

## Study of effect of zoledronic acid on back pain in patients with osteoporosis

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**Conflicts of Interest:** Nil

### Abstract

**Introduction:** Osteoporosis is characterized by low bone mass, microarchitectural disruption, and increased skeletal fragility, resulting in decreased bone strength and increased risk of fracture. Zoledronic acid is a bisphosphonate which can be given once in a year IV, has better patient compliance and good clinical efficacy compared to other oral bisphosphonates. The present study aimed to evaluate the effect of Zoledronic acid in patients with low back pain due to osteoporosis.

**Materials and Methods:** This longitudinal study was conducted among the patients attending OPD / admitted with low back pain at the KLES DR. Prabhakar Kore

Hospital and Medical Research Centre and Charitable Hospital, Belagavi in between 1<sup>st</sup> January 2021 to 31<sup>st</sup> December 2021, over a period of one year. The patients were assessed for the BMD, BMI, VAS, ODI, FRAX score at the various interval of time till one year. Outcome measures were analyzed using the SPSS (Statistical package for social sciences) program.

**Results:** Total of 120 patients included with mean age of 63.43±9.38 yrs and 60 percent were female patients. There was insignificant change in the BMD, T-score, and significant improvement in VAS among the patients compared to the baseline at each visit. However, the reduction in the mean score of osteoporotic fracture

probability and the hip fracture probability did not show significant difference in one year follow-up. ( $p>0.05$ )

**Conclusion:** The present study is successful in demonstrating significant improvement in associated pain among the patients with osteoporosis at the end of one year of follow-up and the insignificant change in the bone mineral density at the end of one year follow-up. Long term follow-up treatment is required to assess the change in bone mineral density.

**Keyword:** Bone Mineral Density, Zoledronic Acid, Bisphosphates, Osteoporosis, Mineralization.

### Introduction

Osteoporosis, a disease with decreasing bone-mass, mostly in post-menopausal women, but it can also affect people who have any hidden illnesses/significant risk factors for bone-mineral loss.<sup>1</sup> Peak bone mass (PBM), which refers to the bone mass and strength attained at the completion of the development phase, is crucial in determining the likelihood that an adult would have an osteoporotic fracture. A one standard deviation increase in peak-bone mass is thought to lead to a drop of half in the risk of fracture. The comparative benefaction of peak-bone mass to fracture risk has been determined by analyzing the changes of areal bone mineral density (aBMD) individual values in response to age. If peak-bone mass were almost always irrelevant in defining aBMD and fracture-risk in old life, one could foresee extension in the range of aBMD values with age.<sup>2</sup> Clinicians frequently struggle with managing bone pain, which is mostly seen in older patients. The potential to function and quality of life of someone can be irreparably harmed by back pain. In Europe, 19% of persons have serious chronic pain. In Italy, this number rises to 26 percent.<sup>3,4</sup> According to Klotzbuecher et al., having one vertebral compression fracture raises the risk

of developing another.<sup>6</sup> The antiresorptive zoledronic-acid slows the rate of bone dissolution. Numerous investigations are mentioning that zoledronic-acid, with a handful of the other bis-phosphonates, also has analgesic effects/results, however the mechanism is still being researched.<sup>7-10</sup> In comparison to other oral bis-phosphonates, zoledronic-acid, can be administered intravenously just one time a year, has higher patient compliance plus effective clinical use. Another noteworthy feature is the paucity of studies on osteoporosis prevalence in the Indian-population.

This study evaluates the functional efficacy of yearly infusion of Zoledronic-acid in vertebral osteoporosis.

### Aims and Objectives

**Aim:** To evaluate the effect of Zoledronic acid on patients with back pain due to osteoporosis.

### Objective

1. To measure the bone mineral density among all the included patients
2. To follow-up and assess the effect of Zoledronic acid on the bone mineral density at each follow-up for one year.

**Source of data:** Patients who came to OPD / admitted with Low back pain at the KLE'S DR. Prabhakar Kore Hospital and Medical Research Centre and Charitable Hospital, Belagavi in between 1<sup>st</sup> January 2021 to 31<sup>st</sup> December 2021, over a period of one year.

