ORIGINAL ARTICLE

Effect of Raloxifene on T Score of Bones in Post Menopausal Women

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ABSTRACT

Aim: To study the effect of 60 mg/ day Raloxifene on bone mineral density in post menopausal women in one year.
Study design: A case control study conducted among 30 cases at Defence Hospital and Surgimed Hospital, Lahore from 2011 to 2012.
Inclusion Criteria: Age > 50 years, taking 60mg/day Raloxifene >1 year, Menopause > 1 year
Exclusion Criteria: Age < 50 years, Bone pathologies, Drug intake, Endocrine pathologies
Methods: The patients were divided in two groups; group 1 taking Raloxifene 60 mg/ day for > 1 year, group 2 not taking Raloxifene. All patients were given a questionnaire about age, parity, history of pain & fractures, height shortening, awareness about preventive measures. Then T score of calcaneum bone of both groups measured in OPD by machine. In both the groups value of t score, questionnaire and various bone problems like pain, fracture, height shortening was noted and evaluated statistically, $p < 0.05$ was significant.
Results: There were significantly different results in group 1 and 2. In group 1, t scores were better about above 1.5 (p=0.00), less fractures (n=4) 4% (p=0.003) and no height shortening (n=0) p=0.001 as compared to group 2, whereas pain (n=20) 67% p=0.266 in group 1 and in group 2 (n=22) 76% not significant in both groups.
Conclusion: Raloxifene 60 mg/ day significantly increases bone mineral density after 12 months of therapy.
Keywords: Osteoporosis, Raloxifene, post menopausal

INTRODUCTION

Osteoporosis is most common metabolic bone disease emerging as health problem in ageing post menopausal woman, due to increased life expectancy from recent advances in biomedical research. The severity of problem can be understood by these facts about osteoporosis that by the age of 70 years percentage loss of bone mass among woman is 50% as compared 20% among men. By 80 years of age 25% women have hip fractures out of which 20% are dead within a year and 25% disabled for life. Only 30% are fully recovered. Death rate from hip fracture is more than cancer of breast and endometrium combined.

Osteoporosis is histologically characterized by low bone mass and deterioration in bone architecture which predisposes to fragility fractures. The dynamic tissue of bone undergoes bone remodeling cycle initiated by osteoclast, which secrete hydrochloric acid and cathepsin k dissolving bone mineral and collagen respectively. It is followed by osteoblastic activity laying bone matrix, which then undergoes mineralization. There is balance of osteoclastic and osteoblastic activity. Osteoclastogen is under control of receptor activator of nuclear factor – k b (RANK) whose expression and production increases at menopause when estrogen concentration drops by 75%. Rank also increases in cases of rheumatoid activities, multiple myeloma, periodontal disease, osteolytic bone metastasis, and drugs like tamoxifene.

Bone mineral density measured by dual energy x-ray absorption (DE XA). The bone mass can be measured by ultrasound of calcaneum bone by T score, if less than -2.5 signifies osteoporosis. -1 and -2.5 shows osteopenia whereas 0+0 1 is considered to be normal.

MATERIAL & METHODS

A case control study was conducted among 60 post menopausal women coming to gynae OPD from July 2011 to July 2012. Post menopausal women > 50 year taking Raloxifene 60 mg/ day for the year with menopause > 1 year were included while women < 50 years, bone diseases, endocrine disorder and drug intake were excluded from the study. All patients were divided into two groups, Group 1 taking

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Raloxifene > year and Group 2 served as control taking no medicine or placebo. A questionnaire was given to all patients. Data was obtained about age, obstetrical history, menopausal year, history of bone pain and fractures, height shortening, awareness about preventive measures. Then the t score of calcaneum bone was measured by machine and values were recorded. In both the groups t score value, effect of Raloxifene on bone pain, fractures, height shortening and questionnaire was evaluated statistically and $p < 0.05$ was considered significant.

