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Parathyroid functions and trace metal elements in hemodialysis patients

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ABSTRACT

Objective: The aim of the study was determine whether there were an important differences in levels of Ca (calcium), Mg (magnesium), P (phosphorus), cholesterol, HDL-cholesterol, triglyceride, and plasma PTH (parathyroid hormone) between hemodialysis and healthy groups, besides whether there were any correlations between elements, lipid profiles and PTH in all groups. **Material and methods:** The study included 47 hemodialysis patients who were dialyzed with a range of 2-16 years. This group called as a "Hemodialyis group". Blood samples were taken before (pre-hemodialysis) and after (post-hemodialysis) hemodialysis session. "Control group" included 23 healthy volunteers. **Results:** PTH (p = 0.01), Mg (p = 0.001) levels were lower and HDL-cholesterol (p = 0.001) levels were higher in group of control than pre-hemodialysis. Levels of PTH (p = 0.05) were higher in post-hemodialysis than the control group. Mg (p = 0.001) and P (p = 0.01) levels were significantly higher and cholesterol, triglyceride (p = 0.05), HDL-cholesterol (p = 0.001) levels were lower in pre-hemodialysis patients than post-hemodialysis patients. In patients pre- and post-hemodialysis, a positive correlation between P and Cholesterol (respectively r = 0.553, r = 0.679, p = 0.001) were determined. In pre-hemodialysis patients, correlation between Ca and triglyceride were negative (r = -0.392, p = 0, 05). In control group, correlation between PTH and Mg were (r = 0.509, p = 0.05) statistically significant. **Conclusions:** Our findings indicated that the levels of Mg, P, cholesterol, HDL-cholesterol and triglyceride altered during dialysis session. PTH levels showed significant differences when we compared the groups of control and pre-, post-hemodialysis. Moreover, the correlation between P and cholesterol levels in hemodialysis groups demonstrated that there were association between P and cholesterol. Further extensive studies are necessary to clarify the effect of P levels on lipid parameters.

KEYWORDS

Hemodialysis;
Lipids;
Parathyroid.

INTRODUCTION

Although most research on uremic toxicity has focused on retention or removal of organic solutes, subtle changes in concentration of inorganic compounds are also important because these compounds may have significant clinical consequences[1]. Especially the levels of electrolytes such as Na^{+1}, K^{+1}, Ca^{+2}, Mg^{+2}, Cl^{-1}, H^{+1} must be kept in a rather narrow physiological range, otherwise life-threatening events may occur[2]. On the basis of the results, the abnormal metabolism of trace metals contributes to a part of the uremic symptoms, which is unresolved by maintenance hemodialysis[3].

Uremic patients, who are undergoing hemodialysis, present with lipid abnormalities, i.e., hypertriglyceridemia and increased levels of lipoprotein (a) and VLDL[4]. Despite relatively low plasma total cholesterol levels, a substantial number of patients have low HDL-cholesterol, low Apo-A, and high Apo-B levels[5].

It has been concluded that magnesium might affect lipid metabolism in hemodialysis patients and also the increase of serum magnesium levels in hemodialysis patients might worsen dyslipidemia[6]. The researchers[7] determined that relative hypoparathyroidism (= 200 pg/ml) was prevalent in hemodialysis patients, with unknown pathogenesis and prognosis. Besides, hyperparathyroidism is related to disturbances of lipid metabolism[8]. In this respect, patients with end stage renal disease display a variety of endocrine disturbances[9].

Serum magnesium levels play an important role in regulating the secretion of PTH. In fact, it is considered that Mg may be able to modulate PTH secretion in a way similar to Ca. Since renal excretion is the major route of elimination of Mg from the body, a positive Mg balance would be expected in patients with renal insufficiency. The Mg balance may be normal or even decreased in uremic patients. This is possibly due to decreased dietary intake combined with impaired intestinal absorption. Thus, in patients with chronic renal failure (CRF), although reduced nutritional intake, impaired absorption from the intestine, vomiting, diarrhea, the use of diuretics, and acidosis may result in a negative balance of Mg, reduced renal excretion may cause accumulation of Mg, resulting in increased Mg concentration in serum in CRF patients[10].

The aim of the present study was to determine whether there were statistically differences between hemodialysis patients and control (healthy) groups according to level of serum calcium, phosphorus, magnesium, lipid profiles and plasma parathyroid hormones and besides whether there were any changes in these parameters between the groups of pre- and post-hemodialysis. Moreover, it has been aimed to find out whether there were any correlation coefficients of trace elements with lipid profiles, PTH in these groups.

MATERIALS AND METHOD

Study was materialized with the 2001/130 numbered permission, approval and financial support of the Committee of Selcuk University of Scientific Research Projects Coordination Department. Present study involved 47 hemodialysis patients (34 female, 13 male), who were treated in Polyclinic of Hemodialysis in Department of Nephrology of Medical Faculty of Selcuk University. The mean ages of the patients were 50,26±16,36 yr. All patients were dialyzed three times a week and each session was at least 4 hour. They were dialyzed with polysulfone dialyzing membrane. The duration of dialysis range were 2-16 yr. Those patients who had Hepatitis B, acute medical events, were using Al-containing drugs, were excluded in this study. This group called as "Hemodialysis Group".