**Study Design:** Longitudinal Study

**Study Period:** 1<sup>st</sup> January 2021 to 31<sup>st</sup> December 2021

**Sample Size:** 120

**Sampling Method:** Simple Random Sampling

**Selection Criteria**

**Inclusion Criteria**

1. Patients of either sex aged 40 years and above.

2. Patients with back pain more than 4 weeks of duration.
3. Patients with degenerative arthritis.
4. No known malignancy, no prior trauma / surgery, no known abdominal cause for low back pain.
5. Patients willing to give written informed consent.

#### Exclusion Criteria

1. Patients less than 40 years old.
2. Patients with prior trauma/surgery.
3. Patients with features of neurological deficit due to spine pathology.
4. Patients with impaired renal clearance.
5. Patients with abdominal pathology causing back pain.
6. Patients on hormone replacement therapy, oral bisphosphonates or any other active management except calcium and vitamin D.
7. Patients with any infective pathology like tuberculosis, discitis, and malignancy.
8. Patients with Prolapsed intervertebral disc, spinal canal stenosis, spondylolysis, spondylolisthesis.
9. Patients not willing to be part of the study.

#### Methods

**Procedure:** The patients who come to OPD with backpain in KLE'S Dr Prabhakar Kore Hospital & Research Centre and Charitable Hospital, Belagavi their thorough history, clinical examination and routine investigation will be carried out to rule out causes of back pain.

The patients after matching with the inclusion criteria on Xray of spine and FRAX score assessment. Eligible patients were subjected to Bone mineral density assessment. The patients who were diagnosed to be osteoporotic according to WHO guidelines<sup>2,4,5,11</sup>, was admitted as per expert advice of the treating consultant as an inpatient after counselling 5 mg of IV Zoledronic

acid was infused after proper hydration (50 ml normal saline before infusion and 50 ml after infusion of zoledronic acid) of the patient over a period of 15 to 20 minutes.

Normal: T score  $\geq -1$  SD

Osteopenia: T score between -1 and -2.5 SD

Osteoporosis: T score  $\leq -2.5$  SD

#### Visit 1/ Day1/ Initial or baseline assessment-

1. Screening for inclusion of study and taking informed written consent.
2. Details of patient's demographic characteristics, and medical histories, concomitant medications and detailed physical/clinical evaluation was recorded.
3. Assessment of symptoms by VAS and modified Oswestry scales.
4. Routine investigations like Complete blood picture, Renal function tests, serum calcium, phosphate, Vitamin D, alkaline phosphatase, radiograph of thoracolumbar spine, Bone mineral density using DEXA were recorded.
5. Eligible patients were admitted as per expert advice of the treating consultant as an inpatient after counselling. 5mg intravenous Zoledronic acid was infused after proper hydration (50 ml normal saline before infusion and 50 ml after infusion of zoledronic acid) of the patient over a period of 15 to 20 minutes, with their informed written consent.
6. They were discharged from the hospital after observing for any acute reactions like generalized body-ache, fever for one day in-patient if needed.

#### Visit 2/ Week 12

1. Assessment of symptoms by VAS scale and modified Oswestry scale.
2. All observed or spontaneously volunteered adverse events was recorded.
3. Pulse rate and blood pressure were recorded.

4. The modified Oswestry back pain questionnaire were given and its score recorded.

#### Visit 3/ Week 24

1. Patients improvement with respect to pain was assessed using VAS scale, FRAX score and modified Oswestry back pain questionnaire were recorded.

2. All observed or spontaneously volunteered adverse events were recorded.

3. Pulse rate and blood pressure were recorded.

4. Patients improvement radiologically and clinically at 6 months.

#### Visit 4/ 1 year

1. Patients improvement with respect to pain was assessed using VAS scale and modified Oswestry back pain questionnaire was recorded.

2. All observed adverse events were recorded.

3. Pulse rate and blood pressure were recorded.

4. Patients improvement radiologically and clinically with respect to Bone mineral density were recorded using DEXA.

**Does the study require any investigations or interventions to be conducted on patients or other humans or animals?**

**YES,**

1. X-Ray Spine AP and Lateral views

2. DEXA/BMD

3. Routine Investigations: Blood: Hb percent, TLC, DLC, ESR, Calcium, Phosphorous, Vit D3, Alkaline Phosphatase.

4. USG abdomen (if needed)

5. Renal Function Tests (if needed)

#### Results

1. Total of 120 patients fulfilling inclusion criteria willing to be part of study were included. the mean age of the participants was found to be  $63.43 \pm 9.38$

years, among them 60 percent were female patients and 40 percent were male patients, with female preponderance (female to male ratio 1.5:1)