RESULTS

Table 1: There were total 60 patients, 30 cases in group 1 and 30 in group 2. When the results of questionnaire were compared, it was noted that age, parity and year of menopause did not affect t score among both groups as (p=0.08), (p=0.5) (p=0.31) respectively. The level of awareness was significantly (p=0.00) different n=25 (83%) in group 1, and n=15 (46%) in group 2 affecting the t score among both the groups. Similarly the preventive measures taken like diet, exercises, calcium and vit. D intake in both the groups significantly (p=0.000) affected bones as in group 1 n=26 (84%) and in group 2 n=4(10%) were taking these preventive measures.

Table 1:

	Cases (n=30)	Control (n=30)	P value
Age	64	65	0.008
Menopausal year	7	8	0.5
OBH	5	4	0.31
Awareness	25(83%)	15(46%)	0.00
Prevention	26(84%)	4(10%)	0.000

Graph 2, it shows the comparison in t scores values plotted graphically among group 1 and group 2. There is an obvious significant difference p=0.000 in bone loss among two groups. The t score of all patients group 1 (taking Raloxifene > 1 year) were above 1.5 showing effectiveness of SERM in storing bone mass and preventing resorption. In the group 2 majority of patients trace t score less than (-2) and have developed osteoporosis.

Comparison of bone mineral density (P = 0.00)

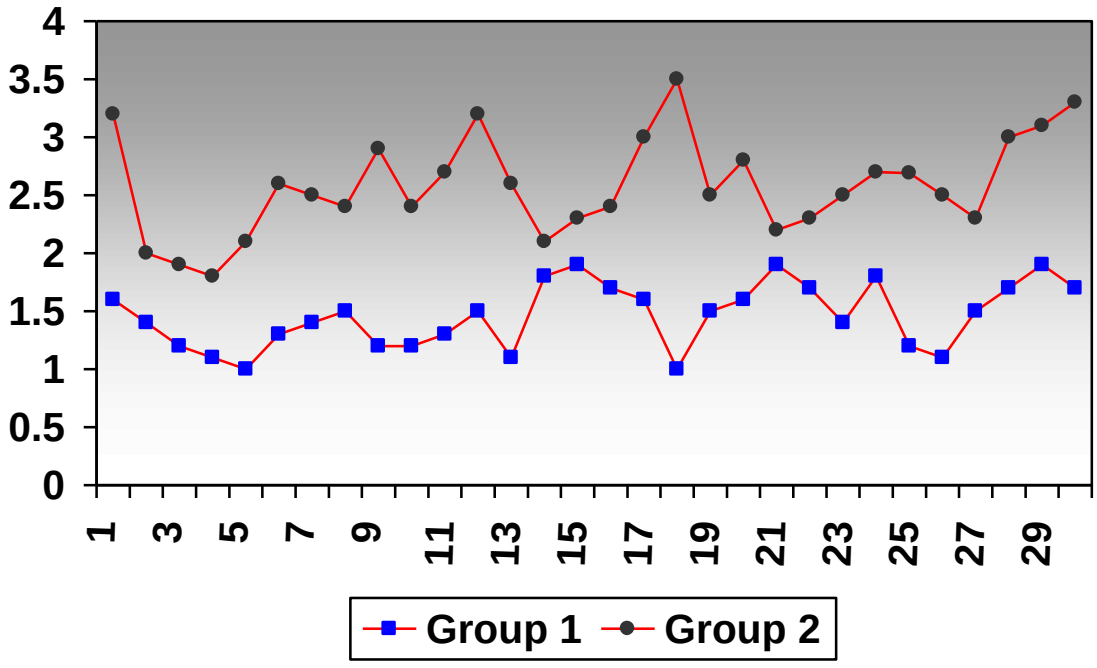


Fig. 1 shows the effect of Raloxifene in women on fractures shows significant increase (p=0.003) in fracture in group 2 n=26 (87%) as compared to n=4 (13%) in group 1 respectively.

