The Impact of Alendronate on Bone Mineral Density of Osteoporotic Patients

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Abstract- The present study assessed the real life therapeutic effects of weekly doses of alendronate in treating a group of osteoporotic patients in Iran. The present historical cohort was conducted on patients who had undergone two or more bone mineral densitometry within an interval of 1.5-2 years in Shariati Hospital bone mineral density department between 2002 and 2010.patients were asked by phone about consumption of alendronate. The mean increase in the BMD values at different sites was calculated. There was a significant increase in the body mass index (BMI) values of both the individuals taking alendronate and the control group (P<0.001). Taking the weekly dosage of the drug was associated with a 7.67% increase in the BMD values at the femoral neck, 8.68% at the total hip, and 3.17% at the lumbar spine. Moreover, our results showed a significant difference between the height decline in the two groups (alendronate taking: 0.7±2.4 vs. control: -0.7±2.6, P<0.001). Comparing the results of the present study with that of previous ones revealed the drug is beneficial in improving bone mineral density in Iranians; as well alendronate is more effective in Iranian postmenopausal women when compared with the Americans.

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Keywords: Alendronate; Bone density; Osteoporosis

Introduction

More than 10 million individuals suffer from osteoporosis in the US and the statisticians estimate that the number would reach 14 million by 2020 (1). In Iran, similarly, the prevalence of the disease is high; the latest figures have revealed that 4.8% of males and 7.7% of females have osteoporosis and osteopenia is seen in 36.8% of males and 39.3% of females (2,3).

Considering the fact that the aging population is a global phenomenon and the risk of fracture increases with age, osteoporosis is considered to impose a heavy burden on the society (4). Moreover, the condition is responsible for a high number of deaths as well. One in every five patients suffering from osteoporotic-related hip fracture would die in the first year after fracture (5). This is while about one third of sufferers would need home care after discharge, and only one third would regain their pre-fracture activity (6).

alendronate, the most common bisphosphonates, is widely used particularly in postmenopausal women. The drug has also shown promising results in men suffering from the condition (7). Many randomized clinical trials have confirmed the efficacy of alendronate in improving bone mineral density (BMD) and lowering the risk of osteoporotic fracture (8,9). While previous studies have reported that taking 10 mg/d of the drug is not only effective but also associated with the least risk of developing side effects (10-12), now the weekly dosage of the medication is gaining more popularity. Many studies, however, have reported no significant difference in the therapeutic effects of different dosages of the drug (13,14).

To our knowledge, the present study is the first research designed to assess the real life therapeutic effects of weekly doses of alendronate in treating a group of osteoporotic patients in Iran. Moreover, all the previous studies conducted in this field, were randomized clinical trials, (RCTs) and so their results could not be generalized to the whole population.

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Hence, to address these concerns, we have conducted the present study evaluating the real life therapeutic effects of weekly doses of alendronate in treating a group of osteoporotic patients in Iran.

Materials and Methods

The present historical cohort was conducted on patients referring to the bone mineral density department of Shariati Hospital affiliated to Tehran University of Medical Sciences between 2002 and 2010. All the patients who underwent two or more bone mineral densitometry within an interval of 1.5-2 years during the study period were recruited.

The results of bone mineral density along with the patient's demographic information (age, weight, height and gender) were all extracted from the patients' medical reports. All the patients who had at least 2 bone mineral densitometry with an interval of 1.5 to 2 years were asked by phone calls about consumption of alendronate and calcium and vitamin D. Those who had used alendronate were compared with the group who had not used alendronate (control).

All the patients had undergone both an L1–L4 anteroposterior lumbar spine and a hip (total hip and femoral subregions: trochanter and neck) DXA study with a Lunar DPXMD densitometer (Lunar 7164, GE, Madison, WI) by a trained operator in accordance with the manufacturer's recommendations. Instrument validation was determined regularly by a weekly calibration procedure using a phantom supplied by the manufacturer. Precision error for BMD measurements was 1-1.5% in the lumbar and 2–3% in the femoral regions. The least significant change was calculated through multiplying these values by 2.8.

The mean increase in the BMD values at different sites was calculated using the following equation: Mean increase = (BMD2-BMD1)/BMD1*100

The patients were also asked about their daily calcium intake (the amount of milk and yoghurt they consumed on the regular basis, using a predesigned questionnaire. In order to calculate the average daily calcium consumption, each glass of milk was considered to have 300 mg and each bowl (half a glass) of yoghurt to have 200 mg of the compound (15).

