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Original Research Article

Comparison of the Effects of Teriparatide & Alendronate in Postmenopausal Women Suffering from Osteoporosis

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Abstract:

Background: Osteoporosis is a skeletal disorder largely affecting postmenopausal women. It decreases the bone mineral density & deteriorates the bone architectures leading to frequent fractures & low quality of life.

Aims & Objectives: to evaluate the efficacy of Teriparatide & Alendronate in improving the bone mineral density and biochemical markers of bone turnover in postmenopausal women suffering from osteoporosis

Material & Methods: This prospective randomized study was conducted in the Department of Orthopedics, of our tertiary care hospital for 12 months from March 2022 to October 2023. The study recruited 70 postmenopausal women (Age range 30-65yrs) with osteoporosis suffering from back pain. The recruited women were divided into two groups: Group A: 20 µg S.C. of recombinant human parathyroid hormone (rhPTH 1–34) injections once daily (n=35). Group B: 10 mg orally of alendronate, once daily (n=35). Both Groups received 1,000 mg of elemental calcium daily and 800 IU of vitamin D daily for 18 months. At baseline & each visit, serum alkaline phosphatase (ALP), urinary cross-linked N-telopeptides corrected for creatinine (NTX), and serum 1,25-dihydroxyvitamin D were measured. Serum calcium levels were estimated 4–6 h after injection at each visit. The BMD of the lumbar spine and the proximal femur was measured by dual-energy X-ray absorptiometry at baseline and 12 months.

Results: On intragroup comparison, at 12 months, the BMD increased significantly in the postmenopausal women in both Group A & Group B($p<0.05$). On intergroup comparison, BMD at lumberspine was significantly higher in Group A than in Group B at 12 months ($p<0.05$). The percentage increase in lumber spine BMD in Group A was 3.6% more than in Group B ($p<0.05$), which increased to 9.2% at the end of 12 months. Group A observed a mean fracture of 2±1.4 and in Group B it was 4±2.7. About 4.7% of women observed back pain in Group A as compared to 21.5% in Group B. ALP & NTX increased significantly in Teriparatide groups at all time intervals while it decreased in Alendronate group ($p<0.05$).

Conclusion: Teriparatide exerted significant anabolic effects with a resultant increase in bone mineral mass & reduction of fracture risk as compared to alendronate with minimal side effects.

Keywords: Postmenopausal women, Osteoporosis, Teriparatide, Alendronate.

Introduction

In elderly women, Osteoporosis is the most common bone disease post-menopause which leads to fractures & considerable morbidity & financial loss. [1] .According to the World Health Organization (WHO), 30 % of postmenopausal women suffer from osteoporosis [2]. Khinda et al study 2022 observed the prevalence of osteoporosis to be 30.50%, in postmenopausal women of Punjab. [3, 4] Globally, every 1 in 3 women & 1 in 5 men past the age of 50 will be going to experience osteoporotic fractures. [5]

Treatments for osteoporosis include improving the bone mass & strength, thus decreasing the fractures. These include antiresorptive agents like bisphosphonates and selective estrogen receptor modulators. [6] Bisphosphonates are the first line of treatment that directly reduces the number and activity of osteoclasts, thereby reducing bone turnover, including bone formation. Thus, a positive bone balance is reached, following which a new equilibrium is established at a reduced turnover rate, increased bone mineral density (BMD) & deposition. [7]

Another potent bone formation agent is Teriparatide (rDNA origin) injection. It is the amino-terminal fragment of human parathyroid hormone. It acts on osteoblasts & increases their formation rate & prevents apoptosis, thus the

number of osteoblasts increases & the rate of new bone formation increases. Studies have demonstrated that daily administration of Teriparatide injection subcutaneously increases bone density and improves trabecular architecture, cortical geometry, and strength. [8]

A recent meta-analysis by Yuan F et al 2019 comparing Teriparatide & Bisphosphonates concluded Teriparatide to be having good efficacy in reducing vertebral fracture risk in postmenopausal women with osteoporosis. It also increases the bone mineral density(BMD) in the lumbar spine and femoral neck with a long duration of use. [9] Fan G et al 2020 stated teriparatide significantly reduces the incidence of vertebral and nonvertebral fractures in osteoporosis patients.

Thus this study aimed to evaluate the efficacy of Teriparatride & Alendronate in improving the bone mineral density and biochemical markers of bone turnover in postmenopausal women suffering from osteoporosis (measured at lumbar spine and proximal femur).

