TRACE ELEMENTS ALTERATIONS IN CHRONIC HEMODIALYSIS PATIENTS WITH CHRONIC RENAL FAILURE AND PROTEINURIA

T. TETIKER*
S. PAYDAS*
G. YÜREGIR*
Y. SAGLIKER*

SUMMARY : The levels of serum copper (Cu_s), zinc (Zn_s), magnesium (Mg_s); erythrocyte Zn (Zn_e) and Mg (Mg_e) levels were studied in 24 patients undergoing hemodialysis (HD), 85 patients with chronic renal failure (CRF), 71 proteinuric patients and 32 healthy subjects. Zns and Zne levels were significantly lower in the HD patients ($p<0.02$, $p<0.02$) and patients with CRF ($p<0.02$) compared to the control group. Post-HD Mg_s levels were higher than pre-HD Mgs levels ($p<0.02$). But Mg_s levels were not different in hemodialysis patients compared to controls. Zn_s levels were found low in all of the proteinuric patients according to control group ($p<0.05$). According to these results the zinc deficiency in uremic patients may be related to reduced dietary zinc intake more than due to hemodialysis. The levels of Zn_s and Mg_s were lower in proteinuric patients. The low level of serum zinc may be a result of increased urinary loss and/or decreased intestinal absorption of zinc.

Key Words : Renal failure, proteinuria, copper, zinc, magnesium.

INTRODUCTION

In chronic hemodialysis patients and uremic patients, the abnormalities of Cu (1), Zn (2, 3) and Mg (4) were reported previously. Thompson *et al.* found significant alterations; such as a decrease of Zn in plasma and red cells, a reduction in red cell Cu, an increase in plasma aluminium (Al) in the chronic ambulatory peritoneal dialysis (CAPD) patients (5). Armstrong *et al.* (6) found that Zn_s and Cu_s levels were within the normal range in hemodialysis patients.

In this study we wanted to test the alterations of trace elements (Cu, Zn, Mg levels of serum erythrocyte and urine) in chronic HD patients, patients with renal failure and proteinuric patients.

* From Department of Internal Medicine, Faculty of Medicine, Çukurova University, 01330 Balcali, Adana, Türkiye.

MATERIALS AND METHODS

The patients were classified into 3 groups. Group I included 24 chronic HD patients undergoing 2 or 3 times weekly dialysis (15 males, 9 females, aged 17-79 years, mean age 42.0 ± 20.3 years). For measurements of Cu_S, Zn_S, Mg_S, levels and Zn_e, Mg_e levels blood samples were obtained pre- and post-HD.

The second group was consisted of 85 patients with CRF (49 males, 36 females, mean age 39.5 ± 13.4 years, range 15-79 years). The creatinine clearances (Ccr) of these patients were as below : Ccr < 5 ml/minute : 16 patients, Ccr = 6-20 ml/minute : 17 patients, Ccr = 21-50 ml/minute : 18 patients and Ccr = 51-70 ml/minute : 34 patients, Cu_S, Zn_S, Mg_S and urinary Zn (Znu) and Mg (Mgu) levels were also measured in Groups II and III and controls. The third group included 71 patients with proteinuria. The severity of proteinuria was as below : proteinuria < 0.5 g/day : 28 patients, proteinuria = 0.5-3 g/day : 27 patients and proteinuria > 3 gr/day : 16 patients). The control group included 32 healthy subjects (20 males, 12

females, mean age 35.4 ± 11.6 years, range 13-70 years).

Urine and blood were taken into acid washed tubes with and without heparin and sent to the laboratory immediately. The sera were separated and stored at -70°C until measurement. The erythrocytes were washed three times with physiological saline and hemolyzed with distilled water. The hemoglobin was measured with the cyanomethemoglobin method. The Zn, Cu and Mg levels of the lysates serum and urine were measured in 2380 model Perkin Elmer atomic absorption spectrophotometer.

Statistical analysis was tested by using the student's t test.

Table 1: In HD patients and control group, serum and erythrocyte levels of Cu, Zn, Mg and statistical analysis (NS: Not Significant).