The gathered data were then analyzed using SPSS version 13. Means±SD were used to express standard descriptive statistics. Categorical variables were expressed as percentages. Paired t-test was used to compare the data between the cases and controls. P-values lower than 0.5 were considered significant.

Considering the fact that many factors have a confounding effect on BMD values, a univariate linear regression analysis was used to assess the confounding effect of the 13 studied factors. The variables, with p-values lower than 0.20, were entered in the multivariate linear regression analysis. Those with p-values lower than 0.05 were reported to have the confounding effect.

Results

Four hundred and four osteoporotic patients were studied in the 8-year historical cohort. Among them, 89.4% (n=361) were females. Their mean age was 52.7±11.4 years, ranging from 20 to 79 years. Two hundred and thirteen (52.7%) of the studied group took alendronate during the study period.

Table 1 outlines the demographic characteristics of the two groups. There was a significant increase in the body mass index (BMI) values of both the individuals taking alendronate and the control group (P<0.001).

Table 1. The difference of the two groups regarding the studied variables.

	alendronate (n=213)	Control (n=191)	*P*-value*
Age	52.7±11.5	52.8±11.3	NS
Male/Female	23/190	20/71	NS
Smoking	4 (1.9)	1 (0.5)	NS
Baseline BMI	25.0±7.3	22.27±10.4	0.002
BMI (2 yrs later)	25.1±23.7	22.2±10.4	<0.002
Menarche age	13.4±1.5	13.6±1.4	NS
Menopause age	46.3±8.1	45.4±8.1	NS
Steroid[1]	30 (14.1)	13 (6.8)	0.023
Ca-vit D supplements[2]	187 (87.8)	191 (100)	< 0.001
Levothyroxin	16 (11.9)	14 (14.3)	NS

*Fischer test

1-Taking at least 5 mg of prednisolone or equivalent doses of other types of corticosteroids in their life

2- Taking at least 500 mg of calcium per day

Table 2. The difference between BMD values at different levels in the two groups following treatment.

BMD		Baseline (Mean±SD)	Post Treatment (Mean±SD)	Within group p-value	between groups (post – pre TX Difference) *P* value
Femoral neck	alendronate +	0.8±0.1	0.9±0.1	0.001	0.037
	alendronate -	0.8±0.1	0.8±0.1	NS	
Total Hip	alendronate +	0.9±0.1	0.9±0.1	<0.001	0.001
	alendronate -	0.9±0.1	0.9±0.1	NS	
Lumbar spine	alendronate +	1.0±0.2	1.0±0.2	NS	NS
	alendronate -	1.0±0.2	1.0±0.1	NS	

Some 10.6% of the studied individuals had a positive history of taking steroid (defined as taking at least 5 mg of different types of the medication in their life). There was a significant difference between the number of individuals taking steroids in the two groups (30 in the alendronate vs. 13 in the control group, *P*-value=0.018).

There was no significant difference between the daily intake of calcium, calculated through summing up the amount of milk and yoghurt taken by each individual, in the two groups (alendronate: 649.1±289.1 vs. control: 649. 9±222.9, *P*-value=NS).

Table 2 outlines the difference between BMD values at different levels in the two groups. Based on the results, there was a significant improvement in the BMD values at the lumbar spine in the whole population, we failed to show a considerable difference between the values reported in the second test between the two groups. As for the femoral neck and total hip, however, the significant difference was only noted in the group who had consumed the medication.

There was a significant difference between the height decline in the two groups (alendronate: 0.7±2.4 vs. control: -0.7±2.6; *P*<0.001). While height decline was significantly correlated with reduced height in the lumbar spine (*P*=0.005, Pearson correlation=0.144), there was no significant association between the mean height decline and the BMD values at the spine before and after treatment (*P*-value=0.586, Pearson correlation=0.028). Reduced height of the L1-L4 vertebra, on the other hand, were related with the difference noted between BMD values at spine before and after treatment (*P*=0.004, Pearson correlation= 0.144).

Taking the weekly dosage of the drug was associated with a 7.7% increase in the BMD values at the femoral neck, 8.7% at the total hip, and 3.2% at the lumbar spine (Table 3).

Multivariate analysis revealed that the baseline BMD values at the spine are the only factor significantly affecting the influence of alendronate on the BMD values at the spine in women (Table 4). When confining the analysis to women a similar result was reported. As for the femoral neck and total hip, similar results were reported in the whole population and the women.

Table 3. Mean increase in BMD values at different levels in the whole and the female population following treatment.

