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Original article

Comparative effect of alendronate and teriparatide on bone mineral density and bone turnover among Japanese postmenopausal women with history of fragility fractures: A clinical practice-based observational study

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Abstract

A clinical practice-based observational study was performed to compare the outcome of alendronate (ALN) and teriparatide (TPTD) treatment among Japanese postmenopausal women with a history of fragility fractures. Sixty-one Japanese postmenopausal women with a history of fragility fractures were treated with ALN (35 mg weekly, n = 32) or TPTD (20 μg daily, n = 29) for 2 years in our outpatient clinic. Alfacalcidol (1 μg daily) was combined with ALN. The lumbar spine or total hip bone mineral density (BMD) was measured using dual energy X-ray absorptiometry, and bone turnover markers were monitored. ALN decreased the urinary levels of cross-linked N-terminal telopeptides of type I collagen (NTX) (38.3% after 3 months) and the serum levels of alkaline phosphatase (ALP) (25.7% at 24 months), whereas TPTD increased the serum levels of intact procollagen type 1 N-terminal propeptide (P1NP) and ALP (79% and 14.1%, respectively at 24 months). Both ALN and TPTD increased the lumbar spine BMD (8.8% and 15.9%, respectively) and sustained the total hip BMD at 24 months. One patient treated with ALN experienced vertebral fractures, and one patient treated with TPTD experienced a nonvertebral fracture. These results confirmed the differential effects of ALN and TPTD on bone turnover and the greater effect of TPTD on the BMD among Japanese postmenopausal women with a history of fragility fractures.

Keywords: Alendronate; Teriparatide; Bone mineral density; Postmenopausal women; Fragility fracture

1. Introduction

Osteoporosis most commonly affects postmenopausal women, placing them at a significant risk for fractures. Alendronate (ALN) is widely used for the treatment of postmenopausal osteoporosis. ALN reduces the incidence of vertebral, hip, and wrist fractures in postmenopausal osteoporotic women with existing vertebral fractures and the incidence of vertebral fractures in postmenopausal women with low bone mineral density (BMD) but without vertebral fractures [1,2]. Teriparatide (TPTD) is used for postmenopausal women with osteoporosis at a high risk of fractures [3]. TPTD dramatically increases bone formation and the lumbar spine, hip, and total-body BMD and effectively reduces the incidence of vertebral and nonvertebral fractures in postmenopausal women with osteoporosis [4]. Both medicines appear to be effective for reducing fragility fractures among postmenopausal women with established osteoporosis.

A randomized controlled trial (RCT) demonstrated the 1-year comparative effect of ALN and TPTD on the BMD and the incidence of nonvertebral fractures in postmenopausal women with osteoporosis [5]. TPTD is available for up to 2 years in Japan. To our knowledge, however, no data showing the 2-year comparative effect of ALN and TPTD on the BMD

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and bone turnover in Japanese postmenopausal women with established osteoporosis have been reported. Thus, a clinical practice-based observational study was performed to compare the outcome of ALN and TPTD treatment for a 2-year period among Japanese postmenopausal women with a history of fragility fractures. The primary endpoint was the BMD, and the secondary endpoints were the biochemical markers.

