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Original

Effect of Cinacalcet on Bone Mineral Density in Hemodialysis Patients

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Background: Secondary hyperparathyroidism (SHPT) is the most common cause of renal osteodystrophy in patients receiving dialysis. The calcimimetic drug cinacalcet has been newly introduced for the treatment of SHPT in patients with chronic kidney disease. To determine the effect of cinacalcet on bone mineral density (BMD), we investigated BMD in hemodialysis patients receiving cinacalcet therapy for the treatment of SHPT. **Methods:** Seventeen patients receiving hemodialysis therapy who had been treated with cinacalcet for more than 12 months and whose BMD had been evaluated before and 12 months after cinacalcet therapy were retrospectively enrolled in this study. We divided the patients into two groups according to the change in the BMD (the increased BMD group and the decreased BMD group). We compared various parameters between the two groups. **Results:** Five of the 17 patients showed an increase in BMD at 12 months after the start of cinacalcet therapy. The pretreatment serum i-PTH level was higher in the increased BMD group (1,037.2 ± 337.6 pg/ml) than in the decreased BMD group (728.6 ± 197.9 pg/ml, $p < 0.05$). Positive linear relationship was observed between the change in the BMD at 12 months after the start of cinacalcet therapy and the serum i-PTH level at the start of cinacalcet therapy ($r = 0.486$, $p = 0.048$). **Conclusions:** A higher pretreatment serum i-PTH level was observed in the increased BMD group than in the decreased BMD group at 12 months after the start of cinacalcet therapy. Treatment of SPHT may be effective for improving BMD in patients with relatively severe SHPT.

Key words: bone mineral density, bone metabolism, calcimimetic, hyperparathyroidism, parathyroid hormone

Introduction

Secondary hyperparathyroidism (SHPT) is the most common cause of renal osteodystrophy in patients receiving dialysis[1]. In patients with SHPT, the increased bone loss is mainly manifested as a thinning of the cortical bone because of increased resorption on the endocortical surface[2]. In patients with secondary HPT, a successful parathyroidectomy can lead to the recovery of the bone mineral density (BMD)[2]. Yajima et al reported that a rapid decrease in the serum PTH level after parathyroidectomy appears to suppress bone resorption, as well as causing a transient marked increase in bone formation and an increase in the normal lamellar osteoid seam, leading to an increase in the mineralized bone volume and the strengthening of mineralized bone after a parathyroidectomy[3].

The calcimimetic drug cinacalcet, which increases the sensitivity of the parathyroid calcium-sensing receptors to calcium, has been newly introduced for the treatment of SHPT in patients with chronic kidney disease[4]. Cinacalcet has been available in Japan since January 2008. Malluche et al examined bone biopsy specimens obtained from the anterior iliac crest of hemodialysis patients and found that treatment with cinacalcet reduced bone turnover and tissue fibrosis among most dialysis patients with biochemical evidence of SHPT[5]. Fur-

thermore, after the administration of cinacalcet treatment to hemodialysis patients with high-turnover bone disease, Yajima et al reported a significant decrease in the histomorphometric parameters of bone resorption in bone biopsy specimens obtained from the anterior iliac crest[6]. They also reported that although the disappearance of fibrous tissue lagged behind that of osteoclasts after a total parathyroidectomy for secondary hyperparathyroidism[3], the disappearance of the fibrous tissue preceded that of osteoclasts after cinacalcet therapy[6]. The bone resorption rate was also significantly decreased, indicating that progressive bone loss was suppressed by treatment with cinacalcet[6]. They suggested that the slow regression of serum PTH induced by cinacalcet may be associated with both a significant decrease in the number of osteoclasts with numerous nuclei and the persistence of osteoclasts with a small number of nuclei; this phenomenon, in turn, may be associated with the disappearance of fibrous tissue[6].

A few reports have estimated the effect of cinacalcet on BMD in hemodialysis patients. To determine the effect of treatment of SHPT with cinacalcet treatment on BMD, we investigated BMD in hemodialysis patients receiving cinacalcet therapy for the treatment of SHPT.

