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Original Article

Raloxifene in Reducing the Risk of Postmenopausal Fracture amongst Osteoporotic Subjects

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ABSTRACT

Background: *Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent decrease in bone mineral density (BMD) and increase in bone fragility and susceptibility to fracture. Hence; we planned the present study to assess the effect of raloxifene in reducing the risk of postmenopausal fracture amongst osteoporotic subjects.*

Methods: *The present study included assessment of effect of raloxifene in reducing the risk of postmenopausal fracture amongst osteoporotic subjects. A total of 120 postmenopausal women were included in the present study. All the subjects were broadly divided into two broad groups with 60 subjects in each group; Group A: Subjects who were given placebo for two years Group B: Subjects who were given raloxifene 60 mg/d for 2 years. Assessment of Risk of Postmenopausal Fracture in all the subjects was done by evaluating the bone mineral density (BMD) at two years follow-up time. All the results were compiled and assessed by SPSS software.* ***Results:*** *Non- significant results were obtained while comparing the adverse effects among subjects of both the study groups. Overall incidence of new vertebral fractures among subjects of group A and group B included 6 and 4 percent respectively. Significant results were obtained while comparing the incidence of new vertebral fractures among subjects of group A and group B respectively.* ***Conclusion****: Significant reduction in the risk of fractures occur under the influence of raloxifene in postmenopausal women with osteoporosis.*

Key words: *Bone mineral density, Postmenopausal, Raloxifene*

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INTRODUCTION

Bone remodelling is a dynamic process that repairs microfractures and replaces old bone with new bone. In the last 10 years there has been a remarkable understanding of bone biology so that new therapies can be specifically designed on a biological basis. The realization that RANKL was the final cytokine involved in the resorption process and that marrow cells produced a natural antagonist called Osteoprotegerin (OPG) quickly led to two lines of therapy.[1-3]

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent decrease in bone mineral density (BMD) and increase in bone fragility and susceptibility to fracture.[4-7] Aim of the present study to assess the effect of raloxifene in reducing the risk of postmenopausal fracture amongst osteoporotic subjects.

Hence; we planned the present study to assess and compare two different management protocols for treating patients with multiple knee ligament injuries.

METHODS

The present study was conducted in the Department of Orthopaedics, S.P. Medical College, Bikaner, Rajasthan,

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India. It included assessment of effect of raloxifene in reducing the risk of postmenopausal fracture amongst osteoporotic subjects. A total of 120 postmenopausal women were included in the present study. Inclusion criteria for the present study included:

- Subjects with postmenopausal status for a minimum of 4 years,
- Subjects with positive history of osteoporosis,

All the subjects were broadly divided into two broad groups with 60 subjects in each group;
Group A: Subjects who were given placebo for two years
Group B: Subjects who were given raloxifene 60 mg/d for 2 years.
Assessment of Risk of Postmenopausal Fracture in all the subjects was done by evaluating the bone mineral density (BMD) at two years follow-up time. All the results were compiled and assessed by SPSS software. Chi—square test was used for assessment of level of significance. P- value of less than 0.05 was taken as significant.

RESULTS

Table 1 shows the characteristic of the subjects. Mean age of the subjects of group A and group B was 58.4 years and 59.8 years respectively. Bone mass index of the subjects of the group A and group B was 24.3 and 25.7 Kg/m^2. Mean BMD of the femoral neck of the subjects of group A and group B was 0.69 and 0.68 respectively. Commonly observed adverse effects among subjects of both the study groups included hypertension, Bradycardia, and leg cramps. Non-significant results were obtained while comparing the adverse effects among subjects of both the study groups. Overall incidence of new vertebral fractures among subjects of group A and group B included 6 and 4 percent respectively. Significant results were obtained while comparing the incidence of new vertebral fractures among subjects of group A and group B respectively.

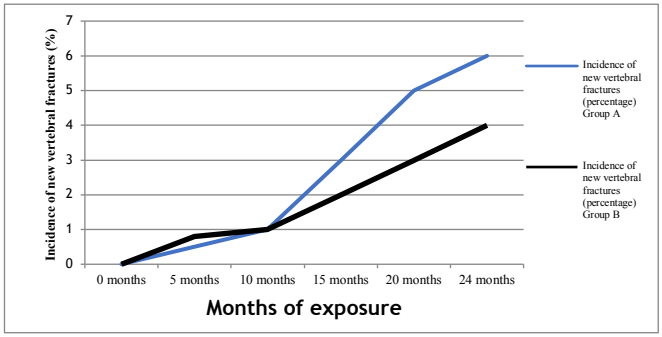
Table 1. Characteristics of the subjects

Characteristics	Group A	Group B
Mean age (years)	58.4	59.8
Body mass index (Kg/m^2)	24.3	25.7
Femoral neck BMD (gm/cm^2)	0.69	0.68

Table 2. Adverse effect

Adverse effect	Group A (n)	Group B (n)	P- value
Hypertension	6	5	0.52
Bradycardia	2	1	
Leg cramps	7	6	
Others	3	3	

