International Journal of Pharmacy and Biological Sciences-IJPBS™ (2020) 10 (2): 167-177
Online ISSN: 2230-7605, Print ISSN: 2321-3272
Research Article | Pharmaceutical Sciences | Open Access | MCI Approved

Effect of Bisphosphonates on Bone Mineral Density in Postmenopausal Women with Osteoporosis: A Retrospective Study

Kusam Harika[1*], Marlabeti Prathyusha, Surepalli Divya Sree, Rentala Praveen, V. Suresh and Singanamala Suman
[1]Pharm-D Intern, Krishna Teja Pharmacy College.
[3,4,5]Pharm-D Intern, Krishna Teja Pharmacy College.
[6]Professor and HOD, Department of Endocrinology, SVIMS, Tirupati.
Assistant Professor, Department of Endocrinology, SVIMS, Tirupati.
Assistant Professor, Department of Pharmacy Practice, Krishna Teja Pharmacy College.

Received: 24 Jan 2020 / Accepted: 20 March 2020 / Published online: 01 April 2020
*Corresponding Author Email: kusamharika239@gmail.com

Abstract

Aim: The aim is to study the effect of Bisphosphonates on Bone Mineral Density in Postmenopausal women with Osteoporosis. **Methodology:** A retrospective study was conducted in department of Endocrinology for a period of 6 months in a tertiary care hospital. Postmenopausal women with Osteoporosis received treatment with Bisphosphonates along with Calcium and Vitamin-D Supplements were included, patients with Chronic kidney disease, Gastro-oesophageal Reflux disease, Liver disease were excluded in the study. **Results:** In a total of 59 patients, this study was demonstrated a statistically significant improvement in mean BMD (5.36% and 4.06%) at Lumbar spine and hip respectively (P<0.001 at both sites), but statistically non-significant improvement in mean BMD (2.1%) at Forearm (P value -0.929). In T-Score, an identical pattern was observed to the BMD changes in all sites namely improvement in all vertebrae, Trochanter, and total hip and no change in Neck of Femur and various Forearm sites. **Conclusion:** In our study, we concluded that the treatment with Bisphosphonates is associated with improvement in Bone mineral density and T-Score of Lumbar spine and Hip. Treatment with Bisphosphonates is associated with maintenance of Bone mineral density and T-Score of Femoral neck and Forearm leading to an improvement in Z-Score.

Keywords
Bisphosphonates, Bone Mineral Density, Postmenopausal women, Osteoporosis, Dual energy X-ray absorptiometry.

*****

INTRODUCTION

Osteoporosis is the most common metabolic bone disease [1]. According to WHO it is "A disease characterized by low bone mass, and deterioration of bone tissue which leads to enhanced bone fragility and a consequent increase in fracture risk" [2]. Clinically bone strength is determined by non-invasive assessment of bone mineral density (BMD) by dual-energy X-ray absorptiometry (DEXA). According to World Health Organisation (WHO), the clinical diagnosis of osteoporosis is based on BMD measurements and presence of fractures [3]. For these diagnostic criteria, BMD is transformed into a T score, which reflects the number of standard

deviations (SD) above or below the mean in healthy young adults. The thresholds for each bone category are shown in the table (1).

Table 1. WHO Definition of Osteoporosis based on BMD

Classification	Bone mineral density	T Score
Normal	Within 1 SD of the mean level of a young adult reference population	T score at -1.0 and above
Low bone mass(Osteopenia)	Between 1 and 2.5 SD below that of the mean level for a young adult reference population	T Score between -1.0 and -2.5
Osteoporosis	2.5 or more below that of the mean level for a young adult reference population	T Score at or below -2.5
Severe or established osteoporosis	2.5 or more below that of the mean level for a young adult reference population with fractures	T Score at or below -2.5 with one or more fractures

According to International Osteoporosis Foundation, Worldwide, 1 in 3 women and 1 in 5 men over the age of 50 years will experience Osteoporotic fracture in their lifetime [4,5,6]. In 2013, sources estimate that 50 million people in India are either osteoporotic (T Score< -2.5) or have low bone mass (T score between -1.0 and -2.5) [7].

Osteoporosis is caused due to aging process in conjugation with decrease in Sex hormones. The bones have deterioration in microarchitecture leading to loss of bone mineral density and increased risk of a fracture. Life style factors are important to the development of osteoporosis including calcium and / or vitamin D deficiency, cigarette smoking [8].

Symptoms of Osteoporosis may have occurred when the bones get weakened. These includes:

- Height loss is a sensitive indicator of compression, but height loss can occur without fractures as a result of narrowing of vertebral disks and postural changes [9].
- Back pain due to a fractured or collapsed vertebra
- Breathing difficulty [10].
- Kyphosis
- Spontaneous bone fractures

Bone mineral density is measured by means of Dual Energy X ray absorptiometry (DEXA) which is the actual expression of the bone in terms of gm/cm2. BMD measurements of hip and spine are used to confirm the diagnosis of osteoporosis to predict future fractures risk and monitor patients [8].

TREATMENT:

As per AACE/ACE guidelines, it provides evidence based information regarding the first-line therapy for the postmenopausal osteoporosis who are at high risk for fractures and drugs include are alendronate, risedronate, zoledronic acid. For those who cannot administer oral therapy and who are at high risk of fracture, use of teriparatide, denosumab or zoledronic acid is recommended [11].

