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Changes in Serum 25-hydroxycholecalciferol and Intact Parathyroid Hormone Status after Hip Fracture

Mayumi SAKUMA[1], Naoto ENDO[1,2], Izumi MINATO[3], Hideki TOYAMA[3] and Einosuke ENDO[1]

[1]Division of Rehabilitation Medicine, Department of Community Preventive Medicine, [2]Division of Orthopedic Surgery, Department of Regenerative and Transplant Medicine, Graduate School of Medical and Dental Sciences, Niigata University, and [3]Department of Orthopedic Surgery, Niigata Rinko General Hospital, Niigata, Japan

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Summary. **The purpose of the study was to examine changes in the levels of serum 25-hydroxychole calciferol (25-OHD) and other biochemical markers in response to hip fracture. Serum 25-OHD, serum intact parathyroid hormone (intact PTH), serum N-terminal crosslinking telopeptide of type I collagen (NTx), and urine NTx were measured during a 6-month period after fracture in 11 patients with acute hip fracture. Bone mineral density (BMD) of the non-fractured hip was measured by dual-energy X-ray absorptiometry (DXA). Serum and urine were sampled at admission, on the day of surgery, and two weeks, four weeks, and either three months or six months after fracture. The mean change in the serum 25-OHD levels was less than ± 10% after fracture. Intact PTH levels after three months were higher than those after two weeks or six months, and intact PTH after six months was higher than after two weeks, the mean change being ± 20%. Urine NTx levels changed until four weeks after fracture, and individual differences were observed; insufficient urine NTx data were obtained for analysis after four weeks, though the changes in the urine NTx level after four weeks were small. Changes in serum NTx were smaller than those in urine NTx and similarly showed no significant changes during the measurement period. In conclusion, serum 25-OHD did not show large changes during hip-fracture healing.**

Key words — 25-OHD, intact PTH, NTx, hip fracture.

INTRODUCTION

The number of cases of hip fracture has been increasing with the aging of society [1], necessitating methods for its prevention. The serum 25-hydroxy cholecalciferol (25-OHD) concentration is an index that reflects nutritional status as determined by the level of vitamin D, which is an important nutrient for bone health and a regulator of calcium metabolism. Vitamin D deficiency leads to an increase in parathyroid hormone (PTH) levels – resulting in bone loss [2], and subclinical vitamin D deficiency is considered to be a risk factor for osteoporotic hip fracture in the elderly; [3,4,5,6] these facts give importance to an evaluation of the vitamin D level in osteoporotic patients with hip fracture. An association of vitamin D with normal bone formation has been established, but there are insufficient data regarding serum 25-OHD changes after hip fracture, and the relationship between 25-OHD levels and hip-fracture healing remains unclear. In evaluating serum 25-OHD in hip-fracture patients, the influence of the fracture on the value of serum 25-OHD and other biochemical markers must be considered. Thus, the aim of this study was to examine the levels of 25-OHD and other biochemical markers, including serum intact parathyroid hormone (intact PTH) and serum and urine N-terminal crosslinking telopeptide of type I collagen (NTx), in patients after acute hip fracture.

Correspondence: Mayumi Sakuma, M.D., Division of Rehabilitation Medicine, Department of Community Preventive Medicine, Graduate School of Medical and Dental Sciences, Niigata University, 1-757 Asahimachi dori, Niigata 951-8510, Japan.

Abbreviations – ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMD, bone mineral density; CLIA, chemiluminescence immunoassay; DXA, dual-energy X-ray absorptiometry; ELISA, enzyme-linked immunosorbent assay; NTx, N-terminal crosslinking telopeptide of type I collagen; PTH, parathyroid hormone; RIA, radioimmunoassay; 25-OHD, 25-hydroxycholecalciferol.