2. Subjects and methods

2.1. Subjects

Sixty-one postmenopausal women with a history of fragility fractures (mean age: 70.8 years) were treated with ALN (35 mg orally, weekly) (n = 32) or TPTD (20 μg subcutaneously, daily) (n = 29) for 2 years at the outpatient clinic of Keiyu Orthopaedic Hospital (Gunma, Japan) between March 2011 and December 2014. Alfacalcidol (1 μg orally, daily) instead of vitamin D supplementation was combined with ALN, because an RCT clarified the efficacy of ALN (5 mg daily) plus alfacalcidol (1 μg daily) versus ALN (5 mg daily) alone in postmenopausal women with severe osteoporosis who were aged 70 years or older and had several risk factors for incident fractures [6]; the combination therapy with ALN and alfacalcidol was more effective for fracture prevention in patients with severe vertebral deformity (semi-quantitative method: grade 3), multiple prevalent vertebral fractures, and for nonvertebral weight-bearing bone fracture prevention. Fragility fractures included vertebral, distal radius, proximal humerus, hip, pelvis, rib or lower leg fractures along with low BMD (<80% of the young adult mean [YAM]). In Japan, the %YAM is used instead of the T score for the diagnosis of primary osteoporosis [7]. The doses indicated in the parentheses are the doses used in Japan for the treatment of postmenopausal women with osteoporosis and have been recognized as being safe and effective [8−10]. The inclusion criteria were postmenopausal osteoporosis, and the exclusion criteria were secondary osteoporosis and other diseases that decrease the BMD [7,11,12]. None of the subjects had ever taken medication for the treatment of osteoporosis prior to the present study. Patients selected the treatment (ALN or TPTD) by themselves after the method of administration and the prices of the medicines had been explained: the monthly cost of TPTD (daily subcutaneous injection) and ALN (weekly internal use) were approximately 52,000 yen and 2600 yen, respectively. Adverse events of TPTD were explained by doctors: nausea, headache, and dizziness, and those of ALN were explained by pharmacists: upper gastrointestinal adverse events. Patients whose data were missing or incomplete were excluded, because they were not followed up adequately.

The preliminary screening included a medical history, physical examination, plain X-rays of the thoracic and lumbar spine, BMD measurements at the lumbar spine or total hip, and blood and/or urinary biochemical tests. Dual-energy X-ray absorptiometry (DXA) was used to measure the BMD of the lumbar spine or the total hip. The BMD was primarily measured at the lumbar spine, but was done at the total hip in patients with severe spondylosis, callus formation after vertebral fractures, and severe aortic calcification, which were thought to significantly affect the lumbar spine BMD. Thus, the lumbar spine BMD was measured in 55 patients and the total hip BMD was measured in 6 patients. Biochemical tests included measurements of the serum levels of calcium, phosphorus, and alkaline phosphatase (ALP) in the ALN and TPTD groups. The urinary levels of cross-linked N-terminal telopeptides of type I collagen (NTX) were measured in the ALN group, while the serum levels of intact procollagen type 1 N-terminal propeptide (P1NP) were measured in the TPTD group.

The serum levels of calcium, phosphorus, and ALP and the lumbar spine or total hip BMD were measured every 6 months after the start of treatment in both groups. The measurement of urinary NTX levels is permitted only twice (just before and within 6 months after the start of medication) in Japan because of health insurance regulations. Thus, we evaluated urinary NTX at 3 months after the start of treatment in the ALN group [13]. The serum intact P1NP levels were measured every 6 months in the TPTD group. After 2 years of treatment, plain X-rays of the thoracic and lumbar spine were taken to assess the incidence of vertebral fractures. The incidence of clinical fractures was also assessed. The outcome of ALN and TPTD treatment for 2 years was then evaluated. The present study was approved by the Ethics Committee of Keiyu Orthopaedic Hospital.

2.2. Assessment of vertebral fractures

Plain lateral X-ray films of the thoracic and lumbar spine were obtained at baseline to detect evidence of morphometric vertebral fractures. According to the Japanese criteria, a vertebral fracture was defined according to the vertebral height on lateral X-ray films [11,12]. Briefly, the vertebral height was measured at the anterior (A), central (C), and posterior (P) parts of the vertebral body, and the presence of a vertebral fracture was confirmed when (1) a reduction in the vertebral height of more than 20% (A, C, and P) compared with the height of the adjacent vertebrae was observed, (2) the C/A or C/P was less than 0.8, or (3) the A/P was less than 0.75. The assessment for vertebral fractures was performed at the T4−L4 level.

2.3. Assessment of clinical fractures

Low-traumatic osteoporotic clinical fractures were assessed. In particular, nonvertebral fractures in terms of major osteoporotic fractures at the distal radius, proximal humerus, hip, pelvis, rib or lower leg were determined, if any, based on clinical symptoms and radiographs.

2.4. Measurement of lumbar spine or total hip BMD

The BMD of the lumbar spine or the left total hip in the anteroposterior view was measured using DXA with a Hologic QDR Explorer apparatus (Bedford, MA, USA). The inappropriate spine within the lumbar (L1−L4) spine for the BMD