Safety and effectiveness of teriparatide vs alendronate in postmenopausal osteoporosis: a prospective non-randomized clinical study

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Summary

In this work we study the safety and effectiveness of teriparatide and alendronate in patients with postmenopausal osteoporosis at high risk of fracture; it was a double-blinded and it was done by examining the comparisons between teriparatide 20 μg/day and alendronate 10 mg/day. Safety and effectiveness analyses were based on data from 355 woman with a mean age of 68 years. Two groups (A and B) with T-score –2.5 at bone mineral density were analyzed and 3 or more vertebral fractures on radiograph. Group A: was treated with teriparatide 20 μg/day and composed from 182 women, in post-menopausal age, without a history of cancer. Group B: was treated with alendronate 10 mg/day composed from 173 women, postmenopausal age, with previous history of cancer (non-active during the study). Clinical evaluations were on bone turnover markers (alkaline phosphatase, procollagen type 1 N-terminal propeptide, and N-telopeptide cross-links), dual-energy X-ray absorptiometry and health-related quality of life (HrQoL). Safety was assessed by reporting of adverse drug reactions (ADRs). The results of this study imply that teriparatide compared with alendronate has a favorable safety profile and is effective in the treatment of patients with osteoporosis at high risk of fracture.

KEY WORDS: osteoporosis; teriparatide; alendronate; bone mineral density; vertebral fracture.

Introduction

The purpose of osteoporosis therapy is to reduce fracture risk. Osteoporosis is a serious public health concern worldwide because of the morbidity and mortality associated with fragility fracture (1, 2) which is expected to affect a large proportion of people (40-50% of women and 13-22% of men) over the age of 50 years. In 2010, osteoporosis was estimated to affect 27.6 million people in Europe. The treatment of osteoporosis consists of lifestyle measures and pharmacologic therapy. Lifestyle measures include adequate vitamin D and calcium, exercise, smoking cessation, counseling on fall prevention, and avoidance of heavy alcohol use. These measures should be adopted universally to reduce bone loss in postmenopausal women (3, 4). Once-daily administration of a parathyroid hormone fragment also increases bone mineral density in men with osteoporosis (5) and in estrogen-deficient women (6-8) and reduces the risk of fracture in postmenopausal women with osteoporosis (8). Whereas all other available treatments for osteoporosis reduce bone resorption, parathyroid hormone therapy increases bone formation. Teriparatide (recombinant 1-34 N-terminal sequence of human parathyroid hormone) is the first anabolic agent approved for the treatment of patients with osteoporosis (9) and has been reported to reduce the risk of fracture by increasing bone formation (10). It increases new bone formation by increasing osteoblast differentiation, osteoblast function, and survival. Teriparatide is recommended for patients with severe osteoporosis and can only be administered by once-daily injection in the thigh or abdomen. The recommended dose is 20 μg per day. The safety and efficacy of teriparatide has been assessed in randomized controlled trials (RCTs) and in observational studies conducted primarily in Caucasian populations. These studies have shown that teriparatide is well tolerated, reduces the risk of vertebral and non-vertebral fractures. It is known to increase bone formation and treatment of osteoporosis with PTH causes a marked increase in vertebral BMD (BMD) and levels of bone turnover biomarkers in osteoporotic patients (5-7). Alendronate belongs to the category of bisphosphonates. These have the ability to inhibit osteoclastic bone resorption. Alendronate increases bone mineral density and reduces the risk of fracture in women (3, 11) and men (9, 12) with osteoporosis. This reduces the risk of bone fractures. In our study we administered 10 mg of alendronate once daily. In the absence of specific contraindications, oral bisphosphonates are considered initial pharmacologic therapy for most postmenopausal women at high risk for fracture. We prefer oral bisphosphonates as initial therapy because of their efficacy, favorable cost, and the availability of long-term safety data.

Materials and methods

The study was conducted between January 2007 and November 2013. The cohort of 355 patients in postmenopausal age was divided into 2 groups that was selected with some inclusion and exclusion criteria, except previous history of cancer (non-acti-
Results

This study will focus on the femoral neck and the total hip, the regions of interest considered to be the most clinically relevant (13, 14). More than half (65.4%) of the patients in group 1 have reported one or more comorbidity. The most frequently reported comorbidities were hypertension (49.6%), hepatic impairment (8.6%), and rheumatoid arthritis (4.2%). Secondary osteoporosis and glucocorticoid-induced osteoporosis were each reported in 3.0% of patients. The patients of group B had in addition to one or more morbidity (72.2%), previous history of tumors. The most frequently comorbidities in this group were hypertension (52.2%), hepatic impairment (10.9%), and rheumatoid arthritis (3.0%). Secondary osteoporosis and glucocorticoid-induced osteoporosis were each reported in 5.1% of patients. The manifestation of adverse reactions into group A was reported in 15 (8.4%) patients. The most commonly reported ADRs in patients were hyperuricemia (1.04%), nausea (1.07%), dizziness (0.42%), headache (0.61%). Into group B, which took alendronate, the rate of adverse reactions was reported in 18 (10.3%) patients. In this group also the most commonly reported ADRs were hyperuricemia (2.16%), nausea (1.12%), dizziness (0.38%), headache (0.71%). There were no significant adverse reactions in any patient in both groups. In this study was to evaluate percentage changes from baseline in biochemical markers of bone turnover, values of bone mineral density (measured at lumbar spine and proximal femur), VAS scale, incidence of new fractures and measurements of HrQoL. There are differences between the results of bone turnover, among those obtained with the administration of alendronate and the administration of teriparatide. The levels of biomarkers for bone formation (PINP, bone ALP) were significantly increased from baseline at all time points during the study. In group A serum levels of PINP increased of 152 and 134% at T12, T24, respectively; bone ALP levels increased of 83 and 69%; NTx levels increased of 102% at T12, of 116% at T24. In group B percent-age changes from baseline of serum levels of PINP were –70 and –75% at T12, T24, respectively; bone ALP levels decreased of 48 and 41%; NTx levels were reduced by 70% at T12, of 74% at T24.

