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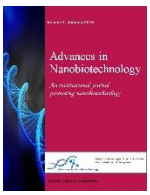

Study of Bone Mineral Density changes in Osteoporosis Therapy

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ABSTRACT

This study focuses on the effect of osteoporosis therapy in elderly. It was a randomized cohort study performed in Isfahan Osteoporosis Diagnosis Center from early 2012 to mid-2015. Data were taken from 350 of the lumbar spine and hip of the referred osteoporotic patients before the start of treatment. Osteoporotic patients who had a bone mineral density (BMD) scan met the inclusion criteria. The appropriate routine treatment was prescribed by their physicians. The second measurements were taken a year later to assess the effectiveness of the treatment. The measurements were taken using a DXA scanner. This study found that more than 85% of the patients who followed the prescribed treatment had a BMD gain in both measured sites of hip and spine.

1. Introduction

The most common bone disease is osteoporosis. It is characterized by low bone mass with micro architectural disruption and skeletal fragility, resulting in an increased risk of fracture [1-3], which leads to considerable morbidity and mortality, and burdens society and the families of the patients [4]. DXA measurements of the spine and hip are recommended because fractures at these sites have the greatest impact on patients' health [5]. Measurement of hip BMD also has the highest predictive value for future hip fracture [6]. In addition, measurement of the spine BMD is also useful, if pharmacological therapy is planned. It shows less variability and can detect responses to therapy earlier than hip BMD can [7, 8]. It has been shown that the pattern of bone loss differs between different ethnic groups and populations because of geographical and economical differences. Therefore, the response to treatment may be different and dependent on the ethnic group [9,10].

Postmenopausal women in Iran demonstrated in a similar study, designed in Iran, that femoral neck T-scores are lower than lumbar spine T-scores [9]. These results demonstrated a clear difference between Iranian populations and most of the others that were studied. Our literature review at the time of this study showed no trace of data on follow-up for the Iranian osteoporotic postmenopausal women and the efficacy of treatment.
In this study, we designhned to determine the efficacy of treatment and patients' compliance with drug therapy and the necessary life-style changes affecting the patients' change in BMD. It can be very useful for clinicians to know what percentage of BMD response they can expect in women treated with osteoporosis therapies.

2. Materials and Methods

This study was a randomized cohort study and was performed on postmenopausal women referred to Isfahan

Osteoporosis Diagnosis Center from May 2007 until March 2009.

Women who were over the age of 50 years, ambulatory, in generally good health, postmenopausal (at least 5 years since their last menstrual periods), had at least 3 vertebral bodies in the lumbar spine (L1 to L4) that were valuable by densitometry (i.e., without fracture or degenerative disease), and had a lumbar spine BMD corresponding to osteoporosis (T-score < -2.5), and osteopenia (-0.1< T-score < -2.5).

Any previous or ongoing condition that could prevent the patient from being able to complete the study. Drug or alcohol abuse, conditions that interfered with the BMD measurements, bilateral hip prostheses, history of cancer in the last 5 years, using medications that could interfere with the study evaluations (e.g., glucocorticosteroids, anabolic steroids, estrogens, selective estrogen receptor modulators, calcitonin, any bisphosphonates, fluoride, strontium, PTH), abnormal clinical laboratory measurements, creatinine clearance less than 30 ml/min, hypo- or hypercalcemia, history of hyperparathyroidism or hyperthyroidism unless corrected, osteomalacia, and lumbar spine BMD corresponding to a T-score of - 5 or lower.

Treatment of osteoporosis consists of non-drug and drug or hormonal therapy. Medications included 70 mg Alendronate every week, 1500 mg Calcium every day and 800 IU of Vitamin D daily for 12 months.

In this study, 350 postmenopausal women over 50 years old with osteopenia /osteoporosis were selected. The patients were divided randomly into three groups: The first group contained 100 patients who completed the course of treatment successfully. The second group of 50 patients did not show any sign of adherence to the treatment. The third group, of 200 patients, did not comply with all the treatment. Using a questionnaire, we gathered data about previous sicknesses and drug use, gynecological history, nutritional habits, physical activity, education level and other life style habits; the questionnaire was one page long and took five minutes to complete. The second DXA scan was performed after a year to monitor the efficacy of treatment; this was performed in the same clinic using the same scanner.