The AACE/ACE recommends that pharmacological therapy should be initiated for [12]:

1) Patients with osteopenia or low bone mass and who have a previous history of fragility fracture at hip and spine.
2) Patients with a T-score of -2.5 or less in lumbar, neck and hip.
3) Patients with a T score between -1.0 and -2.5 if the FRAX 10-year probability for a osteoporoic fracture.

AIM:

The current study deals with comparison of bone mineral density before and after treatment. The aim of the study is to evaluate "The effect of bisphosphonates on Bone mineral density in postmenopausal women with osteoporosis" in tertiary care teaching hospital, SVIMS, Tirupati.

MATERIALS AND METHODS

This **is** a Retrospective study of the data retrieved from the medical records of postmenopausal osteoporosis was carried out in the department of Endocrinology, sri venkateshwara institute of medical sciences, a tertiary care teaching hospital, Tirupati from August 2018 to January 2019. This study was approved by Institutional Ethical Committee (Roc.No.AS/6161/IEC/SVIMS/2017). The medical records are scrutinized to evaluate the effect of bisphosphonates on bone mineral density in postmenopausal women with osteoporosis. After scrutinity of the available medical records, data of 59 patients met the inclusion criteria. A structured patient data collection form was used to collect the patient details like age, gender, menopausal age, weight, height, BMI, date of diagnosis, symptoms prior to diagnosis, duration of menopause at 1st scan, laboratory parameters, before and after treatment with bisphosphonates. This study mainly focuses on postmenopausal women having osteoporosis i.e., T-Score <-2.5 at any one site namely any lumbar

vertebra, neck of femur, and junction of distal one third and proximal 2/3ds of radius who are received treatment with bisphosphonates along with calcium and vitamin D supplementation for ≥2 years, possessing a minimum of two records of BMD spaced ≥2 years apart. A descriptive analysis of the data was done using Microsoft Excel and comparison of two BMD scans before and after treatment with bisphosphonates was done by Paired T test. P value < 0.05 was considered as statistically significant.

RESULTS

This study included 59 patients based on inclusion and exclusion criteria following up at Endocrinology Clinic over the last decade. In this study we assessed effect of bisphosphonates on bone mineral density in postmenopausal women with osteoporosis. All 59 postmenopausal women with osteoporosis had been subjected to DEXA screening at SVIMS Hospital on two occasions at least 2 years apart. Mean duration between the first scan and the most recent scan was 57.7 ± 26.2 months. The treatment given to the patients was bisphosphonates (such as Alendronate, Ibandronate, and Risedronate) along with calcium and Vitamin-D supplements.

The mean age of patients in this study group was 59.06 ± 5.040 years (table 2), with the age ranging from 40 to 75 years. The mean age at menopause was 44.3 ± 7.037 years and hence the duration of menopause at recruitment was14.72 ± 7.26 years (table 2).

Table 2: Patient parameters at the time of initial DEXA scan

Serial No.	Patient parameter	Value (mean± SD)
1.	Age (years)	59.06 ± 5.040
2.	BMI (Kg/m2)	26.09 ± 4.670
3.	Age at menopause (years)	44.305 ± 7.037
4.	Duration of menopause (years)	14.72 ± 7.26
5.	Serum creatinine (mg/dl)	0.766 ± 0.227
6.	Serum calcium (mg/dl)	9.806 ± 0.540
7.	Serum phosphorous (mg/dl)	3.733 ± 0.693
8.	Serum alkaline phosphatise (IU/L)	88. 01 ± 26.01
9.	Serum 25 OH Vitamin D (ng/ml)	24.52 ± 12.80
10.	Serum PTH (pg/ml)	31.055 ± 17.46

AGE:

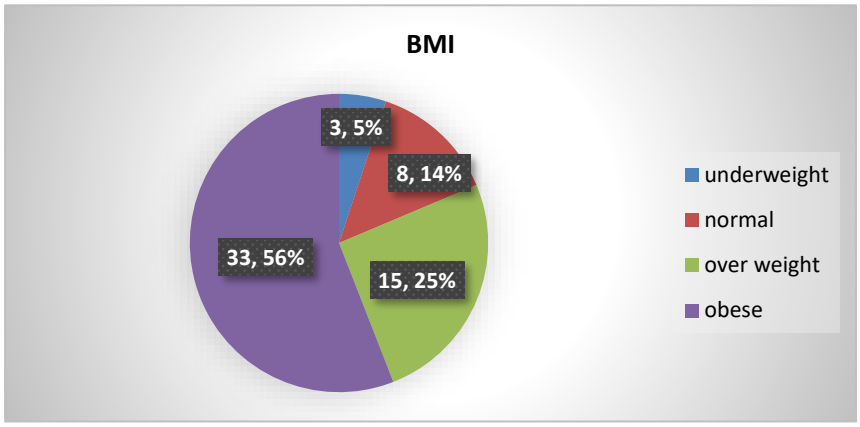
Highest frequency of patients was found in the age group 60-65 years. In the age group of 45-49, 50-54, 55 -59, 60-64, 65-69 the percentage of osteoporosis in postmenopausal women was found to be 3.38%, 15.2%, 27.1%, 38.9%, 15.2% respectively (table 3).

Table 3: Age-wise distribution of postmenopausal women enrolled into the study

S.NO	AGE GROUP (YRS)	Number	Percentage
1	45-49	2	3.38%
2	50-54	9	15.2 %
3	55-59	16	27.1 %
4	60-64	23	38.9 %
5	65- 69	9	15.2 %

BMI

Figure 1: Pie diagram showing the distribution of BMI in the study population.