SUBJECTS AND METHODS

Subjects

Patients with a fresh fracture of the femoral neck who were admitted to a particular general hospital in Niigata, Japan, from February to September 2004 were invited to participate in a prospective study of recovery from hip fracture. Twenty-six patients were recruited, and 15 of these patients could be followed. However, two of the 15 patients were excluded because they had taken active vitamin D_3 before the fracture, and two more patients were excluded because of malignant disease and liver damage, respectively, leaving an enrollment of 11 patients. The average age of the 11 patients (three males and eight females) was 75.3 ± 11.2 years old (range, 55-91 years old); none suffered from renal, liver or malignant disease. The participants took no active vitamin D_3 for six months after the fracture, with the time limit defined by the final blood examination, and serum levels of 25-OHD, intact PTH and NTx, and the urine NTx level were determined during this period. Written consent for participation in the study was obtained from all patients.

Serum, urine, and bone mineral density (BMD) measurements

Serum and urine samples were collected at admission, on the day of surgery, and two weeks, four weeks and three months or six months after the fracture occurred. The average period from fracture to admission was 3.9 days (range, 0-12 days), and the average period from admission to surgery was 3.5 days (range, 1-8 days). Conservative therapy was used for one patient. The blood and urine samples were assayed for NTx, and blood samples were assayed for intact PTH and 25-OHD. The samples were collected in the morning. Serum calcium, serum phosphorus, and serum total protein were determined at admission, using standard methods. Serum creatinine, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels were checked to examine liver and renal function. The BMD of the non-fractured hip was measured by dual-energy X-ray absorptiometry (DXA) (Hologic, QDR Delphi, Bedford, MA, USA).

Table 1. Subject characteristics

Subject number	Gender	Age (years)	BMD of hip (g/cm^2)	Serum total protein (g/dl)	Serum albumin (g/dl)	Serum Ca (mg/dl)	Serum iP (mg/dl)	Serum creatinine (mg/dl)
1	F	55	0.703	6.9	4.3	8.9	3.1	0.6
2	F	70	0.443	5.6	3.1	8.0	2.9	0.4
3	M	91	0.330	5.6	3.1	8.2	2.7	0.4
4	F	88	0.586	5.8	3.7	8.6	3.4	0.5
5	F	80	0.554	6.8	4.3	8.9	3.8	0.4
6	F	74	0.589	6.3	4.0	8.7	2.5	0.5
7	M	83	NE*	7.6	3.0	8.1	2.8	1.5
8	F	78	0.595	6.7	NE	8.8	3.0	0.4
9	M	58	0.630	6.1	NE	8.2	2.6	0.5
10	F	79	NE	7.7	NE	9.1	3.5	0.7
11	F	72	0.806	6.8	NE	8.4	4.6	0.6
Mean ± SD		75.3 ± 11.2	0.582 ± 0.14	6.54 ± 0.73	3.64 ± 0.58	8.51 ± 0.37	3.17 ± 0.62	0.59 ± 0.32

*NE, not examined; BMD, bone mineral density.