2. The mean age of the participants was found to be  $63.43 \pm 9.38$  yrs,

3. Among them 60 percent were female patients and 40 percent were male patients, with female preponderance (female to male ratio 1.5:1)

4. There is no significant change in BMI of the patients at different visits for hospital. ( $p > 0.05$ )

5. On comparison, there is insignificant change in the BMD among the patients compared to baseline.

6. On comparison, there is insignificant change in the T score among the patients compared to baseline.

7. Comparatively, the VAS among the patients has significantly improved from baseline at each visit. ( $p < 0.001^*$ )

8. Comparatively, the ODI among patients has significantly improved from baseline at each visit. ( $p < 0.001^*$ )

#### Discussion

Bisphosphates have a high affinity for bone, are rapidly absorbed, and have a positive impact. They have a long effective concentration in bone and are well tolerated clinically. Previous research has shown that bisphosphonates are useful in the treatment of Osteoporosis and can significantly lower the risk of fracture.

In present study, there are significant changes in VAS among the patients compared to the baseline at each visit, and insignificant change in the BMD and T score checked at first visit and at one year of follow-up. The BMD at 1<sup>st</sup> visit was  $0.707 \pm 0.13$  and at 4<sup>th</sup> visit was  $0.712 \pm 0.145$  ( $p < 0.05$ ). Similarly, the T score at 1<sup>st</sup> visit was  $-3.470 \pm 0.72$  and at 4<sup>th</sup> visit was  $-3.447 \pm 0.728$

( $p < 0.05$ ). There was significant VAS score reduction, with baseline VAS score was  $7.667 \pm 0.844$ , reduced to 2<sup>nd</sup> visit  $6.46 \pm 0.9$ , 3<sup>rd</sup> visit  $5.23 \pm 0.85$  and 4<sup>th</sup> visit  $6.26 \pm 0.73$  ( $p < 0.05$ ) However the osteoporotic fracture probability and the hip fracture probability didn't show significant difference.

Similarly, Cauley et al., documented women with postmenopausal osteoporosis, a once-yearly infusion with zoledronic acid over a 3-year period significantly reduced the number of days that patient reported back pain, limited activity owing to back pain, and limited activity and bed rest owing to a fracture.<sup>6,10</sup>

Because of its annual dosage, zoledronic acid, a bisphosphonate type of drug, has high compliance, and there are early studies claiming its analgesic benefits. The study revealed that zoledronic acid has a considerable pain-relieving effect in people suffering from low back pain caused by vertebral osteoporosis.<sup>5,9</sup> The present study showed a significant change in bone mineral density and reduction of associated pain among the patients with osteoporosis. However, the fracture probability scores did not show significant difference, which can be followed-up for more than one year to assess the effect of the Zoledronic acid on long term.

### Conclusion

The present study successful in demonstrating the significant improvement in associated pain among the patients with osteoporosis at each visit till the one year of follow-up and insignificant change in the bone mineral density was noted at the end of one year.

However, this change in bone mineral density did not have a significant effect on the risk scores. The major osteoporotic fracture probability and hip fracture probability showed a reduced risk at the one year of follow-up.

Hence the long-term follow-up is required to assess the effect on these risk score. No much adverse effects were seen among the patients, making Zoledronic acid safe medication to treat the osteoporosis among the patients and offers significant pain improvement.

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**Legend Tables and Figures**

Table 1: Comparison of score changes at different visits using paired t-test

	Mean	SD	Paired t-test (p-value)
T SCORE 1st visit	-3.470	0.724	0.124
T SCORE 4th visit	-3.447	0.728	

Table 2: Comparison of VAS changes at different visits using paired t-test

	Mean	SD	Paired t-test (p-value)
VAS 1st visit	7.667	0.844	0.001*
VAS 2nd visit	6.467	0.937	
VAS 1st visit	7.667	0.844	0.001*
VAS 3rd visit	5.233	0.858	
VAS 1st visit	7.667	0.844	0.001*
VAS 4th visit	6.267	0.739	