The mean BMI was 26.09 ± 4.670 Kg/m^2. The distribution of BMI is shown in Figure 1.

LABORATORY PARAMETERS:

In the present study mean values of serum calcium among the patients are 9.806 ± 0.540 mg/dl. Mean values of creatinine, phosphorous, alkaline phosphatase and parathyroid hormone among the patients are 0.766 ± 0.227mg/dl, 3.733 ± 0.693 mg/dl, 88.01 ± 26.01mIU/L and 31.05 ± 17.46 pmol/L respectively. The mean value of 25-OH Vitamin-D among the patients was 24.52 ± 12.80 ng/dl. (table 2)

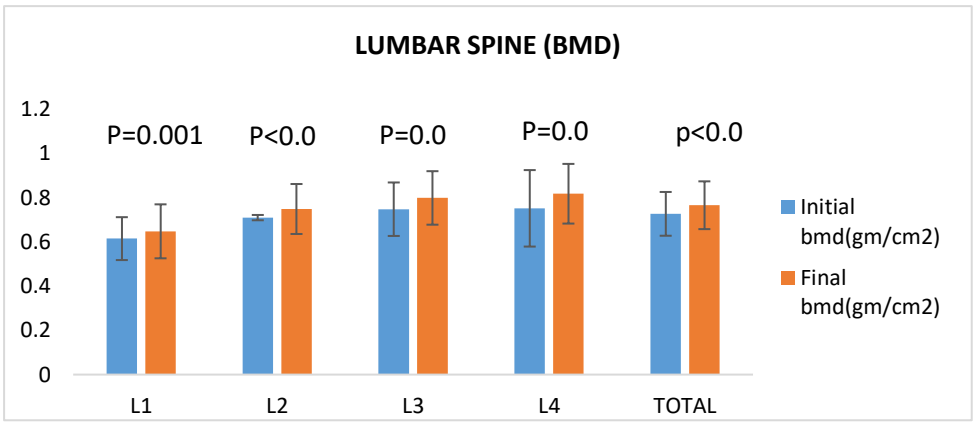
BMD –LUMBAR SPINE

In this study the mean value of initial BMD at the total lumbar spine was 0.727 ± 0.099 and it rose to 0.766 ± 0.108 gm /cm^2 following treatment; p value < 0.001 (table 5). Further an increase in bone density at all lumbar vertebrae was also observed as a result of treatment with bisphosphonates (figure 2).

Table 4: Table comparing BMD at various sites in the Lumbar spine before and after treatment

LUMBAR SPINE	INITIAL BMD (gm/cm^2)	FINAL BMD (gm/cm^2)	P VALUE	% change in BMD
L1	0.615 ± 0.097	0.648 ± 0.122	0.0011	5.36 %
L2	0.710 ± 0.107	0.749 ± 0.113	< 0.001	5.49 %
L3	0.748 ± 0.121	0.799 ± 0.125	0.005	6.81%
L4	0.752 ± 0.173	0.818 ± 0.135	0.006	8.77 %
TOTAL	0.727 ± 0.099	0.766 ± 0.108	< 0.001	5.36%

Figure 2: Comparison of BMD at different sites in lumbar spine before and after the treatment with bisphosphonates.



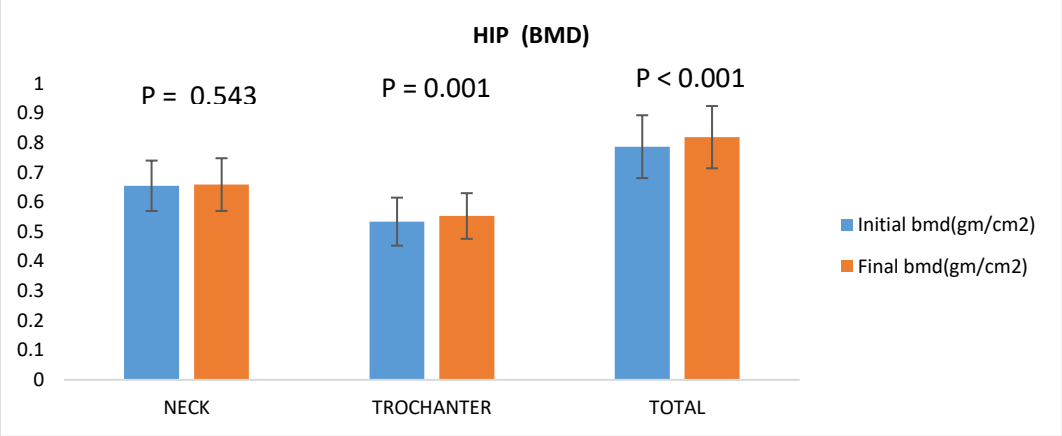
BMD-HIP

In this study the mean value of initial and final BMD at total hip was 0.787 ± 0.106 and 0.819 ± 0.105 which is a significant increase; p < 0.001 (table 6). By comparing BMD in various sites in hip before and after treatment with bisphosphonates, there was an increase in trochanter region but no increase in neck of femur (table 5 and figure 3).