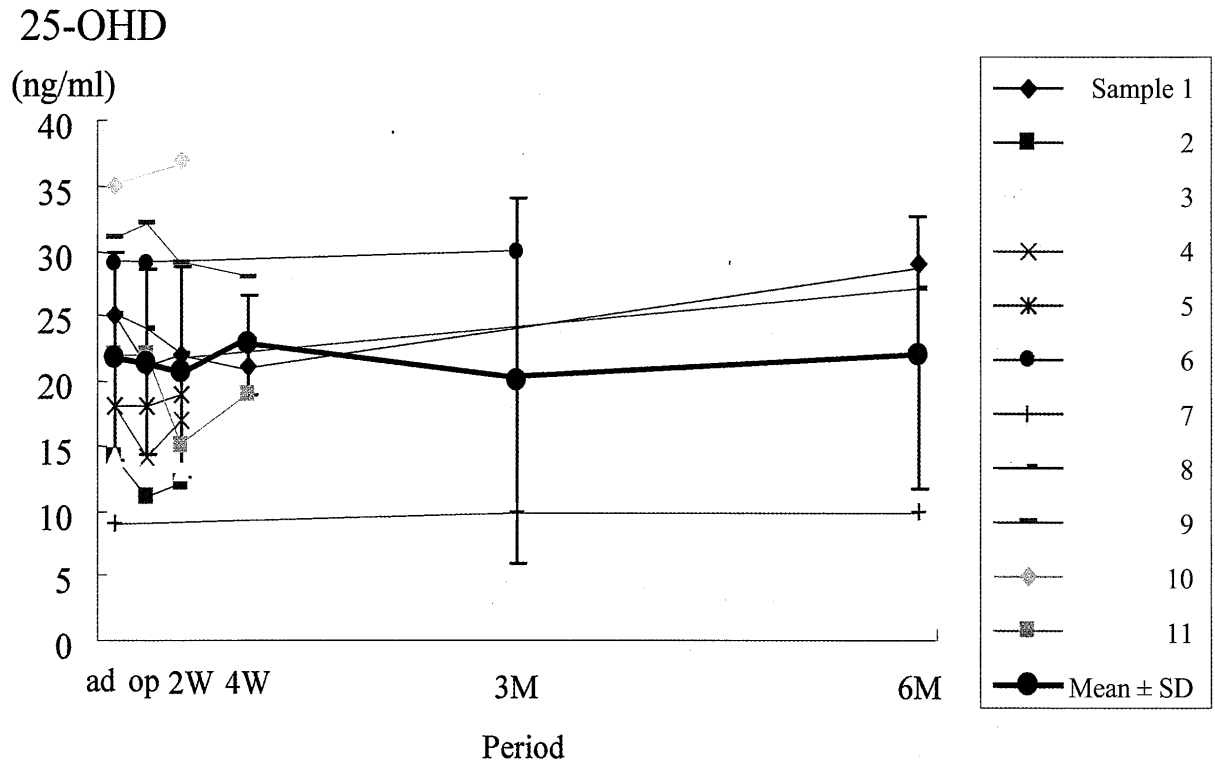

Fig. 1. Plots of the serum 25-hydroxycholecalciferol (25-OHD) level over time for all cases. The average maximum change from the mean value in each case was ± 8.5% (± 1.75 ng/mL).

