased gastrointestinal absorption and loss through dialysis membrane may also contribute and this

will help to explain the low selenium levels in CAPD patients who are usually not on any dietary protein restriction. The patients studied were all in stable conditions and we suspect that during intercurrent illness, eg peritonitis in CAPD patients, with gastrointestinal upset and increase in the degree of tissue oxidant activities, the effect of selenium deficiency may be further aggravated and surely any uraemic or dialysis patient with prolonged complications, especially gastrointestinal problems, should be screened for selenium deficiency.

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