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Comparision of Effect of Teriparatide and Alendronate Sodium on the Bone Mineral Density in Post-Menopausal Women.

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ABSTRACT

Background: Aim: Purpose of this study was to know which one is better modality of treatment for osteoporosis in postmenopausal women – enhancing bone formation or reducing bone resorption. **Methods:** Total 120 patients were included in this study and randomly divided in two groups. Group A patients were given teriparatide injection and Group B patients were given alendronate sodium tablet. Both groups were given Calcium supplement, and vitamin D supplement along with therapy. Bone mineral density (BMD) at the spine and hip was assessed by dual-energy x-ray absorptiometry (DEXA) scan before and after the therapy. **Results:** Average Bone mineral density (BMD) in teriparatide group was - 2.77 in pretreatment and – 1.8767 after one year follow up. Average BMD in alendronate sodium group was -2.78 in pretreatment and – 2.00 after one year follow up. Avearage gain in BMD in Group A was – 0.8933 and in group B was –0.78. **Conclusion:** Teriparatide seems to be better treatment for oeteoporosis as compared to alendronate therapy.

Keywords: Teriparatide, Alendronate, Osteoporosis, BMD.

INTRODUCTION

Osteoporosis is a disease characterized by decreased bone strength predisposing an individual to an increased susceptibility for fracture.[1] Osteoporosis is defined as a bone mineral density (BMD) of 2.5 standard deviations below that of a young adult. This is typically measured by dual-energy X-ray absorptiometry (DEXA).[2]

It is the most common reason for a broken bone among the elderly.[1] Bones that commonly break include the vertebrae in the spine, the bones of the forearm, and the hip.[3] Bones may weaken to such a degree that a break may occur with minor stress or spontaneously. Chronic pain and a decreased ability to carry out normal activities may occur following a broken bone.

Osteoporosis occurs in all country and ethnic groups worldwide .The prevalence however varies considerably between different populations. Several risk factor of lifestyle associated with wealth may also be involved in so called developed country .This mean that in poorer country the risk of osteoporosis will rise with increasing life expectancy and general wealth of the respective population. Based on BMD measurement of the lumbar spine or the femoral neck in person of age 50 years and older the prevalence of osteoporosis is 16.6 % for women and 6% for men.[4,5] Chronic moderate low physical activity is a very frequent cofactor in the development of most form of osteoporosis. Regular moderate gymnastics or especially resistance training is able to maintain bone substance. The negative effects of the hormonal changes induced by excessive high competition sports overcome the benefits of physical activity on bone. Severe vit-D deficiency with very low serum plasma levels causes an under mineralization of bone tissue, i.e rickets in children, or, osteomalacia, in adults.[6]

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MATERIALS AND METHODS

In this study, the women (Post-menopausal) attending outpatient department of orthopedic

surgery >50 year age presenting with backache or fragility fracture of bone were taken under consideration.

All the patients voluntarily entered the study after receiving information and giving informed consent by signing the relevant form. We excluded the patients with other conditions (likely to interfere with bone integrity) like malignancy, endocrine disease (Paget's disease), long term immobilization, chronic renal failure. Also patients with diabetes, bone cancers, fracture by severe trauma were excluded from the study. Total of 134 patients enrolled for study but 3 lost in follow up, 2 died of some unknown cause and 9 got some fracture due to road side accident. So we left with120 patients for study.

All patients BMD calculated by DEXA (dual-energy x-ray absorptiometry) scan before starting the treatment. All patients were divided into two groups randomly on alternate basis. A total of 120 postmenopausal women with low bone mineral density at the hip or spine (a T score of less than –2.5) were included in study. Out of these 60 women were randomly assigned to daily treatment with teriparatide 20 µg subcutaneous injection (Group A). Another 60 women were given alendronate sodium 70 mg per week (Group B) and were followed for 12 months. Each woman (in both groups) received daily supplementation of calcium (1000 mg) and vitamin D (60000 IU) per week. Bone mineral density at the spine and hip was assessed by dual-energy x-ray absorptiometry.

-T score value above	-1SD	Normal
-T score value between	-1 and- 2.5 SD	Osteopenic
- T score value below	-2.5 SD	Osteoporosis
- T score value	< -2.5 SD	Sever osteoporosis

RESULTS

We included only postmenopausal women in our study as osteoporosis is more common in female than male. Most of the patients in our group belong to 60 – 70 years age group (45.83%). All women were given treatment according to their group and followed for one year.

Table 1: Age Distribution

Age group (in years)	No. Of patients (group a + b)	Percentage %
50-60	40 (20 + 20)	33.33 %
60-70	55 (25 + 30)	45.83 %
70-80	25 (15 + 10)	20.84 %

The data were compiled and analysed in SPSS software subscription version. The continuous variables were represented as mean and standard deviation. At 95% confidence interval and and level of significance at 5%, the between group comparisons were made by independent student t test (two-tailed) and within group comparisons for follow up were made by paired student t test (two-tailed).

Table 2: Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
Initial	1.00	60	-2.7700	.22270	.02875
	2.00	60	-2.7800	.20068	.02591
FU	1.00	60	-1.8767	.30330	.03916
	2.00	60	-2.0000	.27433	.03542

The difference in initial mean value of BMD in Group A (-2.77± 0.22) as compared to Group B (-2.78± 0.20) was found to statistically non-significant (p=0.797). Whereas, at the time of follow up after treatment, difference in mean value of BMD in Group A (-1.88± 0.30) as compared to Group B (-2.00± 0.27) was found to statistically significant (p=0.021) when analysed by independent student t-test. So, a significantly better outcome was observed with Group A treatment as compared to Group B treatment.