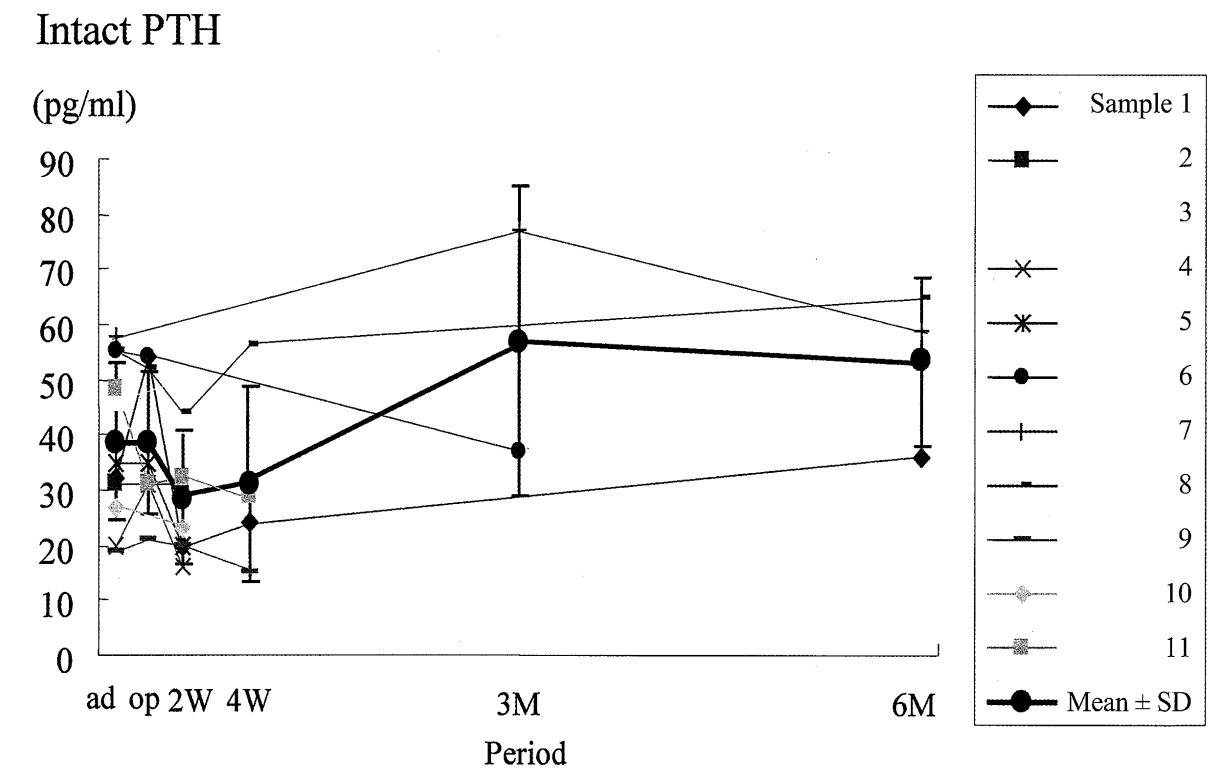

Fig. 2. Plots of the serum intact parathyroid hormone (PTH) level over time for all cases. The average maximum change from the mean value in each case was ± 20.7%.