		Pre HD	Post HD	P	Control	P
Serum	Cu (μg/dl)	104.6±12.6	100.2±11.6	NS	100.6±11.5	NS
	Zn (μg/dl)	83.6±13.1	88.1±15.3	NS	92.9±11.5	p<0.02
	Mg (mg/L)	20.5±1.6	21.7±1.7	p<0.02	21.3±2.2	NS
Erythrocyte	Zn (μg/dl)	14.2±8.9	11.2±3.5	NS	26.1±11.7	p<0.02
	Mg (mg/L)	0.31±0.17	0.24±0.04	NS	0.17±0.06	p<0.02

RESULTS

In HD patients and control group, serum and erythrocyte levels of Cu, Zn and Mg are shown in Table 1. Although the measures were in a normal range, post-HD Mg_s levels (21.7±1.7 mg/L) were higher than pre-HD Mg_s levels statistically significantly (20.5±1.6 mg/L)

Table 2: The patients with chronic renal failure serum and urine levels of Cu, Zn, Mg and comparison with the control group (NS: Not significant).

	SERUM			URINE	
Proteinuria (gr/day)	Cu (μg/dl)	Zn (μg/dl)	Mg (mg/L)	Zh (μg/L)	Mg (mg/L)
Control group (-)	100.6±11.5	92.9±11.5	21.3±2.1	22.8±4.8	51.1±14.1
Ccr<5 ml/min 1.0	102.9±11.0	81.9±14.3	20.3±1.7	30.2±7.7	66.5±20.5
Ccr=6-20 ml/min 2.0	92.2±23.9	72.7±18.0	21.2±1.9	36.8±22.8	69.7±26.1
Ccr=21.50 ml/min 2.9	97.7±14.0	67.2±14.3	20.3±2.4	45.6±22.7	81.5±35.1
Ccr=51-70 ml/min 0.7	96.0±11.8	69.0±13.7	20.0±1.6	57.7±22.7	90.0±28.3
P	NS	<0.02	NS	<0.05	<0.05

Table 3: Comparison of the data between proteinuric patients and the control group (NS: Not significant).

	SERUM			URINE	
Proteinuria (gr/day)	Cu (μg/dl)	Zn (μg/dl)	Mg (mg/L)	Zn (μg/dl)	Mg (mg/L)
Control group	100.6±11.5	92.9±11.5	21.3±2.1	22.8±4.8	51.1±14.1
Proteinuria<0.5g/d	95.6±17.3	72.0±15.6	20.2±2.1	38.0±23.0	92.9±32.2
Proteinuria =0.5-3 g/d	96.1±17.4	75.9±18.0	19.9±1.4	40.2±22.3	80.5±20.8
Proteinuria>3g/d	98.0±16.0	66.0±13.5	19.3±1.8	50.5±22.3	70.1±31.7
P	NS	<0.05	<0.05	<0.02	<0.02

(p<0.02). The Zn_s level of HD group (83.6±13.1 μg/dl) was lower than that of control group (92.9±11.5 μg/dl) (p<0.02). Pre- and post-dialysis Zn_e levels were lower compared to controls (p<0.02), whereas Mg_e levels were higher than control group (p<0.02).

As shown in Table 2, in the second group of patients, Zn_e levels were significantly higher in patients with Ccr<5 ml/minute (81.9 ± 14.3 μg/dl) compared to patients with Ccr=21-50 ml/minute (67.2±14.3 μg/dl) and Ccr=51-70 ml/minute (69.0 ± 13.7 μg/dl) (p<0.02). As a result, Zn_s levels were lower than the control group in all of patients with CRF (p<0.02).

When patients were classified according to proteinuria, no correlation could be observed between daily proteinuria levels and Cu_s , Zn_s , Mg_s levels, but in all of the proteinuric patients Zn_s and Mg_s levels were lower than the control group (p<0.05 and p<0.05) (Table 3). In proteinuric patients urinary Zn and Mg levels were higher than that of the controls (p<0.02).

DISCUSSION

Hosokowa *et al.* reported that in uremic patients Cu_s and Zn_s levels were increased after HD which was attributed to hemoconcentration and for Cu to pass from dialysis membrane (7). However, in a study performed by Paydas *et al.* Zn_s and Cu_s levels were found to be normal in chronic HD patients (8).

In our study, there was no significant difference between pre and post HD Zn_s and Cu_s levels in chronic HD patients, whereas Mg_s levels were found to be high

after dialysis, in which Mg_s levels were not different from the controls. When the data was compared with the control group, only Zn_s levels were significantly low. In these patients pre- and post-HD erythrocyte levels of Zn and Mg were not different, but Zn_e was lower, Mg_e was higher than the control group. Our results were similar to Reimold's and Mahajan's (3) who reported than Zn_e levels were lower than the normal levels.