According to previous studies, the prevalence of osteoporosis is 30%. Therefore, the number required for the present study was calculated to be 100 patients. However, we selected 350 patients, in order to be more confident of having a more definite response to therapy.

The height and weight of each patient were measured before the scan was taken and BMI was calculated as kilograms per square meter.

Bone mineral density assessment BMD measurements at lumbar spine (L1–L4) and hip (hip, Ward's triangle, trochanter) were taken by dual-energy X-ray absorptiometry (DXA) using a Norland XR46 USA scanner. The measurements were taken by specially trained personnel. The precision of the scanner, based on measurements of a phantom during the study period was 0.44%. The precision for the total hip and lumbar spine measurements was <1%.

Statistical Analyses: These analyses included the maximum, minimum and means of the variables (such as age, height, weight, BMI). Then we clustered the continuous variables into groups in order to analyze their frequencies and percentages.

We compared the mean of BMD T-scores of the hip and spine of the three groups before and after treatment and processed the data with SPSS software. We charted the BMD T-scores of the Hip and spine in different groups of variables to find the relationships between them.

Changes of BMD after treatment in each group were evaluated by paired t-tests (SPSS ver.14). We compared BMD of three groups before treatment and after the follow up phase with one-way ANOVA.

3. Results

The baseline characteristics of women in the three subgroups were similar (Table 1).

Table 1. Baseline data in 350 postmenopausal women as mean (SD). Group 1: N=100, completely treated; Group 2: N=5, not treated; Group 3: N=200, partially treated.

Groups	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)
Group1	59.07(6.53)	154.41(7.39)	67.22(10.09)	28.27 (4.40)
Group 2	59.60(7.54)	154.29(5.89)	68.68(10.49)	28.92(4.57)
Group 3	59.66(7.14)	153.61(5.67)	66.90(9.66)	28.35(3.73)
Total	59.48(7.02)	153.93(6.23)	67.24(9.89)	28.40 (4.05)
P- value	0.785	0.524	0.524	0.621

During the 1 year of follow up, the BMD (g/cm2) ±SD of the spine in group one was significantly increased (mean BMD before treatment was 0.83(0.14); after treatment it was 0.86 (0.14), P<001). In group two the BMD of the spine was not significantly changed, mean BMD before treatment was 0.89(0.20) and after treatment was 0.89(0.20) P=0.23. In group three the BMD of the spine was significantly increased, mean BMD before treatment was 0.83(0.18) and after treatment was 0.87 (0.17) P<001.

In addition, the T-score of the spine in group one was significantly increased, mean BMD before treatment was-1.72(0.99) and after treatment was-1.45 (0.93) P<0001.

In group two the T-score of the spine was not significantly changed from mean BMD of -1.44 (1.13) to-1.49 (1.04) after treatment P=0.49. In group three the BMD of the spine, was significantly increased (mean BMD before treatment was -1.68(1.02); after treatment was -1.41 (1.06), P<0.01) (Table 2).

Table 2. Changes in BMD and T-score of spine and hip during treatment in all groups as mean (SD).

Site	Parameter	Group 1, N=100 Completely treated	Group 2, N=50 Not treated	Group 3, N=200 Partially treated	Total, N=350
Spine	0.83 (0.14)	0.89 (0.20)	0.83 (0.1)	0.84 (0.1)	0.83 (0.14)
	0.86 (0.14)	0.89 (0.20)	0.87 (0.17)	0.87 (0.17)	0.86 (0.14)
	-1.72 (0.99)	-1.44 (1.1)	-1.71 (1.0)	-1.68 (1.0)	-1.72 (0.9)
	-1.45 (0.93)	-1.49 (1.04)	-1.41 (1.09)	-1.41 (1.06)	-1.45 (0.93)
Hip	0.73 (0.12)	0.77 (0.14)	0.74 (0.13)	0.74 (0.13)	0.73 (0.12)
	0.74 (0.13)	0.75 (0.12)	0.75 (0.13)	0.74 (0.13)	0.74 (0.13)
	-2.29 (0.72)	-1.90 (1.05)	-2.00 (1.50)	-2.07 (1.27)	-2.29 (0.72)
	-2.21 (0.77)	-1.94 (1.07)	-2.08 (1.14)	-2.09 (1.04)	-2.21 (0.77)

T-test results for spine and hip T-scores and BMDs of all3 groups are tabulated in Table 3.

