ORIGINAL ARTICLE

Changes of serum bone markers in CAPD and hemodialysis patients

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Abstract

Background: A non-invasive method for evaluation of high-turnover and low-turnover bone diseases is the measurement of certain important serum bone markers such as osteocalcin, procolagen-I-propeptide, dioxypiridinoline, hydroxyproline and alkaline phosphatase. Renal osteodystrophy (ROD) in pre-dialysis and dialysis patients, is manifested in 3 forms: high-turnover ROD, related to secondary hyperparathyroidism; low-turnover ROD and mixed ROD.

Material and methods: Serum levels of intact parathyroid hormone (iPTH), osteocalcin (OC), procolagen-I-propeptide (PIPC) and dioxypiridinoline (DYP) were measured in 20 patients on hemodialysis (HD) and 20 patients on continuous ambulatory peritoneal dialysis (CAPD) to assess the prevalence of ROD type in the HD and CAPD groups.

Results: We found lower mean levels of all bone markers in CAPD patients, (iPTH: 219±235 vs. 428±285 pg/ml; $p<0.01$; OC 10.2±7.5 vs. 21.3±7.2 ng/ml; $p<0.01$; PIPC 111±57.3 vs. 218±62.4 ng/ml; $p<0.01$; DYP 7.3±6.4 vs. 55.2±23.3nm/l; $p<0.001$; AP 164±66 vs. 325±188 U/l; $p<0.01$) and lower than normal in 11 of them and higher than normal PTH, AP and some of the other serum markers (PICP; DYP) in 14 HD patients.

Conclusions: The lower levels of the investigated serum bone markers in CAPD patients suggest that low-turnover ROD prevails in these patients than in HD pts. Hippokratia 2007; 11 (4): 199-201

Key words: serum bone markers, osteocalcin, procolagen-I-propeptide, dioxipyridinoline, hydroxyproline, alkaline phosphatase, intact parathyroid hormone, high-turnover ROD, low-turnover ROD

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Renal osteodystrophy (ROD) is a well known bone pathology, appearing in patients with chronic renal failure, especially in pre-dialysis and dialysis patients, manifested in 3 different forms: high-turnover ROD, related to secondary hyperparathyroidism; low-turnover ROD and mixed ROD[1-3]. Circulating serum bone markers and bone biopsy are both methods used for evaluation of bone remodeling and turnover, but they can not always be used equally because serum bone markers are indicators of the hole skeletal metabolism and they are not precise in all cases, while bone biopsy is quite precise but in certain cases reveals only the status of the punctured bone area[3,4]. Nevertheless, bone histology remains the gold standard for the diagnosis of renal osteodystrophy especially for the distinction between high and low turnover bone disease but is a quite expensive and invasive procedure, accompanied by technical difficulties in the processing and studying of the specimens[5]. For this reason, specific and sensitive serum biochemical markers are required for monitoring bone turnover in uremic patients. The ideal biochemical marker of bone turnover should be unique to bone and should reflect total skeletal activity[4-6]. The serum bone markers are enzymes of the bone cells, components of the bone matrix or regulating hormones; some of them are markers of osteoblast activation (osteocalcin, bone alkaline phosphatase, procolagen-I-propeptide), and other are markers of the osteoclast activation (dioxipyridinoline, hydroxiproline, tartrat-resistant acid phosphatase)[3,5,7].

Investigating the above mentioned serum parameters in two groups of patients on different dialysis treatments – hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) - we tried to establish which kind of ROD dominates among patients on HD and CAPD.

Material-Methods

The study included 20 HD patients (1st group) (11 males and 9 females) mean age 46 ± 23 years and mean duration of dialysis 28 ± 20 months; and 20 CAPD patients (2nd group) (10 males and 10 females) mean age 43 ± 22 years and mean duration of dialysis 40 ± 16 months.

The renal failure of the patients in the first group (HD patients) was caused by the kidney diseases as following: pyelonephritis - in 7 patients; glomerulonephritis – in 6 patients; polycystic kidney disease – in 4 patients and; other renal diseases – in 3 patients. In the second group (CAPD patients) renal failure was caused by – pyelonephritis - in 8 patients; glomerulonephritis – in 7 patients; polycystic kidney disease – in 3 patients and other renal diseases – in 2 patients.

Bicarbonate hemodialysis procedures were performed in all patients of the first group and cellulose acetate membranes were used in all cases.

Serum levels of osteocalcin (OC), procolagen-I-propeptide (PIP), dioxipyridinoline (DYP), were measured in all investigated patients of both groups by ELISA; iPTH was tested by radio-immune assay (RIA, Instar,USA) and alkaline phosphatase – by Hitachi 704 auto-analyser.

The blood was collected in the morning for CAPD (2nd group) and in pre- HD session time for HD patients (1st group).

None of the patients had evidence of systemic infection (fever or leukocytosis). No patient suffered from congestive heart failure, active autoimmune disease or received immunosuppressive drugs or had an active form of hepatitis the last 6 months. None of the patients of the second group (CAPD pts.) suffered from peritonitis during the last 6 months before the study.

Statistical analysis was performed routinely: values are given as Mean value ± SD; analysis of variances was applied to assess differences between groups.

Results

We found lower mean levels of all bone markers in CAPD patients, than in HD patients; lower than normal levels of all bone markers in 11 CAPD patients; normal levels – in 7 CAPD patients; higher than normal levels – in 2 CAPD patients. Higher than normal bone parameters were registered in 14 HD patients; normal levels – in 3 patients, and lower levels – in 3 HD patients.