Subjects and Methods

Seventeen patients receiving hemodialysis therapy who had been treated with cinacalcet at Sangenjaya Hospital for more than 12 months and whose BMD had been examined before and 12 months after cinacalcet therapy were consecutively and retrospectively enrolled in this study. Each hemodialysis therapy was performed for 4–5 hours, and the calcium (Ca) concentration of the dialysis fluid was 2.5 mEq/l. Outcomes Quality Initiative (NKF-K/DOQI™) has published Clinical practice guidelines for bone metabolism and disease[7]. The K/DOQI guidelines for stage 5 CKD (estimate glomerular filtration <15 ml/min/1.72 m^2 or on dialysis) recommend treatment goal for intact parathyroid hormone (i-PTH) 150 to 300 pg/ml. So, cinacalcet treatment was started at a dose of 25 mg/day in patients whose (i-PTH) level remained above 300 pg/dl under non surgical and conventional therapies. The patients were advised to take the drug just before the start of the hemodialysis session on the hemodialysis days and at approximately the same time on the non-hemodialysis days as well. Dose of cinacalcet was regulated by nephrologist's discretion. The background data of the study participants (age, gender, duration of hemodialysis, cause of primary end-stage kidney disease) were recorded. All the blood samples were obtained before the first dialysis session of the week. The serum levels of i-PTH, albumin, Ca, phosphorus (P), alkaline phosphatase (ALP) and c-reactive protein (CRP) were measured before and 1, 4, 8 and 12 months after the start of cinacalcet therapy. Routine chemistry profiles were determined using standard methods. The Ca concentration was corrected according to the albumin concentration using the following formula[8].

Corrected Ca (mg/dl) = measured serum Ca (mg/dl) + 0.8 × [4 − serum albumin (g/dl)]

We regulated the dose of vitamin D and phosphate binder to achieve the level recommended by the Japanese Society of Dialysis Therapy guidelines (corrected Ca 8.4–10.1 mg/dl and P 3.5–6.0 mg/dl)[9].

BMD was assessed using dual-energy X-ray absorptiometry (DEXA) scans. The international Society for Clinical Densitometry recommends having DEXA studies at the forearm (one-third radius) for diagnostic classification and follow-up in patients with hyperparathyroidism[10]. So, the absolute BMD values for the 1/3 distal radius were reported. The DEXA scanner was a DCS-600 (Aloka), and the same densitometer was used for all the patients.

We divided the patients into two groups according to the change in the BMD. The increased BMD group was defined as those patients whose BMD was higher at 12 months after the start of cinacalcet therapy than before treatment. The decreased BMD group was defined as those patients whose BMD was lower at 12 months after the start of cinacalcet therapy than before treatment. We compared various parameters between the two groups. We also investigated the relationship between the change in the BMD at 12 months after the start of

cinacalcet therapy and the serum level of i-PTH at the start of cinacalcet therapy.

Approval from the ethical committee of the institute and informed consent from each patients were obtained.

The Dunnett's multiple comparison test was used to identify statistically significant differences vs the baseline measurements. The Student t-test was used to compare continuous variables between two groups. Simple regression analysis was used to examine the relationship between two continuous variables. Data are presented as the means ± SD. A probability value of less than 0.05 was considered to denote a significant difference. All the statistical calculations were performed using JUMP 5.1 software.

Table 1 Baseline characteristics of study participants

Characteristic	
Number (Male/Female)	17 (10/7)
Age (years)	62.9 ± 9.3
Duration of hemodialysis (years)	22.3 ± 9.9
Primary Cause of ESKD, n (%)	
Chronic glomerulonephritis	13 (76.5)
Polycystic kidney disease	1 (5.9)
Diabetic Nephropathy	1 (5.9)
Nephrosclerosis	1 (5.9)
Unknown	1 (5.9)
Phosphate binder use, n (%)	
Calcium carbonate	3 (17.6)
Sevelamer hydrochloride	2 (11.8)
Both	12 (70.6)
VDRA use, n (%)	17 (100)

ESKD: end-stage kidney disease, VDRA: activator of vitamin D receptor.

Results

1. Baseline characteristics

Among the 17 patients, 7 were women and all of these women were postmenopausal. None was treated by steroid during the observation period. Table 1 shows the baseline characteristics of the study participants, including gender, age, duration of hemodialysis and the primary cause of the end-stage kidney disease (ESKD). The mean age was 62.9 ± 9.3 years, and the mean duration of hemodialysis was 22.3 ± 9.9 years. The most prevalent cause of ESKD was chronic glomerulonephritis (76.5%). Three patients used only calcium carbonate as a phosphate binder, 2 patients used sevelamer hydrochloride, and 12 patients used both of these medicines. All the patients used an activator of vitamin D receptor (VDRA).