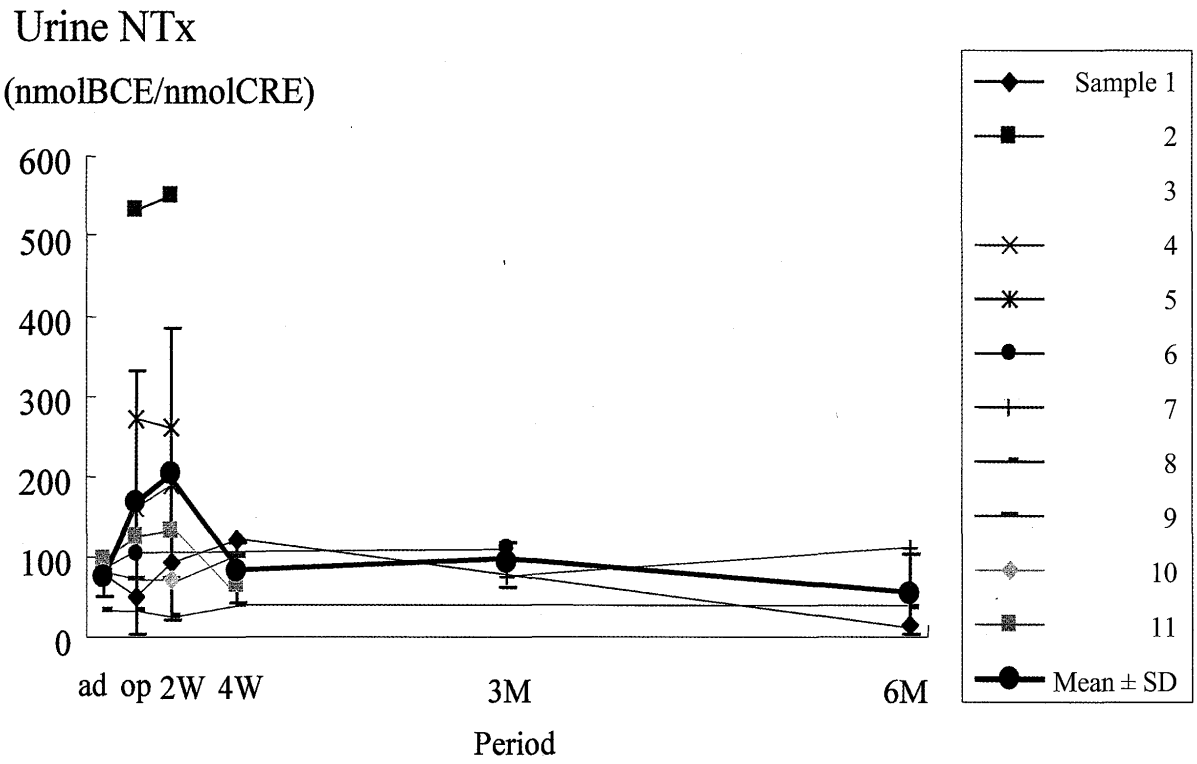

Fig. 3. Plots of the urine NTx level over time for all cases. The average maximum change from the mean value in each case was ± 19.4%.

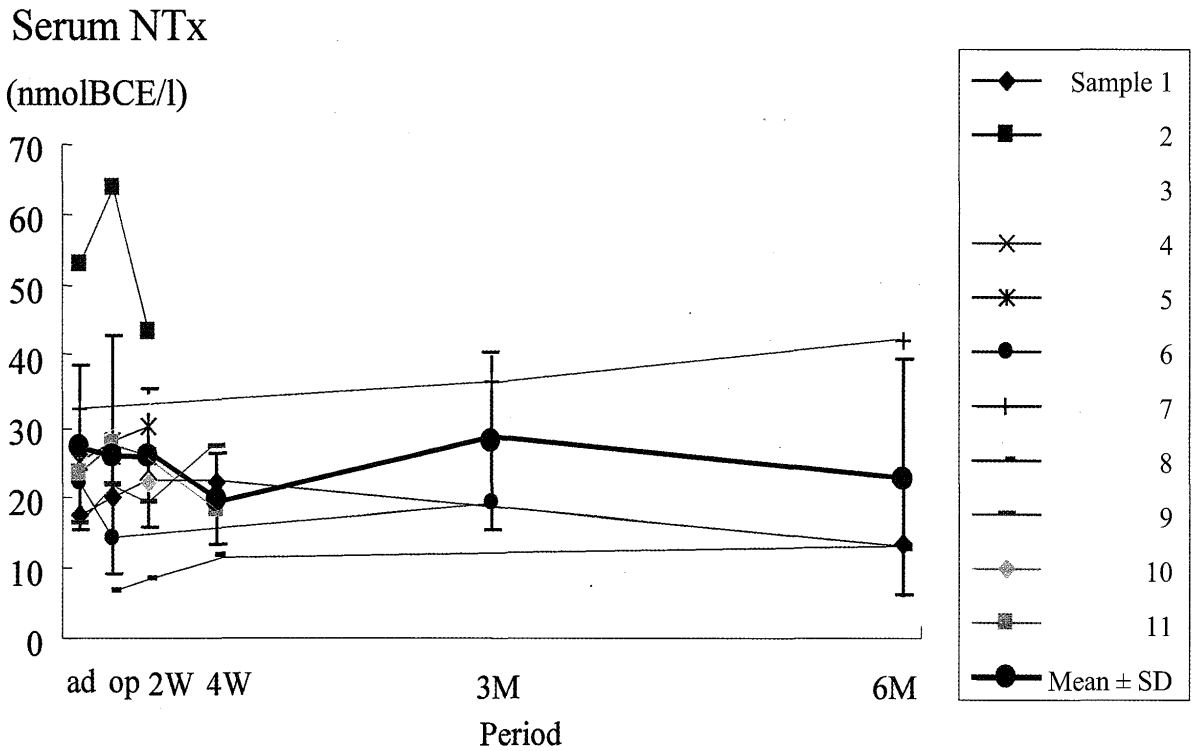

Fig. 4. Plots of the serum NTx level over time for all cases. The average maximum change from the mean value in each case was ± 18.0%.