Halsted *et al.* found decreased Zn_s levels in uremia (9), who reported that Zn has not been affected by HD. In our study too, in all of the HD patients and patients with CRF, Zn_s levels were lower than in the control group. In HD patients pre- and post-HD serum Zn levels were not different. Hypozincemia may be due to decreased intake.

Patients with Ccr<5 ml/min, Znu levels were lower than the patients with Ccr=51-70 ml/min; also patients with Ccr<5 ml/min, Zns levels were higher than patients with Ccr=51-70 ml/min. As a result, it can be said that, there is a positive correlation between Ccr levels and excretion of Zn.

In our study there was not a correlation between Mg_s levels and severity of the renal failure and between the levels of Cu_s, Zn_s, Mg_s and severity of the proteinuria, but Zn_s and Mg_s levels were low in the proteinuric patients. Tumer *et al.* (11) suggest that the patients with nephrotic syndrome may in part be due to decreased intestinal absorption of Zn. Freeman *et al.* (10) state that in the patients with nephrosis, there is a correlation between proteinuria and zincuria, which is shared by us, too. We can add to it that there is a lineer correlation between the severity of the proteinuria and the increased Znu levels. We have also observed that a correlation between the decreased Mgu levels and the severity of the proteinuria does exist, which may be explained by hypoproteinemia or tubular defect in these patients.

In conclusion, there are some trace elements alterations besides other metabolic defects in uremic patients and proteinuric patients. It can be stated that uremia causes low serum level of zinc and that the reason of hypozincemia is not due to hemodialysis, but to the decreased intake of zinc.

In nephrotic syndrome, serum levels of Mg and Zn are low and urinary zinc is increased, whereas urinary magnesium is decreased.

REFERENCES

1. Smythe WR, Alfrey AC, Craswel PW, Crouch CA, Ibels LS, Kubo H, Nunnelley LL, Rudolp H : Trace elements abnormalities in chronic uremia. Ann Intern Med, 96:302-310, 1982.

2. Hosokawa S, Tomoyoshi T, Yoshida O : Zinc transport during hemodialysis. Artif Organs, 10:30-36, 1986.

3. Mahajan SK, Parasad AS, Rabbani P, Briggs WA, Mc Donald FD : Zinc Deficiency: A reversible Complication on uremia. Am J Clin Ntr, 36:1177-1183, 1982.

4. Belyne GM, Benair J, Szwarchberg J, Kaneti J, Donovitch GM, Kaye M : Increase in bone magnesium content in renal failure in men. Nephron, 9:90-33, 1972.

5. Thompson NM, Stevens BJ, Humpherey TS, Atkins RC : Comparison of trace elements in peritoneal dialysis, hemodialysis and uremia. Kidney Int, 23:9-14, 1983.

6. Armstrong VW, Buschmann U, Ebert R, Fuschs C, Rieger J, Scheler F: Biochemical investigations of CAPD: Plasma levels of trace elements and aminoacids and impaired glucose tolerance during the course of treatment. Int J Art Org, 3:237-241, 1980.

7. Hosokawa S, Imai T, Nishia T, et al. : Changes in copper and zinc in hemodialysis patients, EDTA - ERA Abstracts, p 81, 1984.

8. Paydas S, Albayrak A, Yüregir G, Sagliker Y, Demirci C, Gürçay A : Trace elements in hemodialysis patients. Third International Congress on Trace elements in Healt and Disease, p 615, 1989.

9. Halsted JA, Smith JC : Plazma zinc in Health and Disease. The Lancet, 14:322, 1970.

10. Freeman RM, Richards CS, Rames LK : Zinc Metabolism in Aminonucleoside-Induced Nephrosis. Am J Clint Nutr, 28:699, 1975.

11. Tumer N, Baskan S, Arcasoy A, Çavdar O, Ekin M : Hypozincemia in nephrotic syndrome. Nephron, 52:95, 1989.

Correspondence:
S. Paydas
Çukurova Üniversitesi
Tip Fakültesi,
Dahiliye Bölümü,
01330 Balcali,
Adana, TÜRKIYE.