Table 3. T-test results for spine and hip T-scores and BMDs of all groups, results are as mean (SD) and p-value.

Site	Parameter	Group 1, N=100, Completely treated	Group 2, N=50, Not treated	Group 3, N=200 Partially treated
Spine	2nd BMD v 1st BMD	-0.04 (0.11) 0.001	-0.01 (0.04) 0.23	-0.04 (0.10) 0.001
	2ndT-score v 1stT-score	-0.27 (0.69) 0.0001	0.05 (0.51) 0.49	-0.30 (0.76) 0.01
Hip	2nd BMD v 1st BMD	-0.01 (0.03) 0.001	0.20 (1.33) 0.30	-0.01 (0.03) 0.001
	2nd T-score v 1st T-score	-0.08 (0.22) 0.001	0.03 (0.24) 0.38	0.08 (1.11) 0.33

Spine and hip BMD changes in all groups are shown in Table 4.

Table 4. Spine and hip BMD changes in all groups, data are presented as Numbers (%). For spine x^2=15.07, d.f=0.4, p<0.01 and for hHip x^2=15.8, d.f=0.4, p<0.01.

Site		Group 1, N=100 Completely treated	Group 2, N=50 Not treated	Group 3, N=200 Partially treated
Spine	Bone loss	8 (8)	7 (14)	15(7.5)
	No change	40 (40)	31 (62)	95 (47.5)
	Bone gain	52 (52)	12 (24)	90(45)
	Total, N=350	100%	100%	100%
Hip	Bone loss	16 (16)	17 (34)	47 (23.5)
	No change	40 (40)	25 (50)	67 (33.5)
	Bone gain	34 (34)	8 (16)	86 (43)
	Total, N=350	100%	100%	100%

In group one, 52(52%) had a positive change in spine BMD, 40(40%) had no change, and 8(8%) had a negative change. In group two, 12 (24%) had a positive change in spine BMD, 31 (62%) had no change and 7(14%) had a negative change. In group three, 90 (45%) had a positive change in spine BMD, 95 (47.5%) had no change, and 15 (7.5%) had a negative change (x2 = 15.07, d.f. = 4, p< 0.01).

Hip BMD in group one also increased, mean BMD before treatment was 0.73 (0.12) changing into0.74 (0.13) P<001 after the treatment. In group two, the BMD of the hip did not significantly decrease, mean BMD before treatment was 0.77 (0.14) and after treatment was 0.75 (0.12) P=0.30). In group three, the BMD of the hip was significantly increased (mean BMD before treatment was 0.74 (0.13); after treatment was 0.75 (0.13), P<001).

The T-score of the hip in group one was significantly increased (mean BMD before treatment was -2.29 (0.72); after treatment was -2.21 (0.77), P<0001). In group two, the T-score of the hip, was no significantly decrease (mean BMD before treatment was -1.90 (1.05); after treatment was -1.94 (1.07), P=0.38). In group three the BMD of the hip did not significantly change (mean BMD before treatment was -2.00 (1.50); after treatment was -2.08 (1.14), P=0.32) (Table 2).

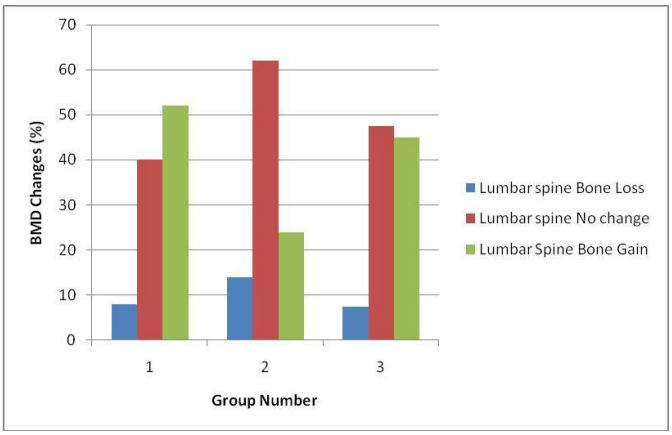

Fig. 1. Column chart of spine BMD changes in three groups.