Fig. 1: Fractures

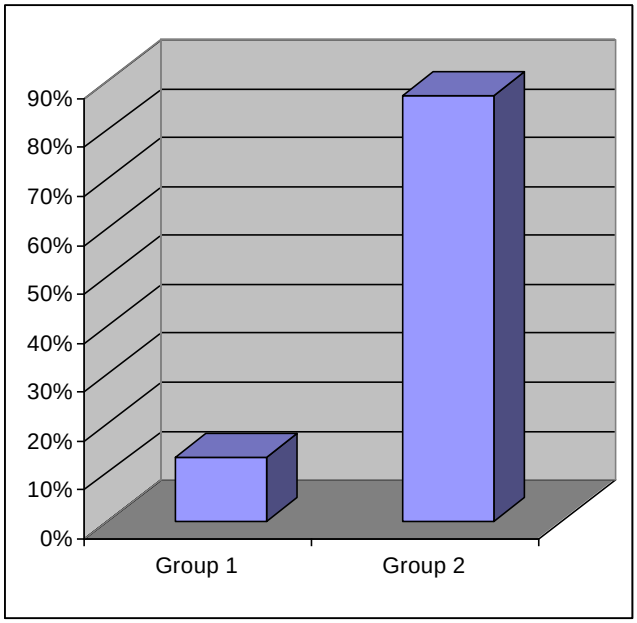


Fig. 2 shows effect of Raloxifene on height showing there was no height shortening n=0 (0%) in group 1 whereas in group 2 there was significant (p=0.01) n=24 (85%) cases of height shortening.

Fig 2: Height shortening

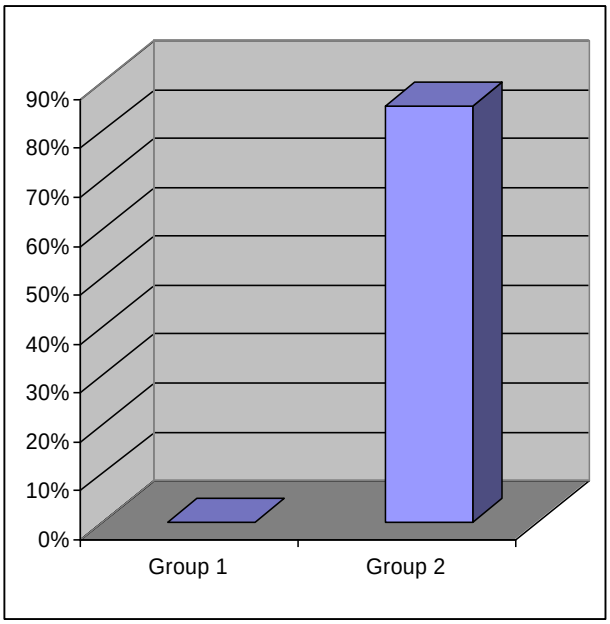
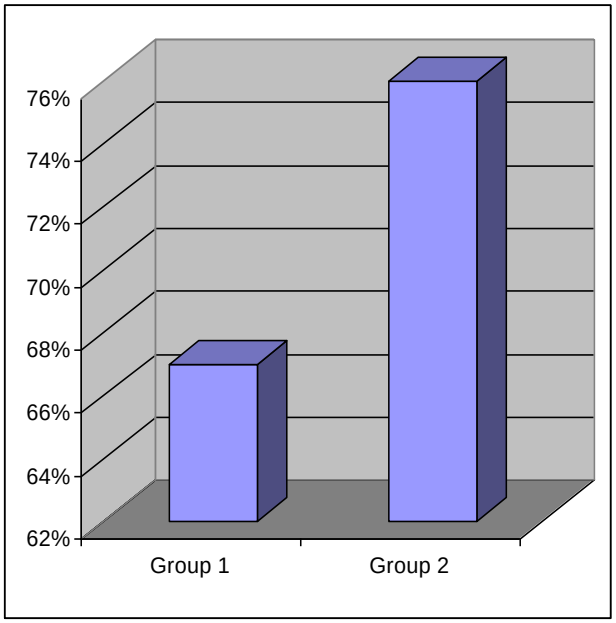


Fig 3 shows effect of Raloxifene on bone pain. It was noted that there was not significant difference in bone pain in both groups as (p=0.266) as n=20 (67%) in group 1 and n=22 (76%) in group 2 respectively.