2. Changes in BMD and laboratory parameters

Table 2 shows the changes in the values of the various examined parameters and the BMD. Cinacalcet therapy resulted in an immediate decrease in the serum i-PTH level from the pretreatment level of 819 ± 276 pg/ml to 468 ± 383 pg/ml ($p = 0.001$) at 1 month and further to 218 ± 133 pg/ml

Table 2 Changes in BMD and laboratory parameters

Months after treatment	Before	1 month	4 months	8 months	12 months
i-PTH (pg/ml)	819 ± 276	468 ± 383 **	393 ± 345 ***	274 ± 150 ***	218 ± 133 ***
Albumin (g/dl)	4.0 ± 0.3	3.9 ± 0.2	3.9 ± 0.3	4.0 ± 0.2	4.0 ± 0.3
Corrected calcium (mg/dl)	10.0 ± 0.5	9.4 ± 0.5 *	9.7 ± 0.4	9.6 ± 0.5	9.4 ± 0.7 *
Phosphorus (mg/dl)	5.9 ± 1.2	5.1 ± 0.8	5.3 ± 0.7	5.6 ± 1.0	5.3 ± 1.1
ALP (IU/l)	356 ± 151	393 ± 208	330 ± 175	306 ± 135	295 ± 118 *
C-reactive protein (mg/dl)	0.29 ± 0.37	0.24 ± 0.25	0.22 ± 0.15	0.22 ± 0.14	0.28 ± 0.32
Dose of phosphate binder					
Calcium carbonate (g/day)	1.6 ± 1.5	2.1 ± 2.0	2.1 ± 1.5	2.2 ± 1.7	2.3 ± 2.0
Severamer hydrochoride (g/day)	2.7 ± 1.9	2.3 ± 1.7	2.0 ± 1.8	1.9 ± 1.7	1.5 ± 1.7
Dose of VDRA					
Maxacalcitol (μg/week, n = 13)	17.9 ± 15.0	18.5 ± 14.7	19.7 ± 19.6	16.9 ± 19.4	12.1 ± 9.9
BMD (g/cm^2, all cases)	0.492 ± 0.142				0.477 ± 0.146
Dose of cinacalcet (mg/day)		25	33.1 ± 14.6	40.4 ± 21.4	43.4 ± 24.3

Values are expressed as mean ± SD.

BMD: bone mineral density, i-PTH: intact parathyroid hormone, ALP: Alkaliphoshatase, VDRA: activator of vitamin D receptor.

All assigned P values are in comparison to pre-treatment level.

* $p < 0.05$, ** $p < 0.001$, *** $p < 0.0001$.

Table 3 Comparison between the increased BMD group and the decreased BMD group

	Increased group	Decreased group	p
Number	5	12	
Age (year)	59.5 ± 10.1	64.3 ± 9.0	ns
Duration of Hemodialysis therapy	21.9 ± 12.2	22.4 ± 9.4	ns
Baseline BMD			
BMD	0.502 ± 0.124	0.488 ± 0.154	ns
T score	− 3.88 ± 1.73	− 4.00 ± 2.22	ns
Z score	− 2.94 ± 1.21	− 2.00 ± 1.66	ns
Biochemical data			
i-PTH (pre, pg/ml)	1,037.2 ± 337.6	728.6 ± 197.9	0.031
i-PTH (12 m, pg/ml)	270.4 ± 145.3	196.2 ± 126.9	ns
⊿ PTH (after 12 m, pg/dl)	− 766.8 ± 294.3	− 532.4 ± 229.4	ns
ALP (pre, IU/l)	403.2 ± 220.0	388.8 ± 212.7	ns
ALP (after 12 m, IU/l)	287.2 ± 94.7	298.2 ± 129.9	ns
⊿ ALP (after 1 m, IU/l)	36.8 ± 52.3	37.4 ± 102.1	ns
⊿ ALP (after 12 m, IU/l)	− 79.2 ± 160.4	− 53.3 ± 81.3	ns
Corrected Ca (pre, mg/dl)	10.0 ± 0.4	10.1 ± 0.5	ns
Corrected Ca (after 12 m, mg/dl)	9.5 ± 0.6	9.4 ± 0.7	ns
⊿ Ca (after 12 m, mg/dl)	− 0.5 ± 0.7	− 0.7 ± 1.0	ns
Medication			
Phosphate binder			
Calcium carbonate, n (%)	0 (0)	3 (25.0)	
Sevelamer hydrochloride, n (%)	0 (0)	2 (16.7)	
Both, n (%)	5 (100)	7 (58.3)	
VDRA			
use, n (%)	5 (100)	12 (100)	
Dose			
Increase, n (%)	2 (40.0)	0 (0)	
Decrease, n (%)	2 (40.0)	11 (91.7)	
Unchanged, n (%)	1 (20.0)	1 (8.3)	

BMD: bone mineral density, i-PTH: intact parathyroid hormone, ALP: Alkaliphoshatase, VDRA: activator of vitamin D.