In Group A patients, the initial mean BMD was -2.77 ± 0.22 which improved to -1.88 ± 0.30 after treatment at the time of follow up. This change in mean BMD was found to be statistically significant (p<0.001) when analysed by Paired samples T-test.

In Group B patients, the initial mean BMD was -2.78± 0.22 which improved to -2.00± 0.27 after treatment at the time of follow up. This change in mean BMD was found to be statistically significant (p<0.001) when analysed by Paired samples T-test.

Safety

Both treatments were safe and well tolerated. Compliance with oral and injectable medications was good. 10 patients in alendronate group complain of gastritis and nausea.

DISCUSSION

We compared the effects of teriparatide, a bone formation agent, and alendronate, a potent inhibitor of bone resorption, on BMD in postmenopausal women with osteoporosis. The improvement in BMD from these approved agents is mediated by distinct and opposite effects on bone cell activity.[7] Both drugs increased BMD in the spine and hip, although the magnitude and nature of these changes differ significantly between drug therapies, consistent with previous findings by Body et al and by Black et al.[8,9]

A negative bone remodeling balance in the presence of high bone turnover is found in untreated patients with osteoporosis, and the reduction of bone turnover and activation frequency has been the objective of osteoporosis treatments for many years.[10,11] Alendronate sodium, a second-generation aminobisphosphonate, achieves that objective by preferentially inhibiting

bone resorption through its action on osteoclasts, thereby decreasing bone turnover. Alendronate preserves existing architecture and reduces the incidence of osteoporotic fractures,[12-15] yet it neither improves nor restores architectural integrity associated with severe osteoporosis.[16-19]

Teriparatide (rDNA origin) injection [recombinant human PTH(1-34)], a bone-forming agent that increases bone remodeling, represents a new therapeutic option for the treatment of osteoporosis.[20] Teriparatide, administered once daily through subcutaneous self-injection, is effective in reducing fracture incidence and increasing BMD.[21-25] However, in contrast to antiresorptive agents, teriparatide preferentially increases bone formation through direct early stimulation of osteoblasts.[26] This increase in new bone formation results in a positive bone balance at the level of individual bone multicellular units (BMUs) and improved bone microarchitecture and quality.[22-30]

Alendronate therapy significantly reduced markers of bone turnover, as reported previously.[31-36] Bone resorption was suppressed after 1 month of treatment, while inhibition of formation occurred by 3 months. A new steady state of reduced bone turnover was achieved after 6 months and persisted through month 12.[37] As a result of these changes in bone metabolism, BMD values increased modestly in the spine and proximal femur. The increase in spine density was more rapid during the first months of treatment, with slower rates of gain noted thereafter. This pattern of BMD response in the lumbar spine is predictable from an understanding of the mechanisms through which inhibitors of bone remodeling increase BMD, including a rapid closure of the remodeling space and a reduced number of new (active) bone remodeling units, resulting in increased time for matrix mineralization.[38,39] In contrast, teriparatide therapy markedly increased the rate of bone formation by the first month of treatment, progressed during the first 6 months, and persisted through month 12. Bone resorption increased modestly between 3 and 12 months. As a result, a positive balance in bone remodeling occurred, resulting in a substantial increase in trabecular bone mass in the spine and hip. Although increased bone remodeling is associated with greater bone loss and increased fracture risk,[40,41] the increased bone turnover with teriparatide improves bone balance that leads to incremental gains in bone mass.[42]

The national osteoporosis foundation has outlined clinical recommendations regarding initiation of therapy for low bone mass and osteoporosis .According to their guideline treatment should be initiated when T score is below -1.5 in the presence of at least one risk factor or if T score is below -2 in the absence of risk factor. T score alone can not be used to judge when drugs are to be prescribed. Low BMD is only one of many risk factors.

The increases from baseline in femoral neck BMD observed with teriparatide and alendronate are consistent with previous reports.[8,31-36,43,44] A greater increase in trabecular BMD was observed with teriparatide than with alendronate, similar to the changes seen in the trabecular BMD of the spine.

A clinical characteristic that differs between treatment with teriparatide and alendronate is the effect of therapy on the incidence of back pain. In this study, fewer patients treated with teriparatide reported new or worsening back pain, particularly with respect to moderate and severe back pain, compared with those treated with alendronate. These findings are consistent with those of Body et al,[8] who found that back pain was reported less frequently by patients treated with teriparatide than with alendronate.

In summary, this study demonstrates that the two treatments, each of which has been previously shown to be effective in the treatment of osteoporosis in postmenopausal women, accomplish their effects by different and, in fact, opposite effects on bone metabolism.

CONCLUSION

We observed that the effect of teriparatide is better as compared to alendronate sodium on increasing BMD in postmenopausal women. The availability of two distinct treatment options for the management of osteoporosis provides the opportunity to select the optimal treatment strategy for a given patient based on different clinical and pathophysiological characteristics. The challenge facing clinicians and clinical investigators is to identify those attributes in an individual patient that would determine whether an antiresorptive agent or an anabolic agent would be most appropriate.

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