BMD (g/cm2)		Whole population		Women	
		Mean increase (Mean±SD)	*P*-value	Mean increase (Mean±SD)	*P*-value
Femoral neck	alendronate	7.7±0.2	0.006	7.8±0.2	0.007
	control	1.2±0.2		1.2±0.2	
Total Hip	alendronate	8.7 ±0.2	0.003	8.9 ±0.2	0.003
	control	2.0±0.2		2.0±0.2	
Lumbar spine	alendronate	3.2±0.2	NS	3.0±0.2	NS
	control	2.1±0.2		1.7±0.2	

Table 4. Multivariate analysis of factors influencing BMD values at the lumbar spine.

Independent variable	Univariate Model		Multivariate Model	
	Standardized Coefficients Beta	*P* value	Standardized Coefficients Beta	*P* value
alendronate	-0.01	0.048	0.06	NS
Age	-0.10	0.041	-0.03	NS
BMI	0.16	0.002	0.06	NS
Ca intake*	-0.11	0.025	-0.07	NS
Baseline BMD at L1-L4	2.4	0.000	0.41	0.000

* calculated based on the amount of milk and yoghurt consumed on the daily routine

1 The effects of Gender, Smoking, the consumption of Calicum plus vitamin D supllement, levothyroxine and steroid were non-significant and omitted from the analysis

As for the femoral neck and total hip, however, the consumption of alendronate was the only factor affecting the difference between the baseline and second BMD values in the whole population (femoral neck: B coefficient= 0.12, *P*=0.027; total hip: B coefficient = 0.14, *P*=0.007) and the females (femoral neck: B coefficient = 0.13, *P*=0.019; total hip: B coefficient = 0.15, *P*=0.005).

Discussion

While the efficacy of alendronate has long been reported in previous studies, the present research is the first to assess the beneficial effects of the drug on the Iranian population. Based on our results, the drug can effectively improve BMD values at different levels in osteoporotic patients.

Bone mineral density accounts for 60 to 80% of the bone's strength in the experimental models (16). Many studies have also shown even mild changes in the BMD of trabecular bones may lead to increased risk of fracture (17). Certain researches have also reported that the association between the declined BMD levels and increased risk of fracture is independent of the baseline values of BMD (17). It could be concluded that BMD is an important predictor of bone strength, therefore preventing from bone loss can prevent fracture (18).

alendronate can increase BMD, diminish skeletal remodeling and reduce the incidence of fractures in different groups, particularly postmenopausal Caucasian and American-African women (10,19,20).

Consuming alendronate helps rapidly reduce bone resorption as indicated by decreases in urinary N-telopeptide of type I collagen (NTx) as well as markers of bone formation, osteocalcin, and bone alkaline phosphatase (BSAP) (10).

In line with our study, taking alendronate for 2 years is shown to contribute to a progressive increase in BMD of the lumbar spine, total hip, femoral neck, and trochanter. A 12-month double blinded study in the US reported that weekly doses of alendronate 70 mg is associated with a 3.7% increase in mean BMD values at the spine, 1.6% at the femoral neck and 2.2% at the total hip in postmenopausal women (21). Another study on a similar group of patients showed a 4.3%, 1.7% and 1.9% increase in the mean BMD values at the abovementioned sites (22). The Chinese study also revealed a similar, but stronger, trend in the consumers of the drug (4.87% at the spine, 2.47% at the femoral neck, and 2.56% at the total hip) (23). We specified significant difference regarding height declines between two groups, in agreement to our results Tucci et al in a study evaluated the Effect of three years of oral alendronate treatment in postmenopausal women with osteoporosis and declared alendronate is effective in reducing height loss, through preventing spinal fracture, in the consumers (9,24).

Corroborating with previous studies, our research revealed that taking the weekly dosage of the drug was associated with a 7.67% increase in the BMD values at the femoral neck, 8.68% at the total hip, and 3.17% at the lumbar spine (24,25).

Our study also revealed the use of Ca-vit D (calcium plus vitamin D) supplements in all the patients who were not receiving any medication for osteoporosis, whereas only 88% of those being treated for their condition were using the supplements. It could be concluded that many Iranians believe taking Ca-vit D supplements may overcome their need for taking any specific medication for treating osteoporosis. This is while many others only take their medication, claiming that while using osteoporosis medications there would be no need for them to take any supplements. Considering these findings one could point out the need for improving

public awareness regarding osteoporosis.

These results show that alendronate is more effective in Asian postmenopausal women when compared with the Americans. Comparing the results of the present study with that of the above mentioned researches revealed the drug to be more beneficial for the Iranians. The longer follow-up period of the present study with the present study could be among one of the reasons contributing to the reported discrepancy. The differences in the genetic, environment and diet are among the other important factors in this regard.

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