($p < 0.0001$) at 12 months. A significant decrease in the corrected serum Ca level at 1 and 12 months (9.4 ± 0.5 mg/dl, $p = 0.003$ and 9.4 ± 0.7 mg/dl, $p = 0.003$; respectively) compared with the pretreatment level (10.0 ± 0.5 mg/dl). While the serum ALP level tend to be elevated at 1 month (393 ± 208 IU/l), the levels at 12 months were significantly lower (295 ± 118 IU/l, $p = 0.04$) than the pretreatment level (356 ± 151 IU/l). No significant changes in the serum albumin or CRP levels were observed among the patients. The dose of phosphate binders calcium were almost unchanged. Thirteen patients used maxacalcitol as a VDRA, and the remaining 4 patients used calcitriol. The dose of maxacalcitol was not statistically changed. In all 17 cases, BMD was not changed 12 months after the start of cinacalcet therapy.

3. Comparison between increased BMD group and decreased BMD group

Five of the 17 patients showed an increase in BMD at 12 months after the start of cinacalcet therapy. Table 3 compares the increased BMD group and the decreased BMD group. Age was relatively high in decreased group (64.3 ± 9.0 years) compared with increased group (59.5 ± 10.1 years). Z score at baseline tended to be lower in increased group (− 2.94 ± 1.21) than in decreased group (− 2.00 ± 1.66). The pretreatment serum i-PTH level was higher in the increased BMD group (1,037.2 ± 337.6 pg/ml) than in the decreased BMD group (728.6 ± 197.9 pg/ml, $p = 0.031$). The change in the serum i-PTH level at 12 months after the start of cinacalcet therapy tended to be lower in the increased BMD group (− 766.8 ± 294.3 pg/ml) than in the decreased

Table 4 Linear regression analysis of relationships between the change in the BMD and various parameters

	⊿ BMD	
	r	p value
Age (year)	− 0.031	0.907
duration of Hemodialysis therapy	0.053	0.840
Biochemical data		
i-PTH (pre, pg/ml)	0.486	0.048
i-PTH (12 m, pg/ml)	0.316	0.216
⊿ PTH (after 12 m, pg/dl)	− 0.350	0.169
ALP (pre, IU/l)	0.127	0.627
ALP (after 12 m, IU/l)	0.074	0.776
⊿ ALP (after 1 m, IU/l)	0.057	0.827
⊿ ALP (after 12 m, IU/l)	− 0.098	0.708
Corrected Ca (pre, mg/dl)	− 0.082	0.755
Corrected Ca (after 12 m, mg/dl)	0.191	0.463
⊿ Ca (after 12 m, mg/dl)	0.183	0.483

BMD: bone mineral density, i-PTH: intact parathyroid hormone, ALP: Alkaliphosbatase.

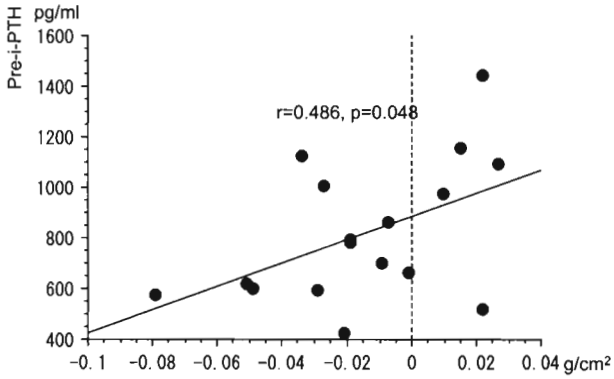

Figure Change of BMD at 12 months after the start of cinacalcet therapy
Relation between the change in the BMD at 12 months after the start of cinacalcet therapy and the serum i-PTH level at the start of cinacalcet therapy. A positive linear relationship was observed between the two parameters (r = 0.486, p = 0.048).