"Control Group" was composed of 23 healthy volunteers (7 female, 16 male) with the mean age 39,52±11,54 yr. Those people had no any medical problem, were not using alcohol and were not smokers.

The blood samples were taken from the hemodialysis patients in their regular monthly check-up testing. No extra blood samples were taken from the patients for those biochemical parameters that were mentioned for this study. Samples were collected immediately before (pre-hemodialysis) and after the dialysis (post-hemodialysis) sessions. In other words, each patient had two samples, which were taken before and after dialysis session. So that, blood samples were not randomly collected.

Samples of control group were taken after 10 hour fasting. Control group was selected from the people who were doing their routine check-up. For those bio-

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chemical parameters analyzing, the samples were used from remains of their check-up blood samples, extra blood samples were not taken.

Blood samples were divided into two tubes (a tube with an anticoagulant (EDTA) and without an anticoagulant). The EDTA anticoagulant samples were centrifuged at 2000 rpm for 10 min at +4°C. Plasma PTH levels were analyzed immediately after taking blood samples. PTH was determined in Immulite 1000 OLYMPUS auto analyzer (BIODPC, Diagnostic Products Corporation 5700 West 96th Street Los Angeles, CA 90045-5597, USA) by using Immulite test kit (catalog no: LKPH1). Serum cholesterol, triglyceride and HDL-cholesterol concentrations were respectively determined by using Immulite test kits (catalog no: OSR6116, OSR6133, OSR6187) in Immulite 2000 OLYMPUS auto analyzer (BIODPC, Diagnostic Products Corporation 5700 West 96th Street Los Angeles, CA 90045-5597, USA). Serum samples were stored into polyethylene tubes at -85°C to analyze the levels of elements (Ca, Mg, P). Elements levels were determined by inductively coupled plasma emission spectrometry (ICP-AES, Varian Australia Pty Ltd, Australia). The period of study, which was used for collecting blood samples from patients and healthy subjects, was 3 months. Some biochemical parameters (cholesterol, HDL-cholesterol, triglyceride, PTH) were analyzed immediately after taking each sample. Besides, elements levels were analyzed totally at the end of 3 months. Elements analyzing carried out in one day.

Statistical analysis

Data were expressed as mean±SE and analyzed with SPSS packet program. Student's t-test and Mann-Whitney U test were used to compare the groups. Pearson Correlation coefficients were applied to evaluate the relationship between levels of trace elements and the other parameters. p value = 0.05, = 0.01, = 0.001 was considered to be significant.

RESULTS

Data concerning to hemodialysis group of pre- and post- levels and control group have been shown in TABLE 1.

TABLE 1 : The levels of parameters in control and patients before dialysis and after dialysis group (x±SE)

Parameters	GROUPS		Post-hemodialysis (C)	P VALUES		
	Control (A)	Pre-hemodialysis (B (B)		P (A vs B)	P (A vs C)	P (B vs C)
Mg (mg/l)	22.05±0.41	31.81±0.70	22.39±0.71	0.000***	0.075	0.000***
Ca (mg/l)	99.87±1.63	101.12 ±2.71	98.48±3.57	0.46	0.25	0.961
P (mg/l)	62.36±2.44	65.17±1.94	55.85±3.01	0.121	0.112	0.006**
PTH (pg/ml)	45.66±6.07	195.52±34.03	187.30±58.36	0.002**	0.027*	0.219
Cholesterol (mg/dl)	195.78±11.29	180.14±8.51	211.10±11.31	0.227	0.426	0.028*
Triglyceride (mg/dl)	170.57±0.15	147.12±13.86	211.31±23.75	0.276	0.531	0.027*
HDL-cholesterol (mg/dl)	42.26±1.95	33.48±1.63	43.21±2.16	0.000***	0.846	0.000***

*** p = 0.05 ** p = 0.01 *** p = 0.001**

In CRF patients before hemodialysis the levels of HDL-cholesterol (p = 0.001) were lower and PTH (p = 0.01), Mg (p = 0.001) levels were higher than levels of controls. There were no significant differences between the control and pre-hemodialysis group in evaluation of Ca, P, cholesterol, triglyceride levels.

Whereas PTH levels (p = 0.05) were higher in post-hemodialysis patients than those in control group, we did not determine significant differences in levels of Ca, Mg, P, cholesterol, HDL-cholesterol, triglyceride between groups of control and post- hemodialysis.

In patients, before hemodialysis session the levels of Mg (p = 0.001) and P (p = 0.01) were significantly higher and the levels of cholesterol, triglyceride (p = 0.05), HDL-cholesterol (p = 0.001) were lower than in patients after dialysis session. In those groups, the levels of Ca and PTH did not show any significant differences.