Material & Methods

This prospective randomized study was conducted in the Department of Orthopedics, of our tertiary care hospital for 12 months from March 2022 to October 2023. The study recruited 70 postmenopausal women (Age range 30-65yrs) with osteoporosis suffering from back pain. (T-score ≤–2.5 at the lumbar spine or femoral neck), the presence of 2 osteoporotic vertebral fractures, previous treatment for osteoporosis. Women with an increased risk of osteosarcoma malignancy, hypercalcemia, comorbid diseases, kidney disease, and liver disease were excluded. Written informed consent was obtained from all the study participants. The study protocol was approved by the Institutional Ethical Committee.

The recruited postmenopausal women were divided into two groups:

Group A: 20 μg s.c. of recombinant human parathyroid hormone (rhPTH 1–34) injections once daily (n=35)

Group B: 10 mg orally of alendronate, once daily (n=35)

Both Groups received 1,000 mg of elemental calcium daily and 800 IU of vitamin D daily for 18 months

For all the patients, sociodemographic details, body mass index(BMI), age at menopause, smoking, alcohol & drug abuse, history of fractures, and family history of osteoporosis were recorded. Venous blood was drawn & sent to the laboratory to assess biochemical markers of bone turnover at baseline, 3, 12, and 18 months. At baseline & each visit, serum alkaline phosphatase (ALP), urinary cross-linked N-telopeptides corrected for creatinine (NTX), and serum 1,25-dihydroxyvitamin D were measured. Serum calcium levels were estimated 4–6 h after injection at each visit. The BMD of the lumbar spine and the proximal femur was measured by dual-energy X-ray absorptiometry at baseline and 12 months. Anteroposterior and lateral radiography of the thoracic and lumbar spine was also done at baseline & 12 months.

Statistical Analysis

The study data was tabulated & statistically analyzed using SPSS version 22.0 for Windows (IBM Corp, India). Quantitative data are presented as mean ± SD. Intergroup comparisons were made using Student's paired t-test. A P-value of 0.05 at a 90% confidence interval was considered to be statistically significant.

Results

This prospective cohort study recruited 70 postmenopausal women with osteoporosis. Both groups were comparable with respect to baseline characteristics. (Table 1) All the patients completed the study protocol & none was lost to follow-up.

Table 1

Demographic characteristics	Group A (n=35)	Group B (n=35)	P value
Age (yrs)	63±8	65±7	>0.05
BMI	24.6±4.2	26.1±3.5	>0.05
History of fractures	32	30	>0.05
Back pain	35	35	>0.05

On intragroup comparison, at 12 months, the BMD increased significantly in the postmenopausal women in both Group A & Group B($p<0.05$). On intergroup comparison, BMD at lumberspine was significantly higher in Group A than in Group B at 12 months ($p<0.05$).

The percentage increase in lumber spine BMD in Group A was 3.6% more than in Group B ($p<0.05$), which increased to 9.2% at the end of 12 months. Fracture percentage reduced significantly in Group A as compared to Group B ($p<0.05$). Group A observed a mean fracture of 2±1.4 and in Group B it was 4±2.7. No difference between the incidences of adverse events observed in both the groups. About 4.7% of women observed back pain in Group A as compared to 21.5% in Group B . ALP & NTX increased significantly in Teriparatide groups at all time intervals while it decreased in Alendronate group ($p<0.05$). Serum calcium levels

& 25-hydroxyvitamin D increased in both groups with a higher increase in Group A. Serum PTH levels decreased significantly in both groups($p<0.05$). (Table II)

Table 2

Outcome Measures	Group A	Group B	P value
BMD at lumber spine	9.5%	6.2%	($p<0.05$)
NTX (12 months)	110% Increase	Decrease 48.9%	($p<0.05$)
			($p<0.05$)
ALP (12 months)	90% Increase	Decrease 50%	($p<0.05$)
			($p<0.05$)
Serum calcium at 6 months	10 (mg/dl)	9.1 (mg/dl)	($p<0.05$)
Serum PTH (at 1 yr)	Decrease	Decrease	($p<0.05$)
Fracture (Mean ±SD)	2±1.4	4±2.7	($p<0.05$).
Back pain	4.7%	21.5%	($p<0.05$)