Fig. 3: Pain in both groups



DISCUSSION

At menopause in woman accelerated bone loss starts 2-3 year prior to menopause due to increased FSH and decreasing serum oestradiol and this loss continues for up to 5-10 year after menopause. Estrogen deficiency increases osteoclastic activity as compared to osteoblastic activity resulting in excessive trabacular and cortical bone resorption[3].

(SERM) selective estrogen agonist receptor [4] are agonist on bone by suppressing bone turn over whereas antagonist on breast and by therefore not increasing the risk of breast cancer. It is prescribed to asymptomatic post menopausal woman with a relatively low bone mineral density in the absence of risk factors for thromboembolism. NICE recommends it in secondary prevention of osteoporotic fractures in post menopausal woman with contraindication or intolerance of biphosphonates[5,6,7].

The Multiple Outcomes of Raloxifene Evaluation (MORE) study demonstrate 30% vertebral (but not non vertebral) fractures risk reduction with a significant (p=0.0002) improvement in lumber spine bone mineral density, treated with Raloxifene 60 mg/ day for 3 years. Similar results obtained from our study showing markedly significant (p=0.000) difference in bone mineral density measured by t

score among group 1 on Raloxifene 60 mg/ day more than one year than group 2 not taking any medicine.

The 5 year long placebo control study, Raloxifene Use for The Heart (RuTH) study of over 10,000 post menopausal woman at risk of coronary heart disease also show 35% reduction in clinical vertebral fracture risk, but also effect on non vertebral fractures. Their results are comparable with out study as risk of vertebral fractures (n=26) 87% in group 2 is high as compared to group 1 taking Raloxifene (n=4) 13%. This shows significant (p=0.003) reduction of fracture among post menopausal woman taking Raloxifene. Similarly there was a significant (p=0.01) difference in height shortening among group 1 and group 2 as there were less chance (n=0) of vertebral fracture among group 1 taking Raloxifene than in group 2 (n=24) 85%. Our study showed non significant (p=0.266) bone pain in both groups. As in group 1 (n=20) 67% and in group 2 (n=22) 76% were complaining of bone pain which is similar to the 4 year study Continuing Outcomes Relevant of Evista (CORE) showing no effect on non vertebral fracture risk.

Then mean SERM like Lasofoxifene, b bazedoxifene have also been studied for effects on bone mineral density and reducing fracture risks. The recently reported outcomes of the Post Menopausal Evaluation And Risk (PEARL) reduction with Lasofaxifen study of over 8,000 women showed that 0.5 mg/ day Lasofoxifen reduced vertebral fracture by 42% at 3 year and non vertebral fracture (but not hip) by 24% at 5 year. Similarly another SERM bazedoxifene has been shown to reduce vertebral fracture by 40% and non vertebral fracture by 50% among 7,000 post menopausal women. Tissue Selectuve Estrogen Complex (TSEC) therapy is also under development. A randomized, double bind placebo controlled phase 3 trial involved over 3,000 post menopausal woman, demonstrated that bazedoxifene + conjugated estrogen given from 2 year presented bone mineral density but risk of fracture prevention is currently unknown. It is in contrast to our study showing significant (p=0.003) reduction in fractures and no (p=0.01) height shortening due to vertebral fracture prevention in group 1 taking Raloxifene as compared to group 2 not taking any treatment.

CONCLUSION

Osteoporosis can be avoided by attaining and maintaining a peak bone mass by healthy life style, balanced diet with optimal calcium and vit. D and physical exercise. SERM Raloxifene 60 mg/ day can be used in young post menopausal woman at a greater risk for vertebral fractures than hip fracture are intolerant to biphosphonates. There is a need for more research for bone preservation and improved bone quality to prevent morbidity and mortality of the osteoporosis[8,9,10].

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