Table 5: Table comparing BMD at various sites in the Hip before and after treatment with Bisphosphonates

HIP	INITIAL BMD (gm/cm²)	FINAL BMD (gm/cm²)	P VALUE	% change in BMD
Neck	0.655 ± 0.085	0.659 ± 0.089	0.543	0.61 %
Trochanter	0.534 ± 0.081	0.553 ± 0.077	0.001	3.55 %
TOTAL	0.787 ± 0.106	0.819 ± 0.105	< 0.001	4.06 %

Figure 3: Comparison of BMD at different sites in hip before and after the treatment with bisphosphonates.



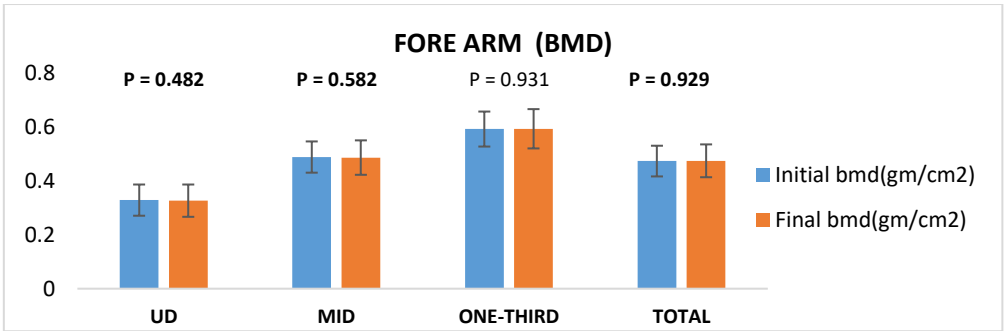
BMD-FOREARM

The mean value of initial and final BMD at total forearm was 0.474 ± 0.057 and 0.475 ± 0.061; which difference was not significant (p=0.929) - vide table 6. By comparing BMD in various sites in forearm before and after treatment with bisphosphonates, there is no change in any site in the forearm (figure 4).

Table 6: Table comparing BMD at various sites in the forearm before and after treatment with bisphosphonates

FOREARM	INITIAL BMD (gm/cm²)	FINAL BMD (gm/cm²)	P VALUE	% change in BMD
UD	0.329 ± 0.058	0.327 ± 0.060	0.482	-0.60 %
MID	0.489 ± 0.058	0.487 ± 0.64	0.582	-0.40 %
1/3	0.593 ± 0.065	0.594 ± 0.073	0.931	0.16 %
TOTAL	0.474 ± 0.057	0.475 ± 0.061	0.929	0.21 %

Figure 4: Comparison of BMD at different sites in forearm before and after the treatment with bisphosphonates



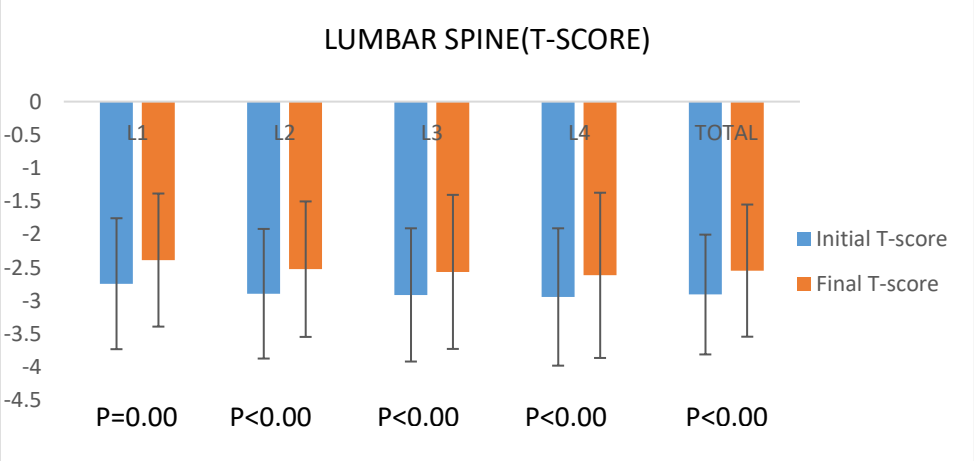
T –SCORE-LUMBAR SPINE

In this study the mean value of initial and final T-score at lumbar spine was -2.905 ± 0.902 and -2.545±0.995 which represented a significant increase (P < 0.001) - vide-table 7. By comparing T score in various sites in lumbar spine before and after treatment with bisphosphonates, there was an increase in T scores at each lumbar vertebra (figure 5).

Table 7: Table comparing T-Score in various sites in the Lumbar spine before and after treatment with Bisphosphonates

LUMBAR SPINE	INITIAL T SCORE	FINAL T SCORE	P VALUE	% Change in T score
L1	-2.742± 0.986	-2.386 ± 1.002	0.0016	12.9 %
L2	-2.893 ± 0.96	-2.523 ± 1.024	< 0.001	12.7 %
L3	-2.911 ± 1.003	-2.564 ± 1.160	< 0.001	11.9 %
L4	-2.942 ± 1.034	-2.616 ± 1.244	< 0.001	11.08 %
TOTAL	-2.905 ± 0.902	-2.545 ± 0.995	< 0.001	12.39 %

Figure 5: Comparison of T Score at different sites in lumbar spine before and after the treatment with bisphosphonates



