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Short Communication

Changes in Bone Mass in Japanese Elderly Patients with Osteoporosis Treated with Anti-RANKL Antibody Following Bone Formation by PTH

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Abstract

Introduction: We have undertaken the modified PTH and anti-RANKL antibody treatment for elder and severe osteoporotic patients in Japan.

Subjects and Methods: After received hip fracture operation, 19 patients treated with daily PTH treatment before anti-RANKL antibody under Japanese insurance at Sakai and Sumoto-Itsuki Hospital.

Results and Discussion: The P1NP levels increased after daily PTH treatment, the NTX levels decreased treated with anti-RANKL antibody, and final % of YAM increased in lumber spine bone mineral compare to hip bone mineral.

Conclusion: Anti-RANKL antibody treatment after daily PTH treatment was useful for even in Japanese elder patients with severe osteoporosis.

Keywords: *Anti-Receptor Activator of Nuclear Factor Kappa-B Ligand (RANKL) antibody; Daily Parathyroid Hormone (PTH); Osteoporosis; Japanese*

Abbreviations

YAM: Young Adult Mean; RANKL: Anti-Receptor Activator of Nuclear Factor Kappa-B Ligand; PTH: Parathyroid Hormone; NTX: N-Terminal Telopeptide; DEXA: Dual Energy X-Ray Absorptiometry; P1NP: Procollagen Type 1 N-Terminal Pro-Peptide; ADFR: Activation Depression Free Repeat

Introduction

Japan is most progressing into an aging society in the world. Only 5 % populations were achieved healthy end in Japan but Japanese is number one healthy life span all over the world. This study examined changes in bone mass (young adult mean [YAM] of the lumber spine and hip bone) in Japanese super elderly patients with a history of femoral neck fracture treated with anti-receptor activator of nuclear factor kappa-B ligand (RANKL) antibody (Denosumab 60 μg / six month each, Daiichi Sankyo Company. Its's cost is Japanese 28,482 yen which is 254 $ / 226 Euro per 6 months) after bone formation by daily parathyroid hormone (PTH, teriparatide 20μg/day, Ely Lilly. Its's cost is 51,871 Japanese yen which is 463$ / 412 Euro per month). This treatment is the strongest treatment for osteoporosis using upper both drugs in the world [1] but not permitted in Japanese health organization. In this study, we evaluated the changes in bone mass in super elderly (≧ 80 years old) Japanese patients with severe osteoporosis treated with anti-RANKL antibody following bone formation by PTH.

Subjects and Methods

We retrospectively studied in 19 patients (all women received surgical operation for hip fracture at aged 80 - 100 years, mean 89 years; body weight 31 - 52kg, mean 44kg) with severe osteoporosis at the Department of Orthopaedic Surgery, Kindai University Sakai Hospital and Sumoto-Itsuki Hospital. We measured procollagen type 1 N-terminal pro-peptide (P1NP: bone formation marker) on administration and after treated with PTH (1 - 24 months, mean 10 months). As the another evaluation, we measured urinary levels of N-terminal telo-peptide (NTX: bone resorbing marker) before and after treatment of anti-RANKL antibody twice or more at outdoor clinic. All patients evaluated bone minerals (in the lumber spine and femur neck bone by dual energy X-ray absorptiometry [DEXA]: DPX-BRAVO. General Electric Company, USA. Its's cost is 4,500 Japanese yen which is 40.1 $ / 37.5 Euro / 6 month) on administration and final consultation.

Results and Discussion

Over 70 years old patients in Sakai showed chronic renal disease (CKD: estimated glomerular filtration rate ＜60 mmL/min/1.73m^2) about 41.6% [2]. Some osteoporotic agent in Japan did not allowed for CKD [3]. PTH efficacy was measured in terms of P1NP level. With PTH treatment, the P1NP level increased in 16 of 19 patients (84.2%) from 47.7 ± 18.4 (range: 13.7 to 80.6) μg/L to 113.4 ± 58.9 (range: 45.2 to 227.3) μg/L (Figure 1-a. t-test: p = 5.85542E-05) significantly. The second treatment was switched to anti-RANKL antibody after a P1NP level increase, the NTX level before and after the second treatment decreased in 13 of 19 patients (68.4%) from 33.4 ± 17.4 (range: 13.0 to 77.7) nmol BCE/mmol CRE to 26.6 ± 7.7 (range: 14.9 to 40.4) nmol BCE/mmol CRE (Figure 1-b. t-test: p = 0.094758) significantly. The YAM of lumber spine increased in 16 of 19 patients (84.2%: not same patients as P1NP) from 64.3 ± 18.0 (range: 40.2 to 110.9) **%** to 68.4 ± 18.2 (range: 44.9 to 116.0) **%** (Figure 2-a. t-test: p = 0.008549) significantly, whereas that of the femur increased only in 6 of 19 (31.6%: decreased 13 patients were not same as NTX) from 62.5 ± 13.9 (range: 44.0 to 102.0) **%** to 59.9 ± 14.1 (range: 43.1 to 96.3) **%** (Figure 2-b. t-test: p = 0.04033) significant tendency. No patient had a serious adverse reaction and/or new clinical bone fracture during the observation period.

