

Analysis of efficacy of intravenous zoledronic acid therapy in osteoporosis with dxa scan

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Abstract

Introduction: Bisphosphonates are one of the commonly used drugs for the treatment and prevention of osteoporosis. Many of the old generation oral bisphosphonates have got lesser affinity to bone mineral matrix and low patient compliance. Newer generation intravenous zoledronic acid has got a better compliance due to once a year dose and it is more effective due to its more affinity towards bone mineral matrix. Hence this study was conducted to evaluate the results of intravenous zoledronic acid in osteoporotic individuals using Dual Energy X ray Absorptiometry.

Materials and Methods: The study was conducted in a tertiary centre between January 2012 to January 2016. The sample size was 36. The patient recruitment was done in a consecutive manner. Patients were diagnosed by DEXA scan and Lumbar spine BMD taken as representative and inj. zoledronic acid was given once a year, repeated every year, total for 3 years duration therapy. Student Paired t-test was used to find the statistical significance. Gender, fracture sustained during the study, complication, hypothyroidism and status of improved were expressed as frequency and the percentage. $p < 0.05$ considered as statistically significant.

Results and Analysis: The mean age of our study population was 67.7 yrs. 12 patients in our study had improvement in BMD (t-score) which was 40% of the whole study group. These 12 patients had an actual percentage rise in BMD by 11.62% on average, detected by DEXA Scan. All these patients were under the age bracket of 65 years. 18 patients did not have any improvement in or worsening of BMD and were above the age bracket of 65 yrs of age. This could be attributed to their medical co - morbid conditions and nutritional status. The incidence of another fracture was 8% among people who had a previous fracture. 10% of the study population had adverse effects like fever and myalgia. There were no other serious adverse effects.

Keywords: Osteoporosis, Zoledronic acid, DEXA.

Introduction

Osteoporosis is a disease involving the skeletal tissue characterized by very low bone mass and decreased normal architecture resulting in increased fragility of the bone leading on to easy fractures.¹ Fragility fractures are very commonly seen these days in geriatric age group even from trivial trauma due to high rates of osteoporosis. Such osteoporotic fractures are very difficult to treat with high rates of treatment failures resulting in prolonged immobility in elderly age group, economic burden to the family and society as well. The incidences of osteoporosis is on the rise in developing countries and modern society due to sedentary life styles. The population of India is expected to reach 1,613 million by the end of 2050, of which nearly 20% will be people aged above 60 years.² Hence prevention of developing early osteoporosis, in turn to avoid fragility fractures, an early diagnosis is very essential. Many different methods are available to diagnose osteoporosis like Radiography, Dual Energy X ray Absorptiometry (DEXA), quantitative computed tomography, radiogrammetry and others. Many modalities are there to reduce the rates of fractures in osteoporotic fractures.¹ Sunlight exposure, calcium and Vitamin D intake will reduce osteoporosis to a certain extent. Among pharmacological modes of treatment of osteoporosis common ones are estrogen, hormone replacement therapy, bisphosphonates, parathyroid

hormone, anabolic steroids and strontium. Among all these bisphosphonates are the commonly used drugs.³ Among all bisphosphonates Zoledronate has got highest affinity for binding to bone mineral matrix.⁴ We have made a study to analyze the effects of intravenous Zoledronic acid therapy in osteoporotic patients with DEXA scan.

Materials and Methods

The study was conducted in a tertiary centre with high input of geriatric patients with osteoporosis and fragility fractures. Study was conducted between January 2012 to January 2016. The study sample size was 36 which contained patients who were either admitted or treated on outpatient basis. The ethical committee clearance was obtained and all the 36 patients were informed priorly about the study and informed consent was obtained. Patients were selected as per the inclusion criteria. Patients were followed up for 3 successive years up to January 2016. This study was a prospective study in which 30 patients were females and 6 patients were males. All the patients were above the age of 50 years and osteoporosis was measured in them by DEXA scan of lumbar spine, BMD was calculated and T-score < 2.5 was considered as osteoporosis. Those with or without fragility fractures, which were either operated or managed non operatively were included in the study.

