

Peritoneal clearance of biochemical markers of bone turnover in children with end stage renal failure on peritoneal dialysis

Aysun K. Bayazıt¹, Nurcan Cengiz², Rüksan Anarat³, Aytül Noyan¹, Ali Anarat¹

¹Department of Pediatric Nephrology, Çukurova University Faculty of Medicine, and ²Department of Pediatric Nephrology and ³Central Laboratory, Adana Hospital Başkent University Faculty of Medicine, Adana, Turkey

SUMMARY: Bayazıt AK, Cengiz N, Anarat R, Noyan A, Anarat A. Peritoneal clearance of biochemical markers of bone turnover in children with end stage renal failure on peritoneal dialysis. Turk J Pediatr 2006; 48: 140-142.

Renal osteodystrophy is one of the important complications in children with end stage renal disease. Non-invasive tools for evaluation of bone metabolism have been proposed in recent years. The aim of this study was to investigate the markers of metabolic bone disease and peritoneal clearance of these markers in children treated with continuous ambulatory peritoneal dialysis (CAPD). In this study, serum osteocalcin (OC) levels were found significantly higher in patients (107.98 ± 99.99 ng/ml) than in the healthy control group (41.94 ± 12.94 ng/ml; $p < 0.05$). Mean peritoneal clearance (Clp) of OC was 0.87 ± 0.91 ml/min. There was no correlation between serum OC and Clp-osteocalcin. There was a positive correlation between serum phosphorus (P) and OC ($r = 0.394$, $p = 0.031$), alkaline phosphatase (ALP) and OC ($r = 0.520$, $p = 0.003$), and parathyroid hormone (PTH) and OC ($r = 0.441$, $p = 0.017$), whereas no correlation was found between OC and calcium (Ca) and OC and magnesium (Mg). There was also a significant correlation between serum ALP and PTH ($r = 0.714$, $p = 0.0001$). A positive correlation was found between serum PTH and Clp of PTH ($r = 0.471$, $p = 0.009$). In conclusion, Clp-osteocalcin is of no interest as a non-invasive marker of metabolic bone disease in children treated with CAPD. But significant correlation between serum OC and PTH, P, and ALP shows that serum OC could be used as a valuable non-invasive biochemical marker of metabolic bone disease.

Key words: osteocalcin, peritoneal clearance, renal osteodystrophy, children.

Renal osteodystrophy (ROD) is a significant problem in pediatric end stage renal disease (ESRD). The valuable diagnostic method of making a clear-cut distinction between metabolic bone diseases relies on the histological analysis of bone biopsy¹. However, especially in children, various other non-invasive biochemical markers are in use. Serum osteocalcin (OC), intact parathormone (iPTH), alkaline phosphatase (ALP), calcium (Ca), phosphorus (P), and magnesium (Mg) have been considered as useful indicators of bone turnover in metabolic bone disease^{2,3}. Serum levels alone of these biochemical markers are frequently insufficient to clearly distinguish different forms of ROD. Also, in patients on peritoneal dialysis, some of these markers are removed from the circulation through the peritoneal membrane⁴. Therefore,

the aim of this study was to investigate serum levels and the peritoneal clearance (Clp) of biochemical markers of bone turnover in children treated with continuous ambulatory peritoneal dialysis (CAPD).

Material and Methods

Thirty patients with ESRD (14 boys, 16 girls; mean age 12.2 ± 2.4 years) treated with CAPD and 12 age- and sex-matched healthy controls (7 boys, 5 girls; mean age 13.1 ± 1.2 years) were admitted to the study. All subjects gave informed consent to participate in this study. Patients had been treated with CAPD for an average of 18 months (range 3-44). CAPD was performed by the standard technique using four dialysis bag exchanges per day. None of the patients had peritonitis episodes for at least

the preceding two months before the study periods, and no patient showed signs of liver disease or disorders affecting extrasosseous collagen turnover. No patient used drugs known to influence peritoneal permeability. Studies were performed during 24-hour periods with patients on their usual regimen of CAPD. Fasting blood samples were drawn early in the morning. Serum and peritoneal Ca, creatinine, ALP, and Mg were measured by standard laboratory techniques. OC and

