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Serum Zinc Concentrations in the Maintenance Hemodialysis Patients

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A B S T R A C T

Zinc is necessary for growth and cells' division. Its deficiency may seriously affect antioxidant defense system and is usually related to renal failure, gastrointestinal diseases and alcoholism. It is very important to know zinc status in dialyzed patients and to prevent hypo- or hyperzincemia. Serum samples from 89 patients with chronic terminal renal failure on regular hemodialysis were withdrawn for the estimation of zinc concentrations immediately before and after dialysis. Serum zinc concentrations showed to be highly dependent on hemodialysis. In 57 (64%) patients, serum zinc concentrations decreased, sometimes from very high to normal values. In remaining 32 (36%) patients serum zinc concentrations tended to increase, but remained within normal range. Zinc supplementation may be recommended only in the patients with proven zinc deficiency, but for all chronic renal failure patients it is questionable.

***Key words**: zinc, hemodialysis, trace elements*

Introduction

For human beings trace elements are essential nutrients with many important functions. They are indispensable components of many enzymes, have some regulatory functions and may affect immune reactions[1,2]. Zinc is cofactor for many metal enzymes (>90%), including red blood cells carboxyanhidrase, alkaline phosphatase and enzymes involved in RNA and DNA synthesis (polymerase). It is necessary for growth and cells' division. Especially fast-dividing cells in immune system (lymphocytes) are sensitive to zinc deficiency. Zinc is found in red blood cells in 75–88%. In the serum, zinc is completely bound to proteins, 60–70% on albumin, the rest on alfa2-macroglobulin and transferine. Serum concentrations are dependent on daily variations, and abnormalities are related to renal failure, gastrointestinal diseases and alcoholism.

The role of trace elements in hemodialysis (HD) patients has not yet been fully characterized. Abnormalities of trace elements are primarily result of uremia[3,4], but they may be further modified by the dialysis procedure[5]. To prevent complications in chronic HD patients, it is very important to know and regulate the levels of trace elements.

Zinc deficiency may be present in chronic renal failure[6]. It has been associated with anorexia, diarrhea, negative nitrogen balance, acrodermatitis, and impotency. Reports indicate that dysgeusia and impotency may be improved by giving zinc supplements to the patients. Zinc deficiency seems to be correlated with some signs of malnutrition in HD patients[7]. Moreover, a recent randomized study in maintenance dialysis patients has shown that the daily intake of a 2.2 mg zinc sulfate supplement was able to correct serum zinc levels to normal values, and this was associated with an increase in normalized protein nitrogen appearance (nPNA)[8]. Recent studies showed that zinc supplementation also correct the cholesterol level which is often low and is the sign of the malnutrition in HD patients[9].

During HD, elimination of substances is dependent upon concentration gradient between blood and dialysis fluid, hydrophilic characteristics of the substance, binding to proteins, and molecular weight. Alterations of zinc concentrations in serum of dialyzed patients have been previously investigated[3,10–12]. The purpose of this study was to assess the zinc serum concentrations in patients with end-stage renal disease on maintenance HD.

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Materials and Methods

Eighty-nine HD patients were enrolled. Demographic patient's characteristics and dialysis data are shown in table 1. Blood samples were collected before and after HD sessions.

TABLE 1
DEMOGRAPHIC CHARACTERISTICS OF THE PATIENT'S

Characteristic	Value (%)
Gender:	
Male	41 (46%)
Female	48 (54%)
Mean patient's age (years)*	63±11
Mean dialysis duration (years)*	4.98±3.39
Mean ultrafiltration rate in all treatments*	2.6±3.4
Type of dialysis membrane:	
cellulose diacetate	44 (49%)
Polysulfone	45 (51%)
Type of dialysis:	
low-flux procedure (hemodialysis)	66 (74%)
high-flux procedure (hemodiafiltration)	23 (26%)
mean dialysis delivered dose (Kt/V) *	1.21±0.15
Underlying renal disease:	
diabetic nephropathy	25 (28%)
glomerulonephritis	22 (25%)
vascular disease	14 (16%)
pyelonephritis	9 (10%)
polycystic kidney disease	8 (9%)
interstitial nephritis	7 (8%)
other	4 (4%)

* X±SD

Serum concentrations of electrolytes (sodium and potassium) were routinely measured before and after HD by phlame photometry on IL 943 (Instrumentation Laboratory, USA). Additionally, we measured urea and creatinine concentrations as well as concentrations of calcium, phosphorus and glucose using conventional methods on Hitachi 704 autoanalyzer (Roche, Germany).