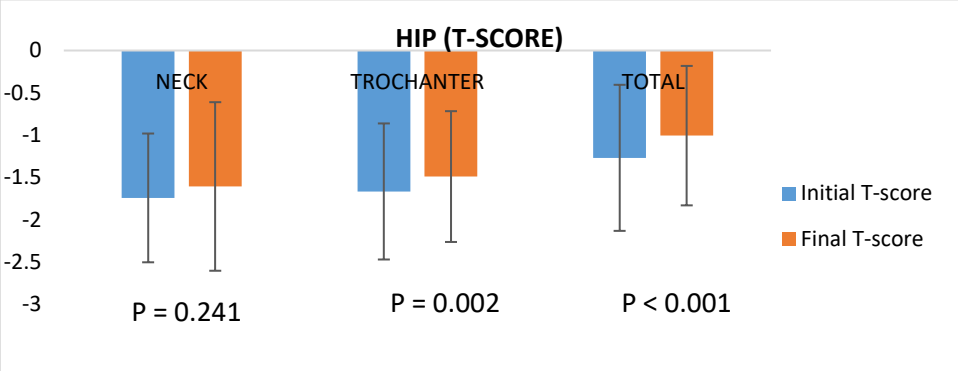
T-SCORE HIP:

In this study the mean value of initial and final T score at hip was -1.267 ± 0.862 and -1.005 ± 0.823 (P value < 0.001) -see table 8. By comparing T score in various sites in hip before and after treatment with bisphosphonates, there is increase in trochanter region but no increase in femoral neck region (figure 6).

Table 8: Table comparing T score at various sites in the Hip before and after treatment with Bisphosphonates

HIP	INITIAL T SCORE	FINAL T SCORE	P VALUE	% change in T score
NECK	-1.740 ± 0.760	-1.605 ± 0.995	0.241	7.75 %
TROCHANTER	-1.664 ± 0.803	-1.488 ± 0.772	0.002	10.57%
TOTAL	-1.267 ± 0.862	-1.005 ± 0.823	< 0.001	20.67 %

Figure 6: Comparison of T score at different sites in hip before and after the treatment with bisphosphonate.



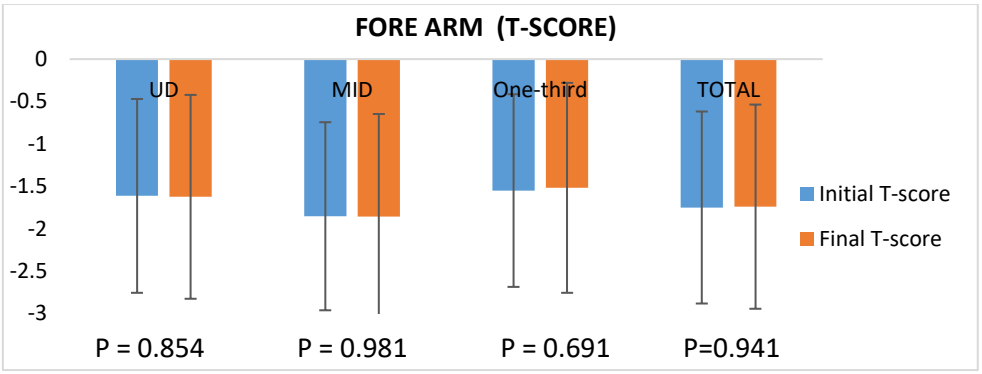
T SCORE-FOREARM

In this study the mean value of initial and final T score at total forearm was -1.75 ± 1.132 and -1.744 ±1.204 (P =0.941)- table 9. By comparing T score in various sites in forearm before and after treatment with bisphosphonates, there is no increase in any site in the forearm (figure 7) as a result of treatment.

Table 9: Table comparing T score at various sites in the forearm before and after treatment with Bisphosphonates

FOREARM	INITIAL T SCORE	FINAL T SCORE	P VALUE	% change in T score
UD	-1.613 ± 1.143	-1.624 ± 1.202	0.854	-0.68 %
MID	-1.853 ± 1.109	-1.851 ± 1.210	0.981	0.10 %
1/3	-1.55 ± 1.136	-1.518 ± 1.238	0.691	2.06 %
TOTAL	-1.75 ± 1.132	-1.744 ± 1.204	0.941	0.34 %

Figure 7: Comparison of T score at different sites in forearm before and after the treatment with bisphosphonate



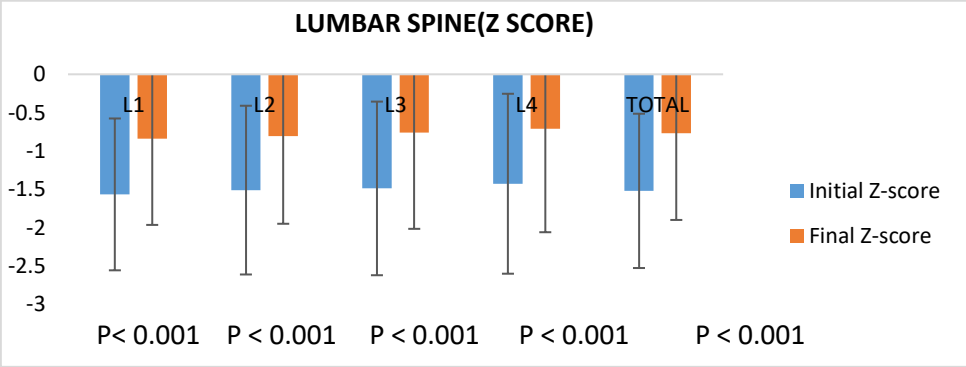
Z SCORE-LUMBAR SPINE

In this study the mean value of initial and final Z-score at lumbar spine was -1.520 ± 1.006 and -0.769 ± 1.130 (P value < 0.001)- table 10. By comparing Z score in various sites in lumbar spine before and after treatment with bisphosphonates, there is increase in bone density at all vertebrae in the lumbar region (figure 8).

