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Original article

Utility of radius bone densitometry for the treatment of osteoporosis with once-weekly teriparatide therapy

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ABSTRACT

Objectives: As clinics that treat patients with osteoporosis do not usually have central dual-energy X-ray absorptiometry (DXA), bone density is often measured with radial DXA. However, no long-term evidence exists for radius bone density outcomes following treatment with once-weekly teriparatide in actual medical treatment.
Methods: We evaluated changes in bone density at 6-, 12-, and 18-month intervals using radial DXA in patients treated with once-weekly teriparatide for more than 6 months.
Results: A significant increase in bone mineral density (BMD) was observed at the 1/3 and 1/10 radius sites 12 months after the initiation of once-weekly teriparatide. We also observed that the rate of change in BMD was greater at the distal 1/10 radius than at the 1/3 radius.
Conclusions: Considering these points, the effect of once-weekly teriparatide therapy can be observed at the radius. In clinics that do not have central DXA, but instead have radial DXA, these findings can help to evaluate the effect of once-weekly teriparatide treatment on osteoporosis.

1. Introduction

Dual-energy X-ray Absorptiometry (DXA) is a type of bone densitometry that allows for differentiation between bone and soft tissue. It uses 2 X-ray beams of different energy levels. Accordingly, bone mass per unit area and bone mineral density (BMD) can be calculated by measuring the X-ray attenuation rate for each beam. BMD measurement using DXA is the gold standard for diagnosing osteoporosis and assessing treatment efficacy as it is very precise with minimal exposure to radiation [1]. Currently, the lumbar spine, femur, and radius are commonly used as measurement sites at the clinic. Japanese guidelines [1] recommend the use of the lumbar spine and the proximal femur for the assessment of bone density. Meanwhile, the radius is used for measurement only if the lumbar spine and proximal femur cannot be used. However, several medical centers do not have central DXA and instead measure bone density using radial DXA. This is because central DXA, which allows for the measurement of the lumbar spine and proximal femur, is expensive and burdensome. Therefore, it is important to assess the change in bone density at the radial distal 1/10 site (abundant spongy bone) and 1/3 site (abundant cortical bone) and to confirm the utility of radial DXA in patients being treated for osteoporosis.

In this study, once-weekly teriparatide was used to assess radial BMD. Teriparatide increases bone density by inducing osteoblast proliferation and promoting bone formation. Although only daily self-injection formats are used abroad, once-weekly teriparatide is additionally marketed in Japan. Daily teriparatide has been reported to increase the bone density in the lumbar spine by 10% after 12 months of use in a phase III clinical trial in Japan, which is more effective than bisphosphonate treatment [2]. In this phase III clinical trial in Japan (Teriparatide Once Weekly Efficacy Research: TOWER Study) [3], once-weekly teriparatide increased bone density at the total proximal femur by 3.1% within 72 weeks of treatment, which resulted in a reduction in the incidence of vertebral fracture by 80%. Since the incidence of vertebral fracture was reduced by 65% after daily teriparatide use [4], once-weekly teriparatide is believed to more effectively reduce the relative risk of osteoporotic damage in comparison to other osteoporosis medications. Once-weekly teriparatide is only used in Japan and its

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time-course effect on radial bone density has only been measured up to 6 months after therapy initiation, as reported by Urushibara et al. [5]. These researchers documented a significant increase in BMD at the 1/10 radius site, but did not examine long-term efficacy and safety. Therefore, we performed this study to determine efficacy and safety of once-weekly teriparatide therapy over an 18-month period.

2. Methods

2.1. Study design

Retrospective study at a clinic in Japan. Subjects received a once-weekly subcutaneous injection of 56.5-μg teriparatide for 18 months. The primary doctor measured BMD at all 3-time points by using radial DXA. Moreover, Institutional Review Board (IRB) approval of the protocol was in place prior to the study.

2.2. Study subjects

Patients that met the following requirements were included in the safety evaluation:

(1) Patients with osteoporosis
(2) Patients that initiated once-weekly teriparatide (56.5 μg/dose) therapy after 2011.