Zinc determination is based on the fact that zinc forms a red chelate complex with 2-(5-brom-2-pyridylazo)-5-(N-propyl-N-sulfopropylamino)-phenol. The increase of absorbance was measured on Opton spectrophotometer and was proportional to the concentration of total zinc[13].

In all laboratory test determinations, commercial quality control samples were used as recommended.

Data were analyzed using the Sigma Plot Scientific Graphing System, Version 6.10. Nonparametric test was performed using Mann-Whitney *U*-test. The differences were considered significant for $p<0.05$. Results are shown as mean value ± standard deviation.

Results

Concentration changes of urea, creatinine, phosphorus, potassium and calcium in patients after HD were significant, as expected (Table 2). In all patients concentrations of urea, creatinine, phosphorus and potassium decreased for 50% or even more ($p<0.001$). HD influenced calcium concentration increasing its values, in some patients for up to 136% ($p<0.001$). Glucose and so-

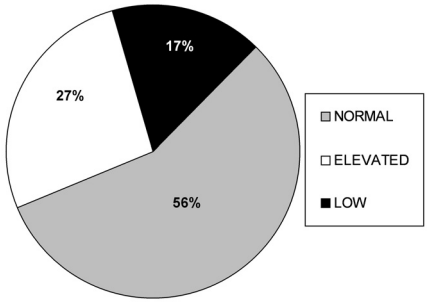

Fig. 1. Serum zinc concentrations in patients before hemodialysis. Percentage of patients with normal, elevated or low zinc concentrations.

TABLE 2
SERUM CONCENTRATIONS OF ZINC, CALCIUM, PHOSPHORUS, SODIUM, POTASSIUM, UREA, CREATININE AND GLUCOSE BEFORE AND AFTER HEMODIALYSIS (N=89)

	Unit	Reference range	Before hemodialysis (X±SD)	After hemodialysis (X±SD)	p
Zinc	μmol/L	10.7–19.5	16.3±7.7	14.2±2.9	ns
Calcium	mmol/L	2.0–2.6	2.3±0.3	2.9±0.2	<0.001
Phosphorus	mmol/L	1.0–1.6	2.2±0.6	1.2±0.2	<0.001
Sodium	mmol/L	133–147	138±4	138±3	ns
Potassium	mmol/L	3.8–5.1	5.4±0.7	3.8±0.4	<0.001
Urea	mmol/L	to 7.5	26.8±7.4	8.4±3.6	<0.001
Creatinine	μmol/L	to 110	722±150	288±81	<0.001
Glucose	mmol/L	to 6.1	6.1±3.1	6.9±2.9	ns