Hormone assays

The 25-OHD level was measured by radioimmunoassay (RIA) using a kit supplied by DiaSorin (Stillwater, MN, USA), and intact PTH was measured by the chemiluminescence immunoassay (CLIA) method using a kit provided by Nichols Institute Diagnostics (San Clemente, CA, USA). Urine and serum levels of NTx were measured by enzyme-linked immunosorbent assay (ELISA), using the Osteomark kit (Inverness Medical Professional Diagnostics, Princeton, NJ, USA).

Statistical analysis

ANOVA followed by the Bonferroni/Dunn test was used to evaluate differences in the data, with P values less than 0.05 considered to be statistically significant. Analysis was performed using StatView for Windows software (version 5.0).

RESULTS

Subject characteristics

The characteristics of the 11 patients are shown in Table 1. On discharge from the hospital, six patients returned home after an average hospitalization period of 32 days, while three patients returned to the hospital or the nursing home at which they had lived before the fracture, and two patients who had lived at home before the fracture moved into a hospital or a nursing home. The BMD of the non-fractured hip was measured by DXA in nine of the 11 patients, and the average BMD was 0.582 ± 0.13 g/cm^2. The average serum total protein level was 6.53 ± 0.7 g/dl. Renal function and liver function, as determined by the serum creatinine level and by serum ALT and AST levels, respectively, were close to the normal ranges, and all patients had normal serum calcium and phosphorus.

The serum levels of 25-OHD are shown in Fig. 1. The average at the time of admission was 20.8 ng/mL (< 20 ng/mL in five of the 11 patients), and in most cases this level changed little in the six months after the fracture occurred: the average maximum change was ± 8.5% (± 1.75 ng/mL), and no significant difference was observed in comparison of serum 25-OHD levels for any pair of time points. The serum levels of intact PTH are shown in Fig. 2. Intact PTH was higher after three months than after two weeks or six months, and higher after six months than after two weeks: the average maximum change was ± 20.7%, but no significant difference was observed in comparison of serum PTH levels for any pair of time points. The urine and serum levels of NTx are shown in Figs 3 and 4, respectively. Urine NTx levels changed until four weeks after fracture, and individual differences were observed; there were, however, insufficient data for urine NTx after four weeks to perform any statistical analysis. The average maximum change in urine NTx was ± 19.4%, though no significant difference was observed in comparison of the urine NTx levels for any pair of time points. Serum NTx levels also increased for two weeks after fracture in six of 11 cases, though smaller changes in serum NTx were observed in comparison with urine NTx; the mean maximum change was ± 18.0%, and no significant difference was observed between data for any pair of time points.

DISCUSSION

The serum levels of 25-OHD showed little change in osteoporotic patients. Tauber et al.[7] found that the blood level of 25-OHD$_3$ is reduced during fracture repair in humans and suggested that this could be related to reduced outdoor activity; however, these results were obtained in patients undergoing prolonged fracture healing. On the other hand, Meller et al.[8] reported that PTH and 25-OHD$_3$ do not show significant changes during the healing period for fractures in young adults. Yu-Yahiro et al.[9] reported that intact PTH levels gradually rise after fracture and are significantly elevated after 365 days, compared with all other time points; however, their study also showed that intact PTH is somewhat decreased 10 days after fracture and returns to a baseline level after 60 days. In our subjects, the intact PTH level was higher three months after fracture than two-four weeks after fracture (not significant), an observation that is not contradictory with previous results. Ingle et al.[10] showed that urine NTx slightly increases following fracture and then decreases from 12 to 52 weeks. In the current study, numerical variation and the small sample size prevented these changes from reaching a statistical significance. Changes in serum NTx were also observed, but these were smaller than the changes in urine NTx. Overall, our data are consistent with previous studies, but the small sample size and lack of data for some variables at certain time points indicate that more detailed studies are needed to confirm these results.

CONCLUSION

The serum 25-OHD level did not change greatly after fracture, in comparison with the levels of intact PTH and NTx.

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