Inclusion Criteria: a) We included following fragility fractures with age > 50 years which were either managed conservatively or operatively:

1. Intertrochanteric fractures.
2. Neck of femur fractures.
3. Vertebral fractures
4. Distal radius fractures

b) Those without fragility fractures with age more than 50 years with Bone Mineral Density (BMD) <2.5.

Exclusion Criteria:

1. Age less than 50 years
2. Patients with secondary osteoporosis.
3. Patients previously treated with other methods.
4. Patients with kidney disease
5. Cardiac patients.

Then DEXA scan was done at the end of each year for 3 consecutive years. So total of 4 scans were performed (0- baseline, before starting therapy, 1,2,3- at the end of 1st, 2nd and 3rd years of treatment respectively. All the patients were followed regularly and informed regularly for a maximum period of 3 years and assessment was done accordingly.

Patients included in the study were started on intravenous Zoledronate after baseline BMD was performed. As per World Health Organization guidelines, Injection Zoledonate was given once in a year for 3 consecutive years. Hence total duration of treatment was 3 years. Patients were routinely checked for renal functions before zoledronate was given. All patients were observed for couple of hours in outpatient

to watch for development of body pain. If patient developed severe body pain, Paracetamol, 1G intra venous infusion was given. Out of 36 patients, 2 patients expired due to various causes unrelated to treatment and 4 patients were lost to follow up. So total number of patients evaluated was 30.

Patients were yearly assessed for improvement in bone mineral density score (T-score) by using DEXA scan. Any incidence of new fractures was recorded. Any improvement less than 5% of previous scan was considered as insignificant. It is a descriptive study and we have used 'paired t-test' for the evaluation of results.

Results and Analysis

Thirty six patients above 50yrs of age with or without fragility fractures with SPINE BMD T-Score of < -2.5 measured by DEXA Scan yearly for 3 yrs have been included in our study. The recruitment period was from January 2012 to January 2013 where the 36 patients were included in the study based on inclusion and exclusion criteria. There were 30 women and 6 men in our study. Out of which 2 patients died are females due to various medical co – morbidities and 4 patients lost to follow up (2 males 2 female). Remaining 30 patients were followed up every year once for maximum period of 3 years up to January 2016.

Table 1: Recruitment and follow up details

Year	Follow Up	Total Patients	Loss of Follow Up	Follow Up %
January 2012-13	Recruitment year	36	-	
Feb 2013-14	1 st Year	34	2	94%
Feb 2014-15	2 nd Year	33	1	92%
Feb 2015- Jan 2016	3 rd Year	30	3	83%

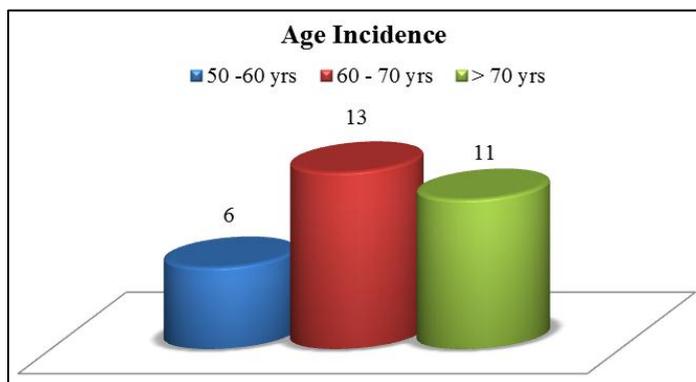


Fig. 1: Age distribution:

Of the remaining 30 patients, mean age was 67.7 years of age. The age groups considered was 54 to 85 yrs. (Fig. 1)