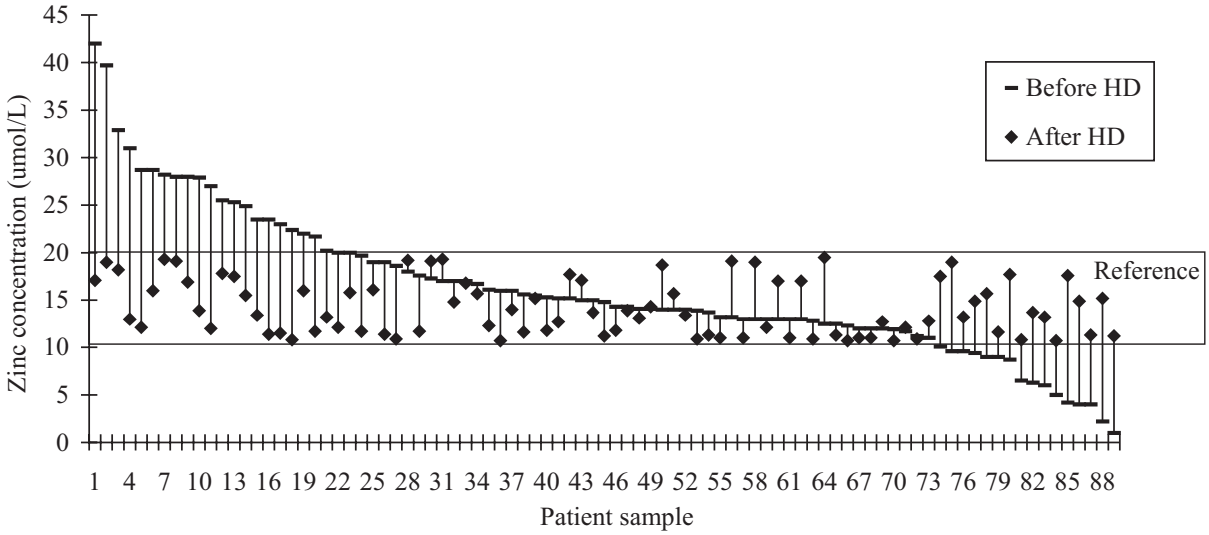

Fig. 2. Alterations in serum zinc concentrations before and after hemodialysis (HD).

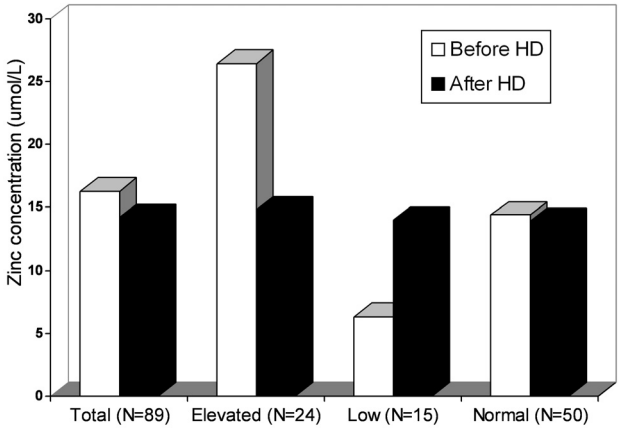

Fig. 3. Changes in zinc concentration after hemodialysis depending on elevated, low or normal concentration before hemodialysis (HD). X – axis represents the groups of patients according to serum zinc concentrations and total patients sample.

dium concentrations did not change. Zinc concentrations showed to be dependent on HD. Before HD, 50 patients (56%) had normal, 15 (17%) low, and 24 (27%) elevated serum zinc concentrations (Figure 1). In 57 (64%) patients zinc decreased from higher values (up to 42 μmol/L) to the final one that remained within normal range (up to 10.7 μmol/L). In remained 32 (36%) patients, zinc concentrations increased (up to 19.5 μmol/ L), but remained within normal range (Figures 2, 3). We compared zinc values and nutritional parameters in HD patients (Table 3).

Discussion

It is well known that patients on chronic HD are at high risk of developing trace element imbalances[11,14], which can further induce different abnormalities in this patients[15–17]. Such abnormalities of zinc metabolism and alterations in serum zinc concentrations have been re-

TABLE 3
COMPARISON OF ZINC VALUES AND NUTRITIONAL PARAMETERS IN HAEMODIALYSIS PATIENTS (X±SD)

Nutritional parameter	Zinc			
	<11.5 μmol/L (N=19)	11.5-18.5 μmol/L (N=43)	>18.5 μmol/L (N=27)	p*
Body Mass Index	24±4	24±4	24±5	ns
Serum albumin (g/L)	38±6	39±5	38±5	ns
C-reactive protein	9.3±6	8.7±5	9.7±5	ns
Cholesterol (mmol/L)	5.5±1.9	5.5±1.9	5.1±17	ns
Serum creatinine (μmol/L)	886±120	792±202	833±177	ns
Protein catabolic rate	0.55±0.05	0.55±0.05	0.57±0.07	ns

