Evaluation of Biochemical Markers of Bone Metabolism in Patients with Secondary Hyperparathyroidism

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We studied the biochemical markers of bone metabolism and bone mineral density (BMD) in 43 male haemodialysis patients. We measured serum levels of carboxyterminal parathyroid hormone (PTH-c), carboxyterminal propeptide of human type I procollagen, calcitonin, intact osteocalcin, cross-linked carboxyterminal telopeptide of human type I collagen, and alkaline phosphatase. We divided all patients into 2 groups (group A and B), those with serum PTH-c levels of 7.5 ng/ml or higher, and those with levels lower than 7.5 ng/ml, respectively. In group A, the levels of markers for bone formation and for bone resorption were notably elevated, while BMD was not significantly decreased. The level of serum markers for bone metabolism appears to be more sensitive than BMD for the clinical assessment of secondary hyperparathyroidism.

Introduction

In patients with chronic renal failure, the bone involvement often occurs during their clinical courses. The evaluation of bone turnover in these patients is considered essential, because they sometimes show intractable symptoms related to bone involvement. Bone biopsy is the most specific examination to investigate the metabolic state of the bone, however, it cannot be performed without compelling medical reasons due to its invasiveness. We, thus, often use dual energy X-ray absorptiometry (DEXA) in order to determine bone mineral density (BMD). However, to be equipped with DEXA may be a financial burden for hospitals, and its repetitive applications have to be cautiously avoided to prevent the possible interference with patients’ reproductivity. Some evidences that several forms of uraemic osteodystrophy could even be caused by DEXA have ushered its clinical application in controversy [1, 2]. In contrast, the measurement of biochemical markers, on the other hand is non-invasive and cost-effectively repeatable. Several markers including carboxyterminal propeptide of human type I procollagen (P1CP) [3], calcitonin [4], intact osteocalcin (i-OC) [5], and alkaline phosphatase [3, 5, 6] have been known to date as the biochemical markers of bone formation. Cross-linked carboxyterminal telopeptide of human type I collagen (1CTP) [3, 5], on the other hand, is known to be useful for the determination of bone resorption.
In order to gain further insight into the usefulness of serum markers, we examined the serum levels of these markers in male patients under periodical haemodialysis and compared results with the assessment of BMD by DEXA.

Patients and methods

Forty-three male patients under periodical haemodialysis due to end-stage renal failure were examined in the present study. The cases with inflammatory diseases, which may raise the serum level of each marker, were excluded from this study. The age of the patients ranged from 32 to 79 years with a mean ± SE of 57.6 ± 1.6 years. The duration of haemodialysis was 7 to 235 months. The patients were dialysed 10–12 hr/m²/week divided into 2 or 3 sessions at a water flow rate of approximately 500 ml/min.

After obtaining informed consent from each patient, the blood samples were collected immediately before the first weekly haemodialysis session. The serum was isolated within 1 hr after collection, and was stored at −80 °C until measurement. Measurements of the serum levels of carboxy-terminal parathyroid hormone (PTH-c), carboxyterminal propeptide of human type I procollagen (PICP), calcitonin, intact osteocalcin (i-OC), cross-linked carboxyterminal telopeptide of human type I collagen (ICTP), and alkaline phosphatase (A1P) were performed by Sumitomo Bio Science (Kanagawa, Japan).

All patients were divided into 2 groups based on the serum level of PTH-c, group A (10 patients) with the level of 7.5 ng/ml or higher, and group B (33 patients) with the level lower than 7.5 ng/ml. Patients with a serum level of 7.5 ng/ml or higher are usually indicated for medical treatment for secondary hyperparathyroidism.

Bone mineral density (BMD) of the radius on the contralateral side of the shunt was measured by dual-energy X-ray absorptiometry (DEXA: Aloka DCS-3000, Tokyo, Japan). The measurement was performed at one sixth portion from the distal edge of the radius, which in a preliminary study was suggested to more sensitively reflect the decreased BMD than lumbar vertebrae (data not shown). The statistical significance (p < 0.01) was determined by the Wilcoxon rank sum test, and by correlation and covariance analysis using Stat View Version 4.0 (Abacus Concepts Inc.; Berkeley, CA, USA).

Results

Table 1 shows the coefficient of correlation between the serum levels of markers examined and PTH-c. The levels of A1P and i-OC were particularly correlated with the level of PTH-c. The calcitonin level did not appear to be correlated with the PTH-c level when all 43 cases were subjected to statistical analysis, whereas a significant correlation was found when limited to group A.