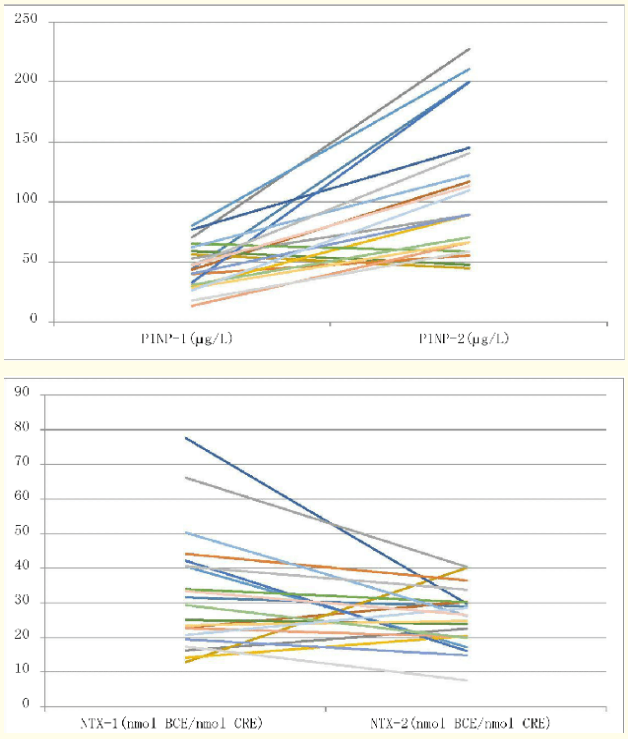

Figure 1: *Changes P1NP level (a) and NTX level (b) before treatment (-1) and after (-2).*

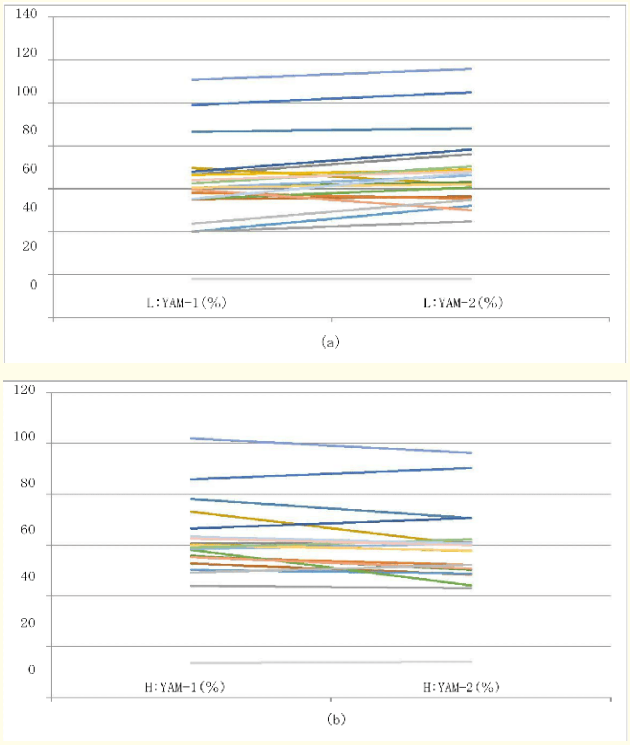

Figure 2: *Changes Lumber YAM level (a) and femoral hip YAM level (b) before treatment (-1) and after (-2).*

Remodeling of bone metabolism: Activation Depression Free Repeat (ADFR) is main concept by Frost [2]. Initial ADFR means that A=vitamin D, D=calcitonin, F=interval, R=continued, but in this study ADFR means that A=PTH, D=anti-RANKL antibody, F and R is not accepted. Treatment with daily PTH and anti-RANKL antibody most potently increases lumber spinal more than hip bone mineral levels [1]; however, combination therapy is not covered under health insurance in Japan. Second recommendation by the same article [1] demonstrated that the anti-RANKL antibody after daily PTH increased YAM of general bone density. Although taking measures against osteoporosis after menopause is important, anti-RANKL antibody treatment after daily PTH increases lumber spine bone mineral levels even in elderly patients with Japanese severe osteoporosis after hip fracture. Therefore, we conclude that treatment is useful and economical advantage for super elder Japanese osteoporotic patients to protect another side hip fracture for several years [4].

Conclusion

We demonstrated that the anti-RANKL antibody treatment after daily PTH treatment was useful for even in Japanese elder patients with severe osteoporosis after hip fracture.

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