*Mann-Whitney U test

ported[10,12]. Most of authors reported low zinc concentrations in serum of patients undergoing HD. Lee at al.[18] have found that 78% of patients on HD had low plasma zinc concentrations and Castro at al.[19] reported that about 20% of such patients were hypozincemic. Krachler et al.[11] found that plasma concentrations of zinc continuously increase during HD, but always stay at or below the reference range. Low plasma zinc concentrations tending to increase with HD duration were found by Skarupskiene et al.[5]. Striking was the report of Prehn[3] that serum zinc level increases after treatment using the hemodialysis membrane KN 401. He also reported benefit of HD on zinc status in these patients. He found that serum level of zinc is reduced with the progression of chronic renal failure, but also pointed out that in advanced renal failure hypozincemia is more pronounced with conservative therapy than in the patients on regular HD.

Our results strongly suggest that serum concentrations of zinc are normalized after the HD treatment. In the present study, serum samples from 89 patients with end-stage renal failure treated by regular HD were withdrawn for the estimation of zinc concentrations immediately before and after dialysis. Before HD 24 patients (27%) had elevated and 15 patients (17%) had low serum zinc concentrations, regarding the reference range for adult healthy persons (Figure 1). After HD all the results of serum zinc concentrations were within reference range (Figure 2).

Further, we found no correlations between zinc values and nutritional parameters in HD patients (Table 3).

There are many factors that can influence serum zinc concentrations. Bogden et al.[19] reported that certain disposable dialytic coils are contaminated with zinc and release substantial quantities of zinc during HD, producing high post-dialysis plasma concentrations. Low plasma zinc level was more often found in patients with <12 hour/week of HD duration and <12 months of HD treatment (5). At the same time, Castro et al.[20] concluded that the occurrence of hypozincemia was not related to dialysis modality and that zincemia did not reflect low dietary intake of zinc. Still, efficiency of HD and water treatment may play an important role, because increased zinc level in serum after HD can be the consequence of reducing total blood volume in these patients. It was shown that except for aluminum, blood levels of trace metals in HD patients were not related to their medication[18], but that environmental factors, diet, and the aging process may contribute to the trace metal burden in uremia. Even in the case of zinc supplementation, plasma zinc levels were not changed, according to findings of Richard et al.[21].

Alterations of serum zinc during HD are still unclear and are probably affected by individual patient's metabolism and specific illness. Future studies have to address more specific parameters, e.g. alterations in serum proteins, enzymes and antioxidants, specific conditions like osteoporosis, as well as patient's age, duration of HD and medication. In the meantime, although serum concentration of zinc do not reflect the real body status of this trace element, it can be easily determined in routine practice and may give a quick insight and warning about possible disorders of zinc metabolism.

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KONCENTRACIJA CINKA U SERUMU U BOLESNIKA NA REDOVITOJ HEMODIJALIZI

S A Ž E T A K

Cink je neophodan element za rast stanica, njegov manjak može bitno utjecati na antioksidativni obrambeni sustav, obično u svezi sa kroničnom bolesti bubrega, bolestima probavnog trakta i kroničnim alkoholizmom. U bolesnika na dijalizi značajno je znati koncentraciju cinka, te spriječiti hipo i hipercinkemiju. Analizirali smo 89 uzoraka krvi bolesnika sa terminalnim zatajenjem bubrega na redovitoj hemodijalizi. Određene su koncentracije cinka prije i poslije postupka hemodijalize. Rezultati su pokazali da su koncentracije cinka bile ovisne o postupku hemodijalize. U 57 (64%) bolesnika, koncentracija cinka u serumu snižena je postupkom hemodijalize, ponekad od vrlo visokih do normalnih vrijednosti. U preostalih 32 (36%) bolesnika, koncentracija cinka je porasla nakon postupka hemodijalize, ali su vrijednosti ostale u normalnim granicama. Suplementi cinka su preporučljivi samo u bolesnika sa dokazanom deficijencijom cinka, ali u je upitna njihova primjena u svih bolesnika sa kroničnim bubrežnim zatajenjem.