serum OC and Clp-osteocalcin. There was a positive correlation between serum P and OC ($r=0.394$, $p=0.031$), ALP and OC ($r=0.520$, $p=0.003$), and PTH and OC ($r=0.441$, $p=0.017$), whereas no correlation was found between either OC and Ca or OC and Mg. There was also a significant correlation between serum ALP and PTH ($r=0.714$, $p=0.0001$). A positive correlation was found between serum PTH and Clp of PTH ($r=0.471$, $p=0.009$). Results are summarized in Tables I and II.

Table I. Serum Level and Peritoneal Clearance of Biochemical Parameters

	Serum mean±SD median (min-max)	Peritoneal clearance (ml/min) mean±SD median (min-max)
ALP (IU/L)	270.13±287.67 185 (42-1095)	0.04±0.03 0.037 (0.00-0.16)
PTH (pg/ml)	616.00±657.87 0.47 (0.01-2.50)	0.84±1.52 0.22 (0.01-6.50)
Osteocalcin (ng/ml)	107.98±99.99 68.5 (14.70-420)	0.87±0.91 0.58 (0.05-4.27)

ALP: Alkaline phosphatase. PTH: Parathyroid hormone.

Table II. Correlations Among Markers

S-P vs S-OC	$r=0.394$, $p=0.031$
S-ALP vs S-OC	$r=0.520$, $p=0.003$
S-ALP vs S-PTH	$r=0.714$, $p=0.0001$
S-PTH vs S-OC	$r=0.441$, $p=0.017$
S-PTH vs Clp-PTH	$r=0.471$, $p=0.009$

ALP: Alkaline phosphatase. S: Serum. PTH: Parathyroid hormone. P: Phosphorus. OC: Osteocalcin. Clp: Peritoneal clearance.

iPTH were measured by chemiluminescence immunometric assays (Diagnostic Products Corporation, Ca, USA). Clp of OC, ALP and PTH was calculated using the standard formula, Quantitative data were expressed as mean±SD and results were compared by Mann-Whitney U test. Variables were correlated using conventional regression analysis.

Results

Serum OC levels were found significantly higher in patients (107.98 ± 99.99 ng/ml) than in the control group (41.94 ± 12.94 ng/ml; $p<0.05$). Mean Clp of OC was 0.87 ± 0.91 ml/min. There was no correlation between

Discussion

Bone histology remains the criterion standard for the diagnosis of renal osteodystrophy. Because it is an invasive and costly method, several new biochemical markers of bone turnover have been proposed in recent years. To date, there is no specific and sensitive serum biochemical test for monitoring bone turnover in patients with ESRD. The type of dialysis modality influences the levels of biochemical markers of metabolic bone disease^{2,3}. Some investigators have reported that non-invasive markers of bone turnover such as iPTH, total ALP, and bone specific ALP were unable to distinguish among low-turnover bone diseases, normal bone and mild osteitis fibrosa. Further, the measurement of serum Ca and P is unhelpful in distinguishing between high and low bone turnover states^{4,5}. Hypermagnesemia, which is common among dialysis patients, may suppress PTH synthesis and/or release, and may have a role in development of ROD³. Another biochemical marker of bone formation is OC. OC is exclusively synthesized by osteoblasts, and increased circulating levels of OC reflect increased skeletal production, decreased renal