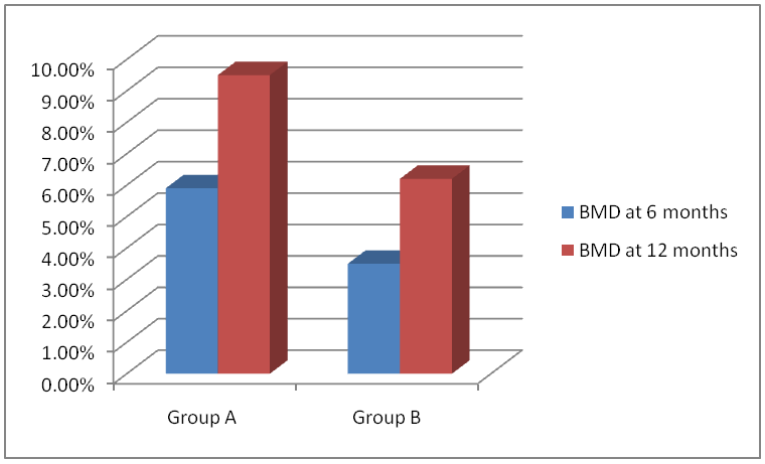

Figure 1: Depicts the BMD at the lumber spine at 6 months & 12 months

Discussion

Teriparatide is a recombinant fragment of human PTH, which consists of its first amino(N)-terminal 34 amino acids. It acts as a potent osteoanabolic agent. It has a positive effect on bone size with direct effects on cortical bone &bone architecture.[11] Numerous trials have been conducted proving its safety & efficacy in the treatment of osteoporosis. [9,10]

In the present study, both groups were comparable with respect to baseline characteristics. On intragroup comparison, at 12 months, the BMD increased significantly in the postmenopausal women in both Group A (Teriparatide) & Group B (Alendronate) ($p<0.05$). On intergroup comparison, BMD at lumberspine was significantly higher in Group A than in Group B at 12 months ($p<0.05$). The percentage increase in lumber spine BMD in Group A was 3.6% more than in Group B ($p<0.05$), which increased to 9.2% at the end of 12 months.

Similarly, Body et al. 2002 study observed once-daily 40 µg teriparatide s.c. injections in postmenopausal women with osteoporosis significantly increased BMD at the lumber spine & hip as compared to 10 mg alendronate. BMD at the trochanter, also significantly increased above baseline. [11] The difference between BMD at lumber spine was statistically significant at 3 months between both the groups. [12] Wang et al 2017, in a meta-analysis involving 618 patients concluded a significant increase in lumbar spine BMD, but not femoral neck BMD, in postmenopausal women from 6 to 18 months. The results were evident in the lumbar spine at 12 months of treatment. [13] In a meta-analysis by Yuan et al 2019, teriparatide was observed to be associated with a decreased risk of vertebral fractures with a mean percent change in BMD of the lumbar spine at 6 months, 12 months and 18 months than bisphosphonates ($p< 0.05$). Also, teriparatide was effective in improving the mean percent change in BMD in the femoral neck at 18 months ($P < 0.05$). No significant difference was observed in terms of adverse events in both groups. [9]

In the present study, the mean fracture percentage reduced significantly in Group A (Teriparatide)as compared to Group B (alendronate). Group A observed a mean fracture of 2±1.4 and in Group B it was 4±2.7($p<0.05$). Accordingly, in a randomized controlled trial conducted by Neer et al 2001, in postmenopausal women with at least one

prior vertebral fracture, 20 mcg of teriparatide administered daily significantly decreased the risk for new vertebral fractures by 65% & nonvertebral fragility fractures by 53%. It significantly increased BMD at the lumbar spine by 9% and at the femoral neck by 3% over a follow-up period of 21 months. [14] A meta-analysis by Wang et al 2017 concluded Teriparatide is not superior to alendronate in the reduction of fracture risk. [13]

In the present study, ALP & NTX increased significantly in Teriparatide groups at all time intervals while it decreased in the Alendronate group ($p<0.05$). Both drugs affect the BMD by different mechanisms as is evident by changes in the bone turnover markers. Teriparatide increases trabecular bone volume and cortical thickness and restores trabecular connectivity (11), whereas alendronate increases the mineralization of the existing bone matrix. Similar findings were observed in the Body et al study. [12]

In a meta-analysis by Yuan et al 2019, teriparatide was observed to be associated with a decreased risk of vertebral fractures with a mean percent change in BMD of the lumbar spine at 6 months, 12 months and 18 months than bisphosphonates ($p< 0.05$). Also, teriparatide was effective in improving the mean percent change in BMD in the femoral neck at 18 months ($P < 0.05$). No significant difference was observed in terms of adverse events in both groups. [9]

Both the drugs were well tolerated by the patients. No difference between the incidences of adverse events observed in both the groups. About 4.7% of women observed back pain in Group A as compared to 21.5% in Group B . Similarly, Body et al study 2002, observed more leg cramps & fewer incidences of back pain in the teriparatide group as compared to the alendronate group. [12] Neer et al 2001 study, concluded a significant reduction in back pain which was observed to be associated with an 80–90% reduction in the risk of vertebral fractures with teriparatide. [14]

Conclusion

Thus the present study, Teriparatide is a potent anabolic agent, effective in increasing the bone mineral density at the lumber spine & proximal femur. Teriparatide also decreases the risk of vertebral fractures & adverse events with both drugs were comparable. Alendronate also increases the bone mineral density significantly above the baseline but showed inferior results as compared to Teriparatide.

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