In hemodialysis patients before and after hemodialysis session, a positive correlation between P and cholesterol (respectively r = 0.553, r = 0.679, p = 0.001) were determined. In control group, correlation between PTH and Mg were (r = 0.509, p = 0.05) statistically significant. Besides, in patients before dialysis group correlation between Ca and triglyceride were (r = -0,392, p = 0.05) found (data were not shown in TABLE 1).

DISSCUSSION

It is well known that the concentrations of trace elements in biological tissues and fluids are important in

health of the human beings. Therefore, deficiency or excessive of trace elements that effecting several diseases' diagnosis and prognosis are also analyzing in hemodialysis patients.

It is stated that patients with chronic renal failure requiring treatment by hemodialysis are also risk of developing trace element imbalances. Trace element disturbances (which cause by medication, the uremic state, the dialysis process and the quality of water used for dialysis) may contribute to clinical abnormalities in dialyzed uremic patients[2].

In addition to, abnormalities in lipid and/or protein content of lipoprotein have been described in patients with chronic renal failure[11]. From the aspect of evaluation of the relation between trace elements and lipids, it has been concluded that the increase of serum Mg levels in hemodialysis patients might worsen dyslipidemia[6]. Moreover, it has been indicated that hyperparathyroidism may be related to disturbances of lipid metabolism[8].

According to our data of Mg levels are consistent with data of Krachler et al[2], Sakurai et al[12], Miura et al[13] and Teraki et al[14]. We determined high P levels in HD patients before dialysis group. These findings are similar with those of Miura et al[13] and Teraki et al[14] and Sakurai et al[12]. In another research, Senft et al[15] concluded that during dialysis, a significant decline of serum Mg levels occurred (below 0.8 mmol/l). When we compare the levels of post-hemodialysis and pre-hemodialysis, we can also suggest significant decreases in serum Mg levels during hemodialysis ($p = 0.001$).

In a study on 32 HD patients receiving magnesium citrate orally at a dosage of 610 mg every other day for 2 months and 12 control group, in which patients receiving only calcium acetate therapy as a phosphate binder, Turgut et al[16] did not find any changes in the mean serum calcium and phosphorus. Also, serum parathyroid hormone level significantly decreased in the Mg group at the end of 2 months. Bilateral carotid intima media thickness was significantly improved in patients treated with magnesium citrate. The authors concluded that the magnesium may play an important protective role in the progression of atherosclerosis in dialysis patients.

Robles et al[6] suggested that magnesium might affect lipid metabolism in hemodialysis patients. They determined that Mg levels were increasing according to increases of cholesterol levels. The patients (who have <200 mg/dl plasma cholesterol levels) had lower Mg levels than the patients who had >251 mg/dl plasma cholesterol levels. Besides, it has been demonstrated a significant linear relationship between total cholesterol and Mg ($r = 0.55$, $p<0.001$). But they did not determine any statistical differences between the groups in levels of P and PTH. Robles et al[6] concluded that further clinical studies were required to determine the optimum levels of serum Mg in patients undergoing maintenance hemodialysis. In our findings, we did not determine a significant correlation between Mg and lipid parameters but we found significant differences between the groups of patients before hemodialysis and after hemodialysis according to levels of Mg, P, triglyceride, HDL-Cholesterol and also a significant correlation between P and cholesterol levels.

Guh et al.[7] have stated that time-dependent PTH levels are associated with age, duration of dialysis and levels of ionized calcium, phosphate, albumin, and magnesium. Although in our study we did not investigate the effect of time-dependent PTH levels on magnesium levels, we determined an important relation between PTH and Mg levels ($r = 0.509$, $p = 0.05$). Seen from this aspect, our conclusion is similar with Guh et al.[7].

It is suggested that buffer and Ca are lost in the ultra filtrate and as a consequence, the acid-base balance and the Ca/P balance become difficult[17]. Our findings concerning to Ca levels in all groups, are inconsistent with the result of Sakurai et al.[12], Teraki et al.[14] and Krachler et al.[2]. Differences in number of the patients, duration of dialysis range and the range of age may cause to obtain the data different. In the present study, Ca levels did not show any significant differences between the groups. Therefore, our results are similar with data of Robles et al.[6].

When we compared the control group with post-hemodialysis, we determined significant differences in only PTH levels. All the other data did not change. We can mention that after dialysis session PTH levels decrease according to pre-hemodialysis but these levels did not reach to control group's levels. More-

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over, after the dialysis session all the other parameters were approximately the same level with the control group.

On the basis of above results, present study is important in determining the relations through lipids, PTH and elements levels in role of acceptable treatment of hemodialysis. Our findings, which show the differences in groups according to levels of PTH, Mg and P and correlation between P and cholesterol levels, suggest that it is important to analyze those biochemical parameters. We think that, to clarify the effects of P levels on lipid parameters, studies that will be performed on different methodology (with the material of e.g. hemodialysis patients with high lipid levels who are using lipid-lowering drugs, collecting samples in different times of dialysis sessions, etc.) are required.

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