P- Value < 0.05



Graph 1: Incidence of new vertebral fractures

DISCUSSION

In the present study, bone mass index of the subjects of the group A and group B was 24.3 and 25.7 Kg/m^2. Mean BMD of the femoral neck of the subjects of group A and group B was 0.69 and 0.68 respectively. Commonly observed adverse effects among subjects of both the study groups included hypertension, Bradycardia, and leg cramps. Non-significant results were obtained while comparing the adverse effects among subjects of both the study groups. Johnell O et al examined whether past use of hormone therapy influences the effects of raloxifene on the risk of new vertebral fracture, cardiovascular events, or breast cancer. The Multiple Outcomes of Raloxifene Evaluation (MORE) trial examined vertebral fracture incidence as the primary endpoint, breast cancer incidence as a secondary endpoint. Cardiovascular events were collected as secondary safety endpoints. The MORE trial enrolled 7705 postmenopausal women. Of the 7682 women who reported their previous HT use status, 29% used HT before screening. Separate logistic regression models analyzed the relationships between prior HT use and the risk of vertebral fracture, cardiovascular events, or breast cancer. Raloxifene 60 mg/d, the clinically approved dose for osteoporosis prevention and treatment, reduced the risk of vertebral fractures by 54% (RR=0.46) and 29% (RR=0.71) in women with and without prior HT use, respectively (interaction P=.05). A lower incidence of invasive breast cancer in women with prior HT use (RR=0.23) and in women without prior HT use [RR=0.31; interaction P=.60] was observed in women receiving raloxifene (pooled doses). Irrespective of prior HT use, women treated with raloxifene (pooled doses) had no change in incidence of cardiovascular events (interaction P=.56). The risk of vertebral fractures was lower in women treated with raloxifene, regardless of prior HT use, but there was a suggestion that the effect was greater in women who had used HT.[8] Ensrud KE et al examined whether the effect of raloxifene treatment on fractures was consistent across categories of fracture risk. In The Raloxifene Use for The Heart (RUTH) trial, women assigned to raloxifene had a lower risk of clinical vertebral fractures but not nonvertebral fractures. However, it is uncertain whether the effect of raloxifene on fractures in this population not selected for low BMD differs according to risk factors for fractures. They randomly assigned 10,101 postmenopausal women >or=55 yr of age with documented coronary heart disease or at high risk for coronary events to 60 mg raloxifene daily or placebo and followed them for a median of 5.6 yr. Fractures (nonvertebral and clinical vertebral) were prespecified secondary endpoints that were reported at semi-annual visits. Fractures were adjudicated and confirmed using X-ray reports or medical records. In older women with or at high risk of coronary heart disease not selected on the basis of osteoporosis or increased fracture risk, treatment with raloxifene for 5 yr reduced the risk of clinical vertebral fractures, but not nonvertebral fractures, irrespective of presence or absence of risk factors for fracture.[9]
Overall incidence of new vertebral fractures among subjects of group A and group B included 6 and 4 percent respectively. Significant results were obtained while comparing the incidence of new vertebral fractures among subjects of group A and group B respectively.
Teriparatide and raloxifene reduce the risk of new adjacent vertebral fractures in postmenopausal women with osteoporosis. Results from two randomized controlled trials.

Bouxsein ML et al determined the influence of the number and severity of prevalent (pre-existing) vertebral fractures on the risk of new adjacent vertebral fractures and to determine whether teriparatide (rhPTH [recombinant human parathyroid hormone]) or raloxifene treatment reduces the incidence of adjacent vertebral fractures in postmenopausal women with osteoporosis. Data from the Fracture Prevention Trial and the Multiple Outcomes of Raloxifene Evaluation trial were analyzed to determine the incidences of new adjacent and new nonadjacent vertebral fractures in the placebo groups and the effect of treatment with raloxifene and teriparatide on the incidence of new adjacent vertebral fractures as compared with that of new nonadjacent vertebral fractures. Of 1226 untreated postmenopausal women with one or more prevalent vertebral fractures at baseline, 196 (16.0%) had a total of 292 new vertebral fractures during the two-year follow-up period, with 108 (8.8%) of the 1226 women having at least one new fracture adjacent to a prevalent fracture. Of the 292 new vertebral fractures, 136 (47%) were adjacent to a previously existing vertebral fracture. The risk of a new adjacent vertebral fracture was 2.5-fold higher than the risk of a new nonadjacent vertebral fracture (4.03% compared with 1.59%). The incidence of new adjacent vertebral fractures increased with both the number and the severity of prevalent vertebral fractures.

Teriparatide reduced the risk of any new, new adjacent, and new nonadjacent vertebral fractures by 72%, 75%, and 70%, respectively, compared with the rates in the placebo group. In untreated postmenopausal women with osteoporosis, nearly half of the incident vertebral fractures occur adjacent to an existing vertebral fracture.

Both teriparatide and raloxifene can significantly reduce the occurrence of new adjacent and nonadjacent vertebral fractures.

CONCLUSION

Under the light of above mentioned results, the authors concluded that significant reduction in the risk of fractures occur under the influence of raloxifene in postmenopausal women with osteoporosis.

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