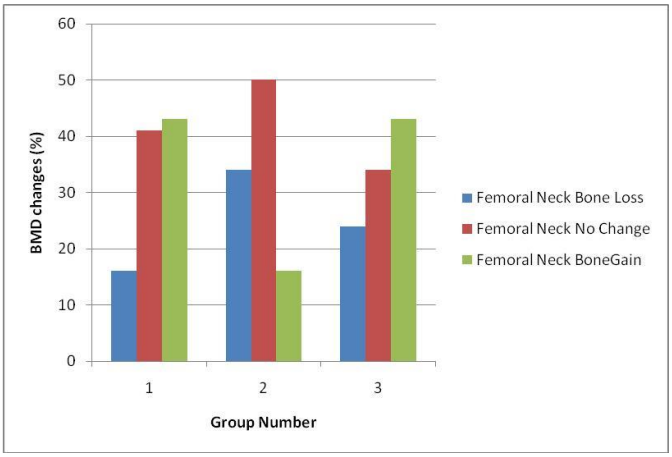

Fig. 2. Column chart of hip BMD changes in three groups.

Change in BMD of the hip in three groups, expressed as a number (percentage) (Table 2, Fig.2). In group one, 34 (34%) had positive change in spine BMD, 41 (41%) had no change, and 16 (16%) hada negative change. In group two, 8 (16%) hada positive change in spine BMD, 25 (50%) had no change, and17 (34%) had negative change. In group three, 86 (43%) had a positive change in spine BMD, 68 (34%) had no change, and 48 (24%) had a negative change ($x2 = 15.8$, d.f. = 4, $p< 0.01$).
Figure 1 and Figure 2 shows the results as column chart of spine and hip BMD changes in all groups.

4. Discussion

The significant findings of this study are a significant increase in BMD both for the spine and hip in group one, 100 cases that received complete treatment. The change of T-score and BMD of spine were significantly more than hip.
In group two 50 cases that received no treatment, the T-score and BMD of hip and spine showed no significant change.
In group three 200 cases who were prescribed drugs but were not certain to have complied fully with their treatment, the T-score and BMD of spine and hip in the second scan were significantly more than in the first scan, but the T-score of hip in the second scan was not significantly higher than in the first scan. Spine mean BMD in the first scan of 0.84 g/cm2and in the second scan of 0.87 g/cm^{2}was higher than the hip mean BMD of 0.74g/cm^2 in the first scan, and 0.74g/cm^2 in the second. Unlike our results, almost all other studies have found a higher hip T-score than spine T-score. But our result is the same as that of a similar study which was planned to take place in Iran [9, 10].
Athansopoulou et al in 2000 in a study of Greek population showed that the spine T-score (-1.18) of women who were 50-59 years old was lower than their hip T-score (0.82) [11]. In the same kind of investigation, Maalouf et al in 2000 showed that the spine T-score (-0. 8) of women in Lebanon who were 50-59 years old was lower than their hip T-score (0.56) [12]. Other studies, such as those of Hammoudeh et al [13] in Qatar, Ghannam et al [14] in Saudi Arabia and Mazess et al [15] in the US report the same results.
For several years, it has been known that there are significant differences in BMD between peer age groups of different sexes and races [16].
In treated patients who adhere to their therapy, a stable or increased BMD is an acceptable response, although those with a stable BMD had fewer fractures than those who lost BMD [17].
To a greater extent than the loss of LSC, the loss of BMD is cause for clinical concern, and may be associated with poor adherence to therapy [18-21], or with previously unrecognized contributing factors that require additional intervention [22].
We also show that if a patient receives the full course of treatment, 92% of them in the spine site, and 84% of them in the hip site respond to treatment and are at lower risk of bone fracture. If drugs alone are prescribed, only 77% of them in the hip site, and 92.5% of them in the spine site, respond to treatment.

5. Conclusion

If osteoporotic patients are not treated, 76% of them in the spine site and 58% of them in the hip site remain in a stable osteoporotic situation or worsen and are under severe threat of osteoporotic fracture. Of 350 patients, 100 completed the treatment successfully, 200 did not complete the treatment and 50 did not take the prescribed drugs. T-tests revealed that for the 100 patients who completed the treatment there were significant ($P < 0.01$) BMD gains in the hip and spine. There were also significant BMD gains for both measured sites ($P < 0.01$) for the 200 patients who did not fully follow the therapy. For the 50 patients who did not undergo the therapy, neither of the sites changed significantly ($P \geq 0.15$).

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