The mean values of the investigated blood parameters in both groups are shown in Table 1.

Table 1. *Mean values of the bone markers in HD and CAPD group*

Bone proteins	1st group (HD)	2nd group (CAPD	p<
OC (3.4 – 10 ng/ml)	21.3±7.2	10.2±7.5	0.01
PIP (69 - 163 ng/ml)	218±62.4	111.2±57.3	0.01
DYP (1.2 – 2.3 nm/l)	55.2±23.3	7.3±6.4	0.001
PTH (9 – 70 pg/ml)	428±285	219±235	0.01
AP (< 270 U/l)	325±188	164±66	0.01

Figures 1 and 2 show the percents of the patients from the 1st (HD) and 2nd (CAPD) group with higher, normal or lower serum levels of the bone markers.

All correlation rates between the investigated bone markers are presented in Table 2.

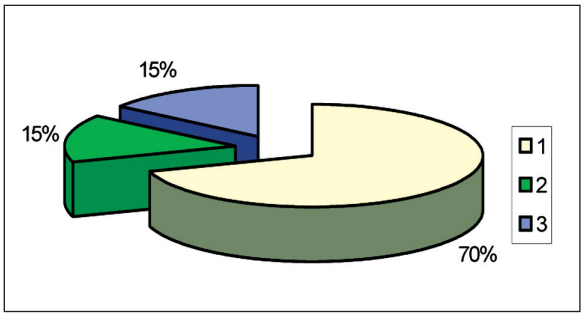

Figure 1. *Percent of patients on HD with higher (1), normal (2) or lower (3) markers of bone turnover*

Table 2. *Correlation ratio (r) between the bone markers in HD group and CAPD group*

1st group (HD)			2nd group (CAPD)		
	r =	p<	r =	p<	
PTH/AP	0. 84	0.001	**PTH/AP**	0.67	0.001
PTH/OC	0.14	NS	**PTH/OC**	0.12	NS
PTH/PIP	0.41	0.05	**PTH/PIP**	0.22	NS
PTH/DYP	0.34	NS	**PTH/DYP**	0.42	0.05
AP/OC	0.45	0.01	**AP/OC**	0.11	NS
AP/PIP	0.55	0.01	**AP/PIP**	0.25	NS
AP/DYP	0.25	NS	**AP/DYP**	0.15	NS
OC/PIP	0.46	0.01	**OC/PIP**	0.38	0.05
OC/DYP	0.14	NS	**OC/DYP**	0.12	NS
PIP/DYP	0.10	NS	**PIP/DYP**	0.08	NS

Discussion

The assay of serum peptides of bone collagen formation and degradation could potentially provide an indirect estimate of the rate of bone turnover in different kinds of bone diseases, including renal osteodystrophy[3,6,8]. In our study we have measured serum levels of OC, a vitamin K-dependent gamma-carboxyglutamic acid containing bone protein; carboxy-terminal propeptide of type I procollagen (PIP) and of AP as markers of bone formation and serum levels of the DYP as a marker of bone resorption; we measured iPTH levels as well, to evaluate the activity of parathyroid glands. Our results showed generally lower than normal mean levels of all investigated bone markers in the 2nd group of patients (CAPD) compared to the 1st group (HD), and mean values of iPTH were lower in CAPD group as well (in detail: we found lower levels of all bone markers in 11 CAPD patients; normal levels – in 7 CAPD patients; higher levels – in 2 CAPD patients. Higher than normal bone parameters were registered in 14 HD patients; normal levels – in 3 patients, and lower levels – in 3 HD patients).These findings suggest that bone metabolism is suppressed in most patients on CAPD treatment and is increased in most HD patients, i.e. low-bone turnover ROD prevails in CAPD group and high-bone turnover ROD – in HD patients.

Correlation table (Table 2) demonstrates a very high

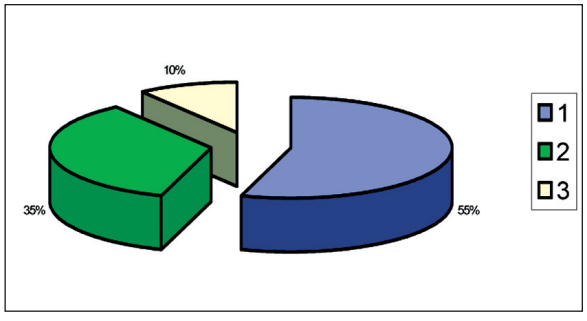

Figure 2. *Percent of patients on CAPD with lower(1), normal(2) or higher(3) markers of bone turnover*

correlation dependence between PTH and AP ($p<0.001$) in both groups, i.e. when hyperparathyroidism is present, bone turnover is higher than normal. Bone formation markers OC, PIP and AP are in a significant correlation each other, may be because they are related to the one side of the bone turnover – bone creation. DYP – the investigated marker of bone resorption, showed an only significant correlation with PTH in 2nd group (CAPD patients). It means that bone resorption is possibly an uncoupled process with bone formation in ROD, especially in high-turnover ROD.

In conclusion our evidence show that in hemodialysis patients predominates high-turnover ROD, and in CAPD patients low-turnover ROD. The reasons for the difference are not clearly defined[9-11] but higher and inconstant levels of calcium and phosphate and unstable acid-based state in the blood of HD patients play probably important role, compared to more constant serum phosphate, calcium and acid-based equation in CAPD patients.

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