BMD group (− 532.4 ± 229.4 pg/ml). The serum ALP level and the corrected Ca level before treatment and 12 months after the start of the therapy did not differ between the two groups. The change in the serum ALP level at 1 month or 12 months after the start of treatment did not differ. The change in the serum corrected Ca level at 12 months after the start of treatment also did not differ. Regarding the VDRA dose, the dose was increased in 2 patients (40.0%), decreased in 2 patients (40.0%), and unchanged in 1 patient (20.0%) in the increased BMD group and decreased in 11 patients (91.7%) and unchanged in 1 patient (8.3%) in the decreased BMD group.

4. Relation between the change in the BMD and various parameters

Table 4 shows linear regression analysis of relationships between the change in the BMD and various parameters. A positive linear relationship was observed between the two parameters (r = 0.486, p = 0.048, also shown in Figure). Change of i-PTH tended to be negatively correlate with change of BMD but it was not statistically significant (r = − 0.350, p = 0.169).

Discussion

To determine the effect of treatment of SHPT with cinacalcet on BMD, we investigated BMD in hemodialysis patients who had received cinacalcet therapy for the treatment of SHPT. Cinacalcet therapy significantly reduced the serum i-PTH level but we could not detect the increase of BMD 12 months after the start of cinacalcet therapy. Five of the 17 patients had an increased BMD at 12 months after the start of cinacalcet therapy. The pretreatment serum i-PTH level was higher in the increased BMD group than in the decreased BMD group. Thus, cinacalcet therapy might be effective for improving BMD in patients whose serum PTH level is rather high.

Calcimimetic agents, such as cinacalcet, have been developed for controlling PTH secretion; these agents act by enhancing the sensitivity of the parathyroid calcium receptors to extracellular calcium ions[11]. Because of its unique mechanism of action, cinacalcet may represent a promising new medical alternative for the treatment of SHPT in Japanese patients undergoing hemodialysis therapy, as in Western populations[12].

In experimental uremic rats, daily NPS-R-568, a prototype of cinacalcet, increased the BMD of cortical bone[13]. Combing the results from 4 clinical trials, randomization to cinacalcet led to significant reductions in the risk of fracture along an improvement in the Body Pain scale[14]. In multiple phase 2 and phase 3 clinical trials, treatment with cinacalcet was

associated with favorable changes in the biochemical markers of bone formation (bone-specific alkaline phosphatase) and resorption (serum N-telopeptide), as well as improvements in bone turnover parameters[15]. Shigematsu et al observed 200 Japanese hemodialysis patients for 52 weeks and found that although the levels of bone resorption markers gradually decreased throughout the study period, the bone alkaline phosphatase level increased significantly during the first 4 weeks and then gradually decreased[16]. The suggested causative mechanism was that the sudden disappearance of PTH suppressed osteoclast activity[17], causing a subsequent increase in calcium influx into the bone and accelerating osteoblast-mediated bone formation[18]. In our study, we also observed a transient increase of in the ALP level at 1 month after the start of therapy and a decrease in the serum Ca level, similar to the changes observed after a parathyroidectomy. This condition is sometimes referred to as hungry bone syndrome.

In 2005, Lien et al examined 8 chronic kidney disease patients (pre i-PTH 912 ± 296 pg/ml) and reported the suppression of plasma i-PTH reverse bone loss in the proximal femur at 26 weeks after the start of cinacalcet therapy, although the treatment did not appear to have any effect on the lumbar spine[19]. Carlos Bergua et al examined 8 renal transplant patients (pre i-PTH 309 ± 120 pg/ml) and reported that after 12 months of cinacalcet therapy, the mean radial BMD increased[20]. Prieto et al observed 27 renal transplant patients (pre i-PTH 258 ± 104 pg/ml) and found a significant improvement in the femoral neck bone mineral density, but not in the lumbar spine, after 6 months of cinacalcet treatment[21]. On the other hand, Peacock et al compared primary hyperparathyroidism patients treated with cinacalcet (40 patients, (pre i-PTH 105 ± 36 pg/ml)) or a placebo (37 patients (pre i-PTH 120 ± 54 pg/ml)) and found that the BMD of the lumbar spine, total femur, and 1/3 distal radius were unchanged at 52 weeks after cinacalcet therapy but that bone resorption and formation markers, such as serum bone-specific alkaline phosphatase (BAP), N-telopeptide (NTx), or urine NTx, had increased[22].