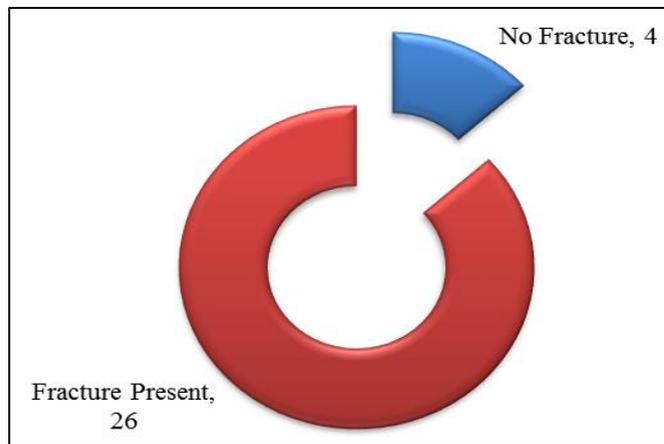


Fig. 2: Incidence of fragility fractures in study population

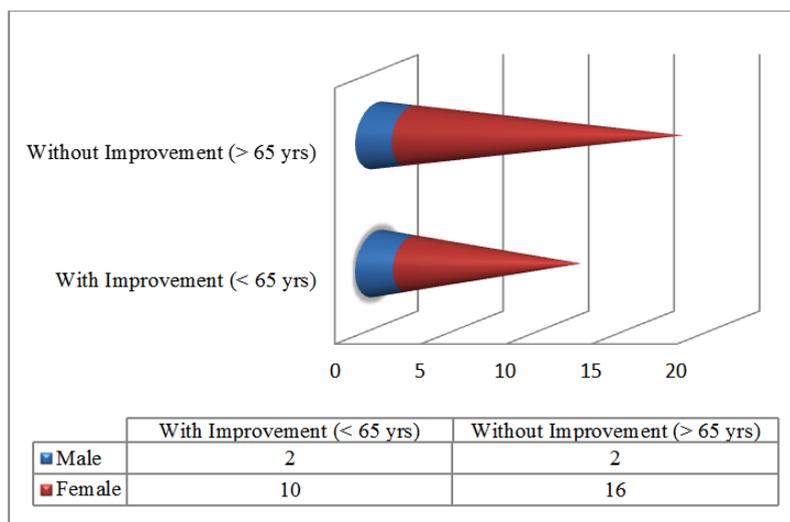


Fig. 3: Percentage of cases with improvement in BMD (Spine) (T-Score):

12 patients in our study had improvement in BMD (t-score), of which 10 patients were females and 2 patients were males (below the age of 65 years). 3 patients had side effects like generalized body ache, fever and malaise.

Thus, percentage of patients with improvement in BMD (T-score) in our study was 40% of the total study group (Fig. 3). Among the 12 patients who had improvement in BMD was proven by *DEXA Scan* and the percentage of actual improvement BMD in these patients was an average of 11.62%. None of them sustained any further fracture during the follow up. All these patients were below the age of 65yrs.

5 patients above 65 yrs did not show improvement of more than 5 %, 4 had no change in BMD and the rest had worsening of BMD which was attributed to nutritional habits and physical activities, medical co morbidities, compliance of drug intake and regular calcium intake (Table 2).

Table 2: Percentage of Improvement in BMD (T-score) in study group:

	Number of Cases	Percentage
Improved	12	40%
Not improved	18	60%
Total	30	

Table 3: Significance:

BMD	Mean	SD	P-Value
Baseline	-3.88	0.13	
Visit1	-3.67	0.13	<0.001
Visit2	-3.63	0.74	<0.001
Visit3	-3.69	0.88	0.043

Paired t - test was used to find the significance difference the baseline and each follow up is showing statistically significant (table-3).

The average percentage of improvement is 11.62 and SD is 0.36 (Fig. 4).

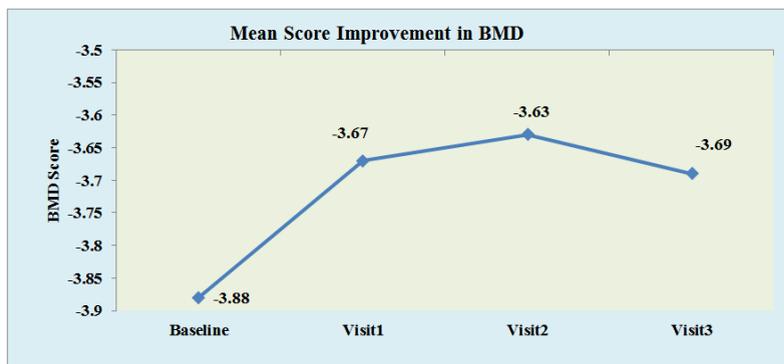


Fig. 4: mean score improvement in BMD

10% of study group showed Complications like fever, generalized body ache for the first infusion and 6% in the second dose. All the three patients with complications were females.