clearance, or both⁶. Transperitoneal removal of these markers might be expected in patients on peritoneal dialysis. In the present study, we have shown that CAPD removes a significant amount of OC and PTH from the circulation. We found that serum OC correlated significantly with serum P, ALP, and PTH concentrations, but did not correlate significantly with Clp of OC and serum Ca and Mg concentrations. Some authors have reported no correlation between serum OC and other biochemical markers [serum Ca, P, ALP, PTH, Mg, aluminum, vitamin D binding protein, and 1,25 (OH)₂D₃] of ROD, but others found significant correlation between them⁶⁻⁹. This discrepancy may be due to differences in the age group and different dialysis modality. Baskin et al.¹⁰ demonstrated that serum OC correlated with bone ALP and iPTH. In their study, it was concluded that bone ALP and OC combined with iPTH level seemed to be useful non-invasive markers of bone metabolism in dialysis patients. The study of Yalcinkaya et al.¹¹, based on the histologic diagnosis of transiliac bone biopsies of children with CAPD, showed that mean serum Ca levels were significantly higher in the low turnover group compared with the patients with high turnover bone disease. A serum iPTH level >200 pg/ml was 100% sensitive and 66% specific in identifying patients with high turnover ROD. Correlation with quantitative bone histology shows that serum OC is a measure of the rate of bone formation¹².

Our data shows that OC and PTH are removed effectively through the peritoneal membrane by CAPD. The transperitoneal removal of OC did not alter OC levels in blood. The correlation between PTH and Clp-PTH shows that transperitoneal removal of PTH seems to alter serum PTH levels. Serum Mg levels did not appear to alter serum PTH and OC levels. Our results indicate no correlations between Clp-osteocalcin and any of the other measured parameters. Therefore, Clp-osteocalcin is of no interest as a non-invasive marker of metabolic bone disease in children treated with CAPD. But significant correlations between serum OC

and PTH, P, and ALP shows that OC could be used as a valuable non-invasive biochemical marker of metabolic bone disease. Using these bone markers in combination will improve the diagnosis and the treatment of metabolic bone diseases.

REFERENCES

1. Urena P, De Vernejoul MC. Circulating biochemical markers of bone remodeling in uremic patients. *Kidney Int* 1999; 55: 2141-2156.
2. Ferreira A, Drueke TB. Biological markers in the diagnosis of the different forms of renal osteodystrophy. *Am J Med Sci* 2000; 320: 85-89.
3. Roe S, Cassidy MJ. Diagnosis and monitoring of renal osteodystrophy. *Curr Opin Nephrol Hypertens* 2000; 9: 675-681.
4. Qi Q, Monier-Faugere MC, Geng Z, Malluche HH. Predictive value of serum parathyroid hormone levels for bone turnover in patients on chronic maintenance dialysis. *Am J Kidney Dis* 1995; 26: 622-631.
5. Fletcher S, Jones RG, Rayner HC, et al. Assessment of renal osteodystrophy in dialysis patients: use of bone alkaline phosphatase, bone mineral density and parathyroid ultrasound in comparison with bone histology. *Nephron* 1997; 75: 412-419.
6. Joffe P, Heaf JG, Hyldstrup L. Osteocalcin: a non-invasive index of metabolic bone disease in patients treated by CAPD. *Kidney Int* 1994; 46: 838-846.
7. Gundberg CM, Hanning RM, Liu YA, Zlotkin SH, Balfe JW, Cole DE. Clearance of osteocalcin by peritoneal dialysis in children with end-stage renal disease. *Pediatr Res* 1987; 21: 296-300.
8. Piscitelli J, Cabansag MR, Silverstein DM. Correlation among markers of renal osteodystrophy in pediatric hemodialysis patients. *J Pediatr Endocrinol Metab* 1999; 12: 879-886.
9. Malluche HH, Faugere MC, Fanti P, Price PA. Plasma levels of bone Gla-protein reflect bone formation in patients on chronic maintenance dialysis. *Kidney Int* 1984; 26: 869-874.
10. Baskin E, Besbas N, Saatci U, et al. Biochemical markers of bone turnover in the diagnosis of renal osteodystrophy in dialyzed children. *Turk J Pediatr* 2004; 46: 28-31.
11. Yalcinkaya F, Ince E, Tumer N, Ensari A, Ozkaya N. Spectrum of renal osteodystrophy in children on continuous ambulatory peritoneal dialysis. *Pediatr Int* 2000; 42: 53-57.
12. Brown JP, Malaval L, Chapuy MC, Delmas PD, Edouard C, Meunier PJ. Serum bone gla-protein: a specific marker for bone formation in postmenopausal osteoporosis. *Lancet* 1984; 1: 1091-1093.