Among those that satisfied the aforementioned criteria, we included those that met the following conditions in the efficacy evaluation:

(1) Measurement using radial DXA was available at the time of dosing.
(2) Once-weekly teriparatide was administered for more than 6 months.
(3) BMD at the radial distal 1/3 site was 70% or more below the young adult mean value at its baseline.
(4) Radial DXA images were taken at 6, 12, or 18 months.
(5) The same part was measured in the study, such as the primary doctor was able to judge that the length of the forearm was measured equally and rotation of the arm was not detected.

2.3. Treatments

We evaluated the change in bone density at the radial distal 1/10 site (abundant spongy bone) and at the radial distal 1/3 site (abundant cortical bone) over time at the baseline and at 6, 12, and 18 months in patients treated with once-weekly teriparatide.

2.4. Evaluation

Safety endpoint: Adverse events that occurred during the study period were evaluated.

Efficacy endpoint: The primary endpoint was change in bone density (distal 1/3 site) after 18 months measured using radial DXA (Dichroma Scan DCS-600EXV, Hitachi Ltd., Tokyo, Japan) for all data. Secondary endpoints were change/rate of change (distal 1/3 site and 1/10 site) of bone density at 6, 12, and 18 months (excluding primary endpoint).

2.5. Statistical analysis

Change in BMD from the baseline was evaluated using a paired *t*-test without considering multiplicity. The rate of change in BMD from the baseline was analyzed using data for which all measurements, from the baseline to 18 months, were available. The correlation between BMD at the 1/10 and 1/3 radius sites was evaluated using Pearson test. Results of the analysis in the full text are expressed as the mean ± standard deviation for continuous variables and number of cases (%) on a nominal scale. A 2-sided significance level of 5% was used. JMP ver. 13.1.0 (SAS Institute Inc., Cary, NC, USA), was used for statistical analysis.

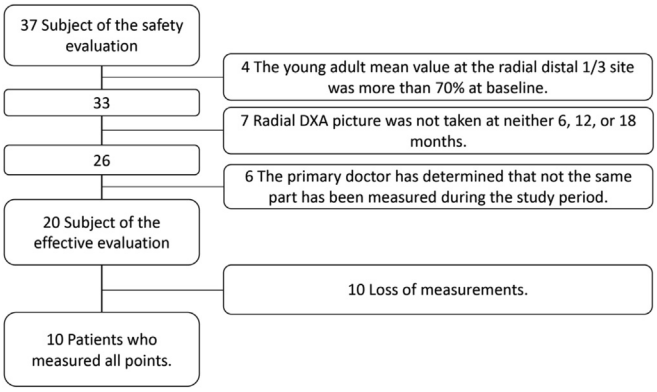

Fig. 1. Participant flow. DXA, Dual-energy X-ray absorptiometry.

2.6. Ethics statement

Although this was a retrospective observational study with anonymization in an unlinkable fashion, written informed consent was obtained from patients after our oral explanation.

This study was conducted with the approval of the ethics committee of the Adachi Kyosai Hospital (March 24th, 2016) (approval number: 2154). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

3. Results

The participant inclusion flow chart is shown in Fig. 1. The baseline characteristics is shown in Table 1. Thirty-seven patients (all female) were evaluated for safety. The mean age of the patients was 77.2 ± 4.4 years old. Of the 37 patients, 28 (75.7%) were undergoing concomitant vitamin D treatment. Change in BMD is

Table 1
Baseline characteristics.

Characteristic	Subject of the safety evaluation (n = 37)	Patients who measured all points (n = 10)
Age, yr	77.2 ± 4.4	76.6 ± 3.4
Height, cm	147.4 ± 4.6	147.6 ± 4.0
Body weight, kg	47.2 ± 6.3	47.6 ± 2.2
Body mass index, kg/m^2	21.7 ± 2.4	21.9 ± 1.2
Therapeutic agent before study (include overlap)		
Minodronic acid hydrate	13 (35.1)	4 (40.0)
Ibandronate sodium hydrate	3 (8.1)	0 (0)
Other bisphosphonate	8 (21.6)	4 (40.0)
SERM	8 (21.6)	2 (20.0)
Activated vitamin D	28 (75.7)	7 (70.0)
Calcitonin	21 (56.8)	3 (30.0)

Values are presented as mean ± standard deviation or number (%).
SERM, selective estrogen receptor modulators.