Table 4: Incidence of fracture in the study group:

	Number of Cases	Percentage
Sustained	26	87%
Not Sustained	4	13%
Total	30	

Table 5: Another fracture during study:

	Number of Cases	Percentage
Yes	2	8%
No	24	92%
Total	26	

In the study group 2 patients sustained another fracture during the course of treatment. These patients were above 70 yrs of age, female sex, associated with hypothyroidism and worsened BMD (Table 4 and 5).

There is only one case of hypothyroidism with improvement in BMD. The rest of the 3 cases did not improve after zoledronic acid infusion.

Discussion

Osteoporosis is a state of physiological disease that every person has to go through in their life span and it is a cause of fragility fractures of distal radius, fracture neck of femur, vertebral fractures and trochanteric fractures. In India, osteoporotic fractures are more common in females and occur at a younger age group than males. Such fractures acute and chronic pain, diminished quality of life and substantial morbidity. Nearly 20% of the osteoporotic fracture patient die within one year of the fracture.⁵

Fractures around hip, vertebral fractures or distal end radius fractures have been found to affect quality of life to a degree that is similar to that seen in other serious chronic diseases such as asthma, chronic obstructive pulmonary disease and osteoarthritis.⁶ So prevention and treatment of osteoporosis has become

important in orthopaedic practice. Along with nutritional supplements like Calcium and Vitamin D, the most commonly prescribed drugs are Bisphosphonates which are used to treat osteoporosis.

Zoledronic acid is the recent generation bisphosphonate which is administered once yearly by intravenous infusion.⁷ Of all the bisphosphonates available, zoledronate has got the highest affinity for binding to the bone mineral matrix. Bisphosphonates with higher affinity like zoledronic acid bind avidly to the bone surface but, spread through bone slowly whereas lower affinity agents like clodronate distribute more widely through the bone, but they have shorter time of residence when the treatment is stopped. The suppression of osteoresorption starts happening three months after the initiation of therapy in oral bisphosphonates, where as in intravenous therapy it occurs more rapidly. Compliance of the patients for oral bisphosphonates is also low resulting in reduced efficacy, where as single yearly infusion may improve the efficacy.⁸

After three years of treatment, bisphosphonates have shown to increase BMD of the hip by 3 - 6% and at the spine by 5 - 8%. In women with osteoporosis zoledronic acid, alendronate and risedronate also reduced nonvertebral fractures by 25-40%, including hip fractures by 40 - 60%.⁹

By taking consideration of all advantages and efficacy of IV bisphosphonates, in our study we prescribed IV Zoledronic Acid infusion. This was mainly because of poor compliance of patients to oral bisphosphonates due to irregular dosing, missing regular intake of the drug, too frequent dosing, irregular follow up, gastro esophageal complications and cost of the drugs. They have been evaluated by *DEXA Scan* yearly for 3 yrs.

Out of the total, 40% of the study population showed significant improvement in BMD (t-score) of about 11.62% (*DEXA* evaluation). With P - value 0.043 by paired t-test which denotes the data significant. Rest of 60 % do not show any Improvement (>5% increase in BMD) or worsening in spine BMD. According to *Black DM, Delmas PD, Eastell R, et al. Study* once - yearly Zoledronic Acid for treatment of postmenopausal osteoporosis showed improvement of

6.71% BMD in spine (DEXA evaluation) where as in our study significant improvement was noted in 11.62% of the cases.¹⁰ Drugs approved by US-FDA for treatment of osteoporosis - 6 to 9 % increase in spine BMD with once yearly zolendronic acid.¹¹

Overall percentage of improvement was 11.62% in our study, which was comparable to other studies when spine BMD was done (Fig. 5). Percentage of

improvement was 38.5% in females and 50% among males. All patients given regular calcium and weekly Inj. Vitamin D3 and advised physical exercises. In patients above the age of 65yrs no improvement was noted, which was due to various factors, adequate exposure to sunlight.