Table 10: Table comparing Z score at various sites in the Lumbar spine before and after treatment with Bisphosphonates.

LUMBAR SPINE	INITIAL Z SCORE	FINAL Z SCORE	P VALUE	% change in Z score
L1	-1.566 ± 0.990	-0.838 ± 1.126	< 0.001	46.4 %
L2	-1.516 ± 1.100	- 0.805 ± 1.144	< 0.001	46.8 %
L3	-1.488 ± 1.132	-0.761 ± 1.254	< 0.001	48.8 %
L4	-1.427 ± 1.173	-0.711 ± 1.348	< 0.001	50.7 %
TOTAL	-1.520 ± 1.006	-0.769 ± 1.130	< 0.001	49.4 %

Figure 8: Comparison of Z score at different sites in lumbar spine before and after the treatment with bisphosphonates



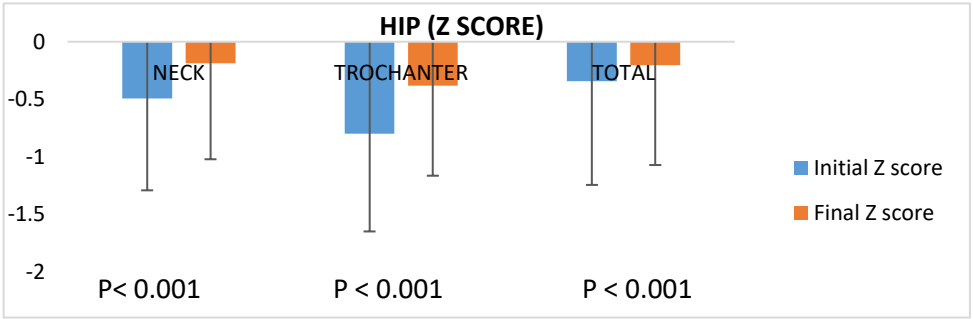
Z SCORE -HIP

In this study the mean value of initial and final Z score at total hip was -0.344 ± 0.900 and -0.205 ± 0.866 (P value < 0.001) which is represented in table 11. By comparing Z score in various sites in hip before and after treatment with bisphosphonates, there is improvement in trochanter region as well as in femoral neck region which is represented in figure 9.

Table 11: Table comparing Z score at various sites in the Hip before and after treatment with Bisphosphonates.

HIP	INITIAL Z SCORE	FINAL Z SCORE	P VALUE	% change in Z score
Neck	-0.494 ± 0.797	-0.188 ± 0.833	< 0.001	61.9 %
Trochanter	-0.779 ± 0.849	-0.383 ± 0.781	< 0.001	50.8 %
TOTAL	-0.344 ± 0.900	-0.205 ±0.866	< 0.001	40.4 %

Figure 9: Comparison of Z score at different sites in hip before and after the treatment with bisphosphonates



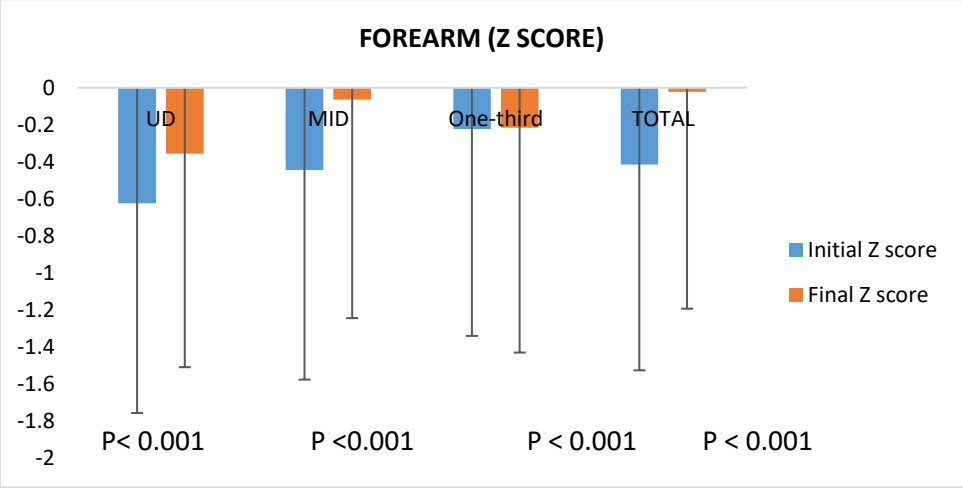
Z SCORE-FOREARM

In this study the mean value of initial and final Z score at forearm was -0.415 ± 1.111 and -0.022 ± 1.171 (P value < 0.001) - table 12. By comparing Z score in various sites in forearm before and after treatment with bisphosphonates, there was improvement in all sites in the forearm -figure 10.