Table 3: Comparison of ODI changes at different visits using paired t-test

	Mean	SD	Paired t-test (p-value)
ODI 1st visit	58.400	7.815	0.001*
ODI 2nd visit	52.267	7.310	
ODI 1st visit	58.400	7.815	0.001*
ODI 3rd visit	47.667	7.260	
ODI 1st visit	58.400	7.815	0.001*
ODI 4th visit	51.667	7.106	

Table 4: Comparison of BMD changes at different visits using paired t-test

	Mean	SD	Paired t-test (p-value)
BMD 1st visit	0.707	0.137	0.365
BMD 4th visit	0.712	0.145	

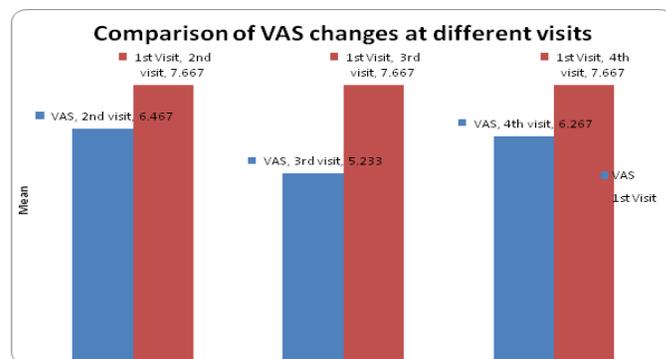


Figure 1: Comparison of VAS changes at different visits

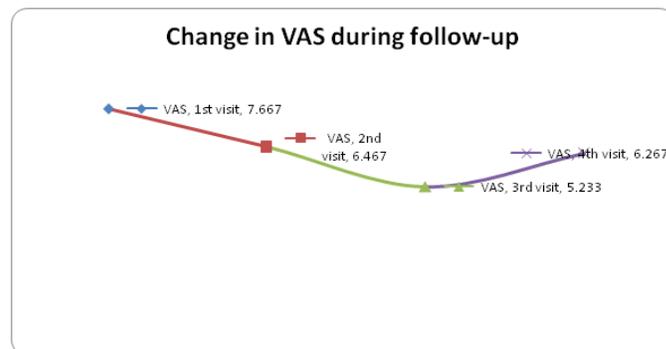


Figure 2: Scatter plot showing the mean VAS changes during follow-up

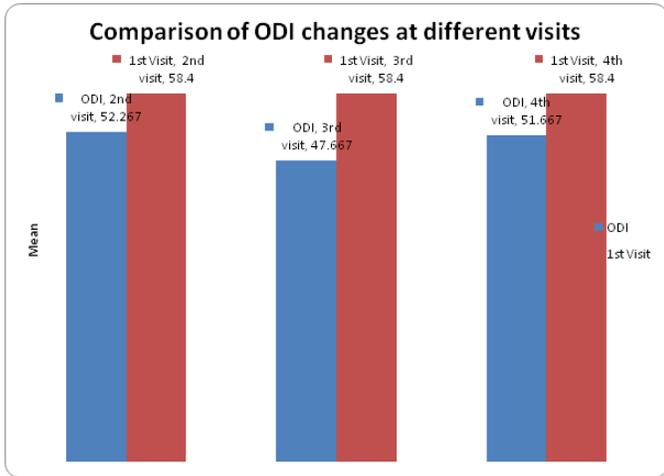