Mean PINP values were 41±7 μg/l at T0, 102±35 μg/l at T12, 97±27 μg/l at T24 in group A (T0 vs T12 r: 0.88, p<0.001; T0 vs T24 r: 0.86, p<0.001) and 78±16 μg/l, 22±14 μg/l, 18±10 μg/l at T0, T3, T12, T24 respectively (T0 vs T12 r: 0.76, p<0.001; T0 vs T24 r: 0.82, p<0.001). In group A mean ALP value at T0 was 68±20 U/L, 120±48 U/L at T12 and 115±38 U/L at T24 (T0 vs T12 r: 0.46, p<0.01; T0 vs T24 r: 0.85, p<0.001); instead, in group B mean ALP was 72±15 U/L at T0, 15±10 U/L at T12 and 41±6 U/L at the end of the study (T0 vs T12 r: 0.53, p<0.001; T0 vs T24 r: 0.65, p<0.001). NTx mean values in group A were 32±6 nmol/mmol Crea, 64±14 nmol/mmol Crea, 67±25 nmol/mmol Crea at T0, T12, T24 respectively (T0 vs T12 r: 0.58, p<0.001; T0 vs T24 r: 0.50, p<0.01) while in group B NTx mean values were 54±6 nmol/mmol Crea at T0, 22±15 nmol/mmol Crea at T12 and 17±10 nmol/mmol Crea at T24 (T0 vs T12 r: 0.58, p<0.001; T0 vs T24 r: 0.70, p<0.001). The BMD values expressed in terms of T-score in our total pool displayed important changes. At month 24, lumbar spine BMD increased by 14.2% in group A compared with group B in which it increased by 4.96%. Specifically, in group A mean T-score at T0 was –3.88±0.70 and mean T-score at T24 was –3.37±0.60 (r: 0.88; p<0.001); instead, in group B, mean T-score at T0 was –3.87±0.75 and mean T-score at T24: –3.72±0.74 (r: 0.98; p<0.001). Back pain significantly (P<0.001) improved from baseline at all time points during the study. In the group A the mean (SD) back pain VAS score at baseline was 40.9 (27.7). The mean (95% CI) change from baseline in back pain VAS scores at 3, 12, 18, and 24 months and in the Last observation carried forward (LOCF) were –10.1 (–12.5 to –7.7), –12.4 (–15.0 to –9.1).
Teriparatide increased remodelling, removed old, more fully mineralised bone matrix and replaced it with new, less fully mineralised bone matrix and improved fracture healing. Surgical fixation did not protect the others bone from probably new fracture, for this reason, are required therapies, able to enhance the bone structure at the systemic level. Therefore, this study evidences that teriparatide represents compared with alendronate, a solution that guarantees of the finest results in severe postmenopausal osteoporosis.

Author contributions

All Authors were involved in the study design, data collection, data interpretation, and statistical analysis, and contributed to the drafting of the manuscript.

Ethical considerations

This study was performed with informed consent of patients and following all the guidelines for experimental investigation with human and animal subjects in accordance with the ethical standards of the institutional and /or national research committees and the Helsinki Declaration of 1975 and the 1983 revision of the same.

Discussion

The effect of teriparatide to increase bone formation, as demonstrated by studies of iliac crest biopsies, bone scans, and positron emission tomography, would be anticipated to increase bone mass and hence BMD. Areal BMD assessed by DXA at the spine and proximal femur is a standard means of identifying patients with osteoporosis, and response to therapy is often assessed by serial BMD testing (1, 15). Teriparatide was shown to have favorable safety and effectiveness profiles in osteoporotic patients at high risk of fracture. Importantly, teriparatide was well tolerated, with no new clinically significant safety concerns identified, and persistence with teriparatide treatment was similar to or higher than that reported in other studies (16, 19). Early significant increases in bone formation biomarkers were followed by subsequent increases in bone resorption biomarkers. Treatment with teriparatide resulted in a greater increase in bone mineral density (BMD). After 24 months women of group A with severe osteoporosis (mean lumbar BMD = −4.01±0.53, mean femoral neck BMD = −3.37±0.60 and with 3 or more vertebral fractures), persistent back pain and previous treatment with bisphosphonates for osteoporosis; and the women belonging group B with menopausal status, affected by back pain, severe postmenopausal osteoporosis (lumbar spine BMD = −3.98±0.46, mean femoral neck BMD = −3.21±0.72 and with 3 or more vertebral fractures) were already treated for osteoporosis with bisphosphonates, we compared the results obtained from patients in group A compared to group B. From this comparison showed that teriparatide has previously treated for osteoporosis with bisphosphonates, we compared those receiving alendronate.

Conclusion

Teriparatide increased remodelling, removed old, more fully mineralised bone matrix and replaced it with new, less fully mineralised bone matrix and improved fracture healing. Surgical fixation did not protect the others bone from probably new fracture, for this reason, are required therapies, able to enhance the bone structure at the systemic level. Therefore, this study evidences that teriparatide represents compared with alendronate, a solution that guarantees of the finest results in severe postmenopausal osteoporosis.
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