Table 12: Table comparing Z score at various sites in the forearm before and after treatment with Bisphosphonates

FOREARM	INITIAL Z SCORE	FINAL Z SCORE	P VALUE	% change in Z score
UD	-0.624 ± 1.132	-0.356 ± 1.153	< 0.001	42.9 %
MID	-0.444 ± 1.132	-0.063 ± 1.181	< 0.001	85.8 %
1/3	-0.256 ± 1.118	-0.215 ± 1.215	< 0.001	16.01 %
TOTAL	-0.415 ± 1.111	-0.022 ± 1.171	< 0.001	94.6 %

Figure 10: Comparison of Z score at different sites in forearm before and after the treatment with bisphosphonate



DISCUSSION

Osteoporossis in postmenopausal women is a major health problem in India. The Delhi Vertebral Osteoporosis Study (DeVOS) showed a prevalence of 17.1% of fractures of spine in 415 women aged more than 50 years recruited into the study [13]. A study from Rohtak showed the frequency of hip fracture to be 159/100,000 in women older than 50 years of age [14]. A reported 34.3/100,000 women suffer from low trauma fractures at hip, spine, and wrist [15]. Khadlikar et al [16] have suggested that in the year 2015, of the 230 million women over the age of 50 years in India about 20% would be suffering from osteoporosis. This gives a very high estimate of 46 million.

There is a huge economic impact of osteoporotic fractures in terms of cost of treatment and need to keep away from productive work. Further, apart from the pain that the patient suffers, there is also reduced motility and an increased risk of mortality particularly in patients with hip fracture. Hence the need to treat osteoporosis, to prevent the development of fractures.

Currently one of the most effective and low cost modality of treatment for osteoporosis is the use of oral or i.v bisphosphonates. Long term trials have shown significant improvement in bone mineral density and a reduction of fractures in postmenopausal women with osteoporosis. These drugs are approved by FDA for the treatment of osteoporosis as defined by WHO (i.e T score < -2.5). In addition, the bisphosphonates are also indicated in the treatment of osteopenia in postmenopausal women where the risk of fracture of the hip is more than 3% in 10 years or overall fracture risk is more than 20% in 10 years as determined by the WHO FRAX score.

The fracture Intervention Trial (FIT) with alendronate is the largest trial till date to document the efficacy of alendronate- an oral bisphosphonate in postmenopausal osteoporosis. In this trial there was an approximately 50% reduction in hip and vertebral fractures in alendronate treated patients along with a 30% reduction in all clinical fractures in 3658 women followed up for 3-4 years [17].

Table 13: Comparison of our study outcome with other study outcome regarding BMD change among Postmenopausal women with Osteoporosis after Bisphosphonates use.

Authors	Subjects	Study duration(yrs)	Type of treatment	Change in BMD Spine%	Change in BMD Hip %	Change in BMD Forearm %
Isaac Sachmechi study	114	4 years	Alendronate	3.1 %	1.9 %	- 9.8%
Bone HG study	994	10 years	Alendronate	13.7%	10.3%	5.4%
Miroslava Hejdova study	32	1 year	Alendronate	7.0%	4.3%	_
Li M study	639	1 year	Low dose Alendronate, Calcium & Vitamin-D supplements	5.6%	3.87%	3.28%
Chailurkit LO study	70	1 year	Alendronate	9.2%	4.6%	3.1%
Our study	59	4 years 9 months	Alendronate, Ibandronate Risedronate	5.36%	4.06 %	0.21%

Improvement with BMD and T scores in women on Bisphosphonates:

This reduction in fracture risk is accompanied by an improvement in the BMD as shown below in (table 13). However, the effect of bisphosphonates on BMD has not been adequately studied in India. We performed a retrospective analysis of changes in BMD, T score and Z score in spine, hip region and forearm before and at least 2 years or more after the commencement treatment with bisphosphonates. After 4.9 years of follow –up, there was an improvement in mean BMD at hip and spine by 5.36% and 4.06% respectively ($p < 0.001$ at both sites). However, at the total forearm there was a non-significant improvement of only 2.1% (p value 0.929). Indeed, there was no improvement in BMD in any region of the forearm or in the total forearm.

Similar results were observed by other authors also. Sachmechi et al [18] showed that even after 4 years of bisphosphonate therapy there was a fall in forearm BMD (-9.1%) as against an improvement in spine and hip BMD. Likewise, in the Bone HG study maximum improvement was observed in the spine followed by hip and then least in the forearm. This is the same pattern observed in our study.

There was no significant improvement in BMD in the neck of femur in our study, while it increased in trochanter and total hip. In the spine BMD improved in all the vertebrae.

With Regard to the t scores, an identical pattern was observed to the BMD changes in all sites; namely improvement in all vertebrae, trochanter and total hip and no change in neck of femur and various forearm sites.

Thus it is clear that there is a differential effect of bisphosphonates on BMD in different parts of the skeleton with more effect on the spine and less on the forearm. Bisphosphonates are anti-resorptive agents. They deposit in the bone matrix replacing the pyrophosphate crystals. They then induce apoptosis in osteoclasts and thereby primarily inhibit bone resorption by osteoclasts. Because of the coupled nature of osteoclastic and osteoblastic responses, secondarily osteoblastic activity is also reduced.

The coupled activity of osteoblasts and osteoclasts occurs at the surface of the bone. Initially osteoclasts resorb a small region of the bony surface called How ship's lacuna. This lacuna is then filled up by osteoblasts with newly formed bone. After the 3rd decade of life each such bone cycle results in a slight negative balance as the amount of bone formed by the osteoblast in response to osteoclastic activity is slightly less than the amount previously resorbed. This loss of bone is accelerated at menopause due to loss of estrogenic inhibitory effect on osteoclasts, thereby leading to more bone turnover per unit time and greater net negative loss.