Figure 3: Comparison of ODI changes at different visits

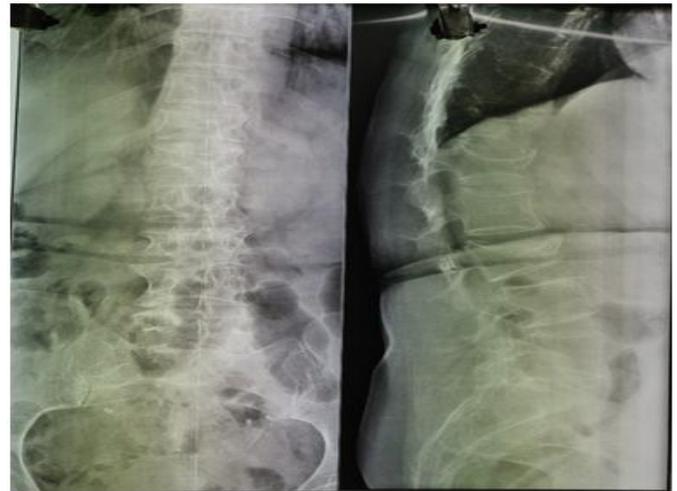


Image 1: X-Ray L-S spine AP and LATERAL

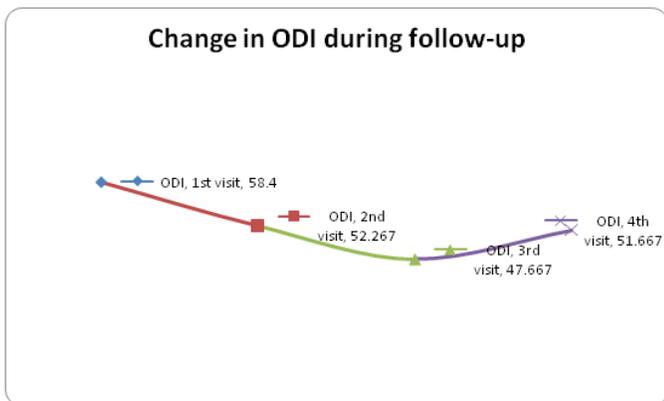


Figure 4: Scatter plot showing the mean ODI changes during follow-up



Image 2: DEXA scan of lumbar spine on GE lunar prodigy dexa BMD scan machine

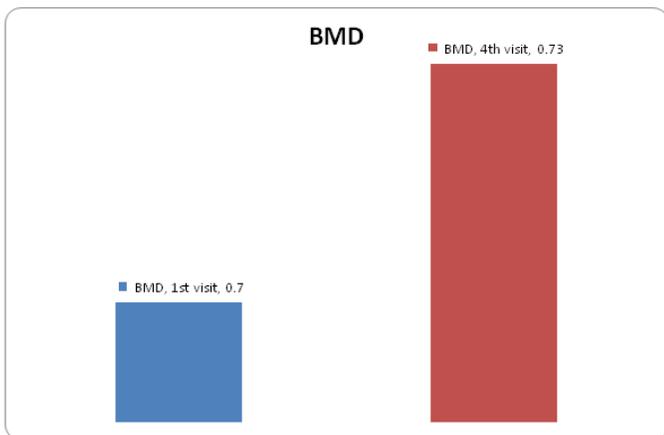


Figure 5: Comparison of BMD changes at different visits



Image 3: Injection ZOLEDRONIC ACID being administered intravenously

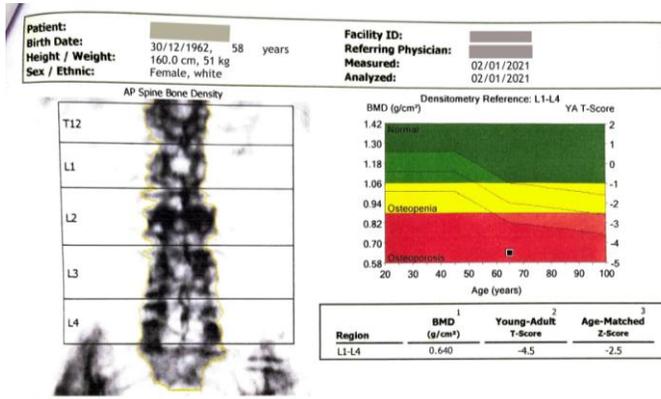


Image 4: DEXA scan report of the patient on the first visit

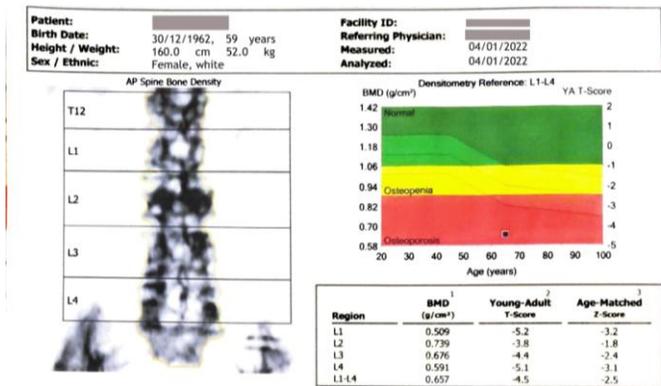


Image 5: Figure: DEXA scan report of the patient on the final follow-up