In our study, BMD was not changed 12 months after the start of cinacalcet therapy. Discrepancy between our results and other studies was not clear. Patients have been on hemodialysis for exceptionally long period of time (22.3 ± 9.9 years) compared to patients in other studies. The explanation could be partly that complication of amyloidosis as the result of long term hemodialysis could affect bone mineral disease, but duration of hemopdialysis was not different between increased BMD group and decreased BMD group. The mean i-PTH after 12 months of treatment was 218 pg/ml, meaning that few patients had i-PTH levels lower than suggested in the guidelines. If we could successfully treated SHPT in all patients, BMD could be increased like other studies.

Five out of 17 patients showed an increase in BMD at 12 months after the start of cinacalcet therapy. The pretreatment serum i-PTH level was higher in the increased BMD group than in the decreased BMD group, and the change in the serum i-PTH level tended to be lower in the increased BMD group than in the decreased BMD group. A positive linear relationship was observed between the serum i-PTH level at the start of cinacalcet therapy and the change in the BMD at 12 months after the start of cinacalcet therapy. The reason why some patients had elevation of BMD whereas it further decreased in others despite cinacalcet therapy and effectively suppressed i-PTH was not clear. One explanation could be that cinacalcet was also administered to patients without severe hyperparathyroidism and without significantly decreased bone mass at baseline. Z score tended to be lower in increased group than decreased group but T score and BMD were almost same. Treatment of SHPT with cinacalcet may be effective for improving BMD in patients whose serum PTH levels are rather high and whose BMD level were reduced by SHPT. The cause of the improvement in the BMD after cinacalcet therapy can be explained by several factors, including a superior PTH control, cyclic changes in the PTH blood level, or a possible direct effect of cinacalcet on bone tissue[23].

Bone remodeling is reportedly more pronounced

in cortical bone than in cancellous bone[22]. In addition, cortical bone constitutes approximately 70% of the systemic bone mass in the normal population, and bone fractures generally initiate in cortical bone[24]. Therefore, an evaluation of the cortical bone history is important. The International Society for Clinical Densitometry recommends having dual energy X-ray absorptiometry studies performed on the nondominant forearm (one-third radius) for diagnostic classification and follow-up in patients with hyperparathyroidism[10]. BMD testing of the forearm using peripheral dual energy X-ray absorptiometry can be accurately and precisely used for the diagnosis of bone abnormalities. We also estimated the BMD of the 1/3 distal radius.

There were several limitations in this study. This study was performed retrospectively, and no clear protocol existed for the doses of medicine that were administered. VDRA is known to contribute to the improvement of BMD[25]. The flexible use of VDRA probably contributed to the modulation of BMD in our study. In the decreased BMD group, the VDRA dose was reduced in 11 patients (91.7%) and left unchanged in 1 patient (8.3%). Compliance of cinacalcet was not clear and some patients might forget to take medicine in some times. The number of patients enrolled in this study was also relatively small and we could not clearly show the effect of cinacalcet on BMD. Further large-scale, prospective studies are needed to estimate the effect of cinacalcet.

Conclusions

Cinacalcet therapy significantly reduced the serum i-PTH level but we could not detect the increase of BMD 12 months after the start of cinaclcet therapy. A higher pretreatment serum i-PTH level was observed in the increased BMD group than in the decreased BMD group at 12 months after the start of cinacalcet therapy. Treatment of SPHT may be effective for improving BMD in patients with relatively severe SHPT.

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シナカルセトが骨密度に与える影響

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〔目的〕二次性副甲状腺機能亢進症は透析患者における骨ミネラル代謝異常をきたす要因として挙げられる．シナカルセトは二次性副甲状腺機能亢進症に対する新たな治療薬であり，骨密度に及ぼす変化について検討した．〔方法〕三軒茶屋病院の外来維持透析患者において，シナカルセト投与後1年以上経過し，投与前と投与後1年に骨密度を測定した17例について retrospective に検討した．骨密度は非シャント側橈骨遠位1/3部を Dual Energy X-ray Absorptiometry 法で測定した．骨密度の増加群と減少群に分け比較した．〔結果〕i-PTH 値はシナカルセト開始前 819±276 pg/ml より1年後 218±133 pg/ml と低下した（$p<0.0001$）．骨密度の増加群5例，減少群12例で，増加群において減少群に比し前 i-PTH 値は高値であった（1,037.2±337.6 vs 728.6±197.9 pg/ml，$p=0.031$）．骨密度の変化量とシナカルセトによる治療前の i-PTH は正の相関を示した（$r=0.486$, $p=0.048$）．〔結論〕シナカルセトは比較的高度な二次性副甲状腺機能亢進症を改善することにより，骨密度を改善する可能性がある．