Bisphosphonates by primarily inhibiting resorption and secondarily affecting bone formation reduce the bone turnover. They also tip the slight negative balance in each bone turnover cycle to a positive one. This allows the BMD to go up in bones which have a large surface area. This is because the action of bisphosphonates in modulating bone turnover

occurs at the surface where osteoclasts and osteoblasts reside.

Vertebrae of the spine are largely cancellous bones, while the hip and forearm are mixed, with the forearm having a higher proportion of cortical bone. As cancellous bones have much higher surface area by virtue of their trabecular meshwork. Cortical bones have only subperosteal and endosteal surfaces. Therefore, it would follow that bisphosphonates would be more effective at the spine, less at the hip and least at the forearm, exactly what we have observed.

Maintenance of BMD and T Scores in Femur neck and forearm:

It would not be true to say that bisphosphonates had no effect on bone in the forearm and neck of femur. Indeed, even no change in BMD over more than 5 years is a significant achievement, because normally the BMD should go down with aging. This is the reason that the z score improved in all the areas including neck of femur and the forearm sites (whereas BMD and t score did not change).

T score is the number of standard deviations by which the observed BMD at any site deviates from the mean BMD of a young woman in the early 3rd decade. It will change only if the BMD also changes. However, the z score is the number of standard deviations by which the observed BMD deviates from the mean BMD of age matched otherwise healthy women. As women age, the mean BMD falls at all sites measured. However, if the observed BMD and the t score are maintained unchanged over a period of time, the z score will improve as the mean BMD of the untreated population at that site would have fallen.

CONCLUSION

Treatment with bisphosphonates is associated with improvement in bone mineral density and t scores of lumbar spine and hip.

Treatment with bisphosphonates is associated with maintenance of bone mineral density and t scores of femoral neck and forearm leading to an improvement in z score.

BIBILIOGRAPHY

1) Shlomo, Melmed, Kenneth Spolonsky, P. Reed Larsen, Henry M. Kronenberg. Williams textbook of Endocrinology. 2012; 12:1312-1320.
2) Consensus Development Conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med. 1993; 94:646-650.
3) Kanis JA, Melton LJ 3rd, Christiansen C, Johneston CC, Khaltaev N. The diagnosis of Osteoporosis. J Bone Miner Res 9; 1994:1137-1141.
4) Compston J., Genant H. Epidemiology and Diagnosis of postmenopausal osteoporosis. In: Rizzoli R.(eds) Atlas of postmenopausal osteoporosis 2010. https://doi.org/10.1007/978-1-907673-28-3-2.
5) Kanis S, J.A& Johnell, O & Oden, A & Serbo, Ingemer & Redlund-Johnell, I & Dawson, A & De Laet, Chris & Jonsson, Brynjolfur. Long-term Risk of Osteoporotic Fracture in Malmo. Osteoporosis International 2000; 11:669-674.
6) Steven W Blume, Jeffrey Curtis. Medical costs of osteoporosis in the elderly Medicare population. National Osteoporosis Foundation of USA.2010;22(6):1835-44.
7) Ambrish Mithal, Beena Bansal, Carey S.Kyer, Peter Ebeling. Division of Endocrinology and Diabetes. Indian J Endocrinol Metab. 2014;18(4):449-454.
8) Tumay sozen, Lale ozisik, Nurselcalikbasaran. An overview and management of Osteoporosis. Eur J Rheumatol 2017; 4:46-56.
9) Siminoski K, Warshawski RS, Jen H,et al.The accuracy of historical height loss for the detection of vertebral fractures in postmenopausal women. Osteoporos Int.2006; 17:290- 296.
10) Lumbardi I Jr, Oliveira LM, Mayer AF, et al., Evaluation of pulmonary function and quality of life in women with osteoporosis. Osteoporosis Int.2005; 16:1247-1253.
11) Osteoporosis Australia http://www.osteoporosis.org.au.2004
12) Kristie N. Tu, Janette D.Lie, Chew King Victoria wan, Madison Cameron, Alaina G.Austel, Jenny K.Nguyen,et al., Osteoporosis: A Review of Treatment options.2018;43(2):92-104.
13) Marwaha RK, Tandon N, Gupta Y, et al. The prevalence of and risk factors for radiographic vertebral fractures in older Indian women and men: Delhi Vertebral Osteoporosis study (DeVOS) Arch Osteoporos 2012;7(1-2):201-207
14) Dhanwal DK, Siwach R, Dixit V, Mithal A, Jameson K, Cooper C. Incidence of hip fracture in Rohtak district, North India. Arch Osteoporos.2013;8(1-2):135.
15) Mithal A, Bansal B, Kver CS, Ebeling P. The Asia-Pacific regional audit-epidemiology, costs, and burden of osteoporosis in India 2003: a report of International Osteoporosis Foundation. Indian J Endocrinol Metab.2014;18(4):449-454.
16) Khadilkar AV, Mandlik RM. Epidemiology and treatment of osteoporosis in women: An Indian perspective. Int J Womens Health. 2015; 7:841-50.
17) Black DM, Thompson DE, Bauer DC, Ensrud K, Musliner T, Hochberg MC. Fracture risk reduction with alendronate in women with osteoporosis: The Fracture Intervention Trial. FIT Research Group J Clin Endocrinol Metab.2000;85(11):4118-24.
18) Isac sachmechi, Ahmed S, Joseph J, et al. Effect of Alendronate on Bone Mineral Density in Postmenopausal women with Type-2 Diabetes Mellitus. Int Endocrinol Metab Disord.2015;1(1): doi http://dx.doi.org/10.16966/2380-548X.103.