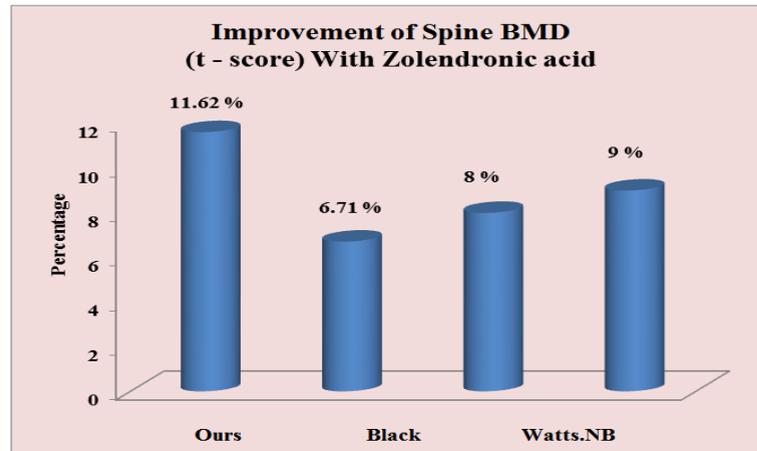


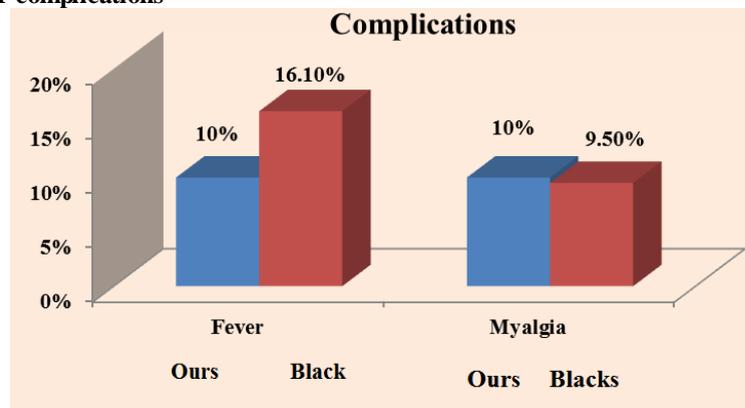
Fig. 5: Comparison of improvement in different studies

Fractures During Study: 87% population already sustained fractures included in study population of which, 8% sustained fracture during our study. According Black DM, Delmas PD, Eastell R, et al. Study once - yearly zolendronic acid for treatment of postmenopausal osteoporosis showed 8% clinical fractures. Rest 13% cases did not show any fracture during the study.

Complications: 10% cases of study population showed adverse effects like generalized body aches and fever. According Black DM, Delmas PD, Eastell R, et al. Study once-yearly zolendronic acid for treatment of

postmenopausal osteoporosis showed 16.1% cases with fever, 9.5% cases of myalgia. 10 % cases showed adverse effects after 1st infusion and 6.6 % in 2nd infusion. No effects were seen after the 3rd infusion. According Black DM, Delmas PD, Eastell R, et al. Study once-yearly zolendronic acid for treatment of postmenopausal osteoporosis showed 31.6%, 6.6%, 2.8% after 1st, 2nd, 3rd infusions of zolendronic acid respectively. There was a 3.7% incidence of cardiac events and 2.8% incidence of stroke in the above mentioned study but there were no serious complications in our study (Fig. 6).

Fig. 6: Comparison of complications



13% patients in our study were associated with hypothyroidism of which 25% showed improvent in BMD, 75% did not show any improvement in our study.

Although our sample size is low it's very difficult to determine the efficacy of Bisphosphonate, IV Zolendronic Acid, to have a therapeutic effect on improving BMD in osteoporotic patients when

compared to Black DM, Delmas PD, Eastell R, et al. Study. However the therapeutic validity of the improvement in BMD is higher in our study than the Black et al. study Hence it can be inferred that bone strength preventing further fragility fractures. But it should be used cautiously keeping in mind of its adverse effects.

Conclusion

From our study we get the impression that there was 40% improvement in BMD (Lumbar Spine taken as representative) (t-score) in the study population who were <65yrs of age through once yearly Zoledronic acid therapy. By these results we can come to the conclusion that Intravenous Zoledronic acid can be prescribed once every year to osteoporotic individuals <65yrs of age to improve BMD. Due to the better compliance of IV Zoledronic acid, once yearly dose was preferred, when compared to oral bisphosphonates. Zoledronic acid therapy was found to be helpful in improving BMD but at the cost of a few side effects. Lesser number of sample size was the limitation of our study.

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