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Efficacy of zoledronic acid infusion on bone mineral density among adult population

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ABSTRACT

Background: Osteoporosis is a skeletal disease characterised by impaired bone strength due to reduced bone mineral density. As a consequence, patients with osteoporosis are at increased risk of fractures. Zoledronic acid is an anti-resorptive agent that acts by slowing down osteoclast medicated bone resorption, thereby increasing bone density. This study was carried out to evaluate the efficacy of Zoledronic acid on bone mineral density.
Methods: This study was carried out as a record based cross sectional study among 30 symptomatic adult patients who visited the outpatient department of Orthopedics for a period of two years. Bone mineral density (BMD) parameters assessed using dual-energy X-ray absorptiometry (DEXA) scan were documented for initial period and after six months of intervention. Documentation of intervention with single dose of zoledronic acid 5 mg by intravenous infusion was verified and noted.
Results: There was a significant difference in the mean scores for both femoral neck and lumbar spine with respect to BMD values and T-score values between baseline parameters and values measured after 6 months of Zoledronic acid infusion. The difference was statistically significant ($p<0.05$).
Conclusions: Single dose of zoledronic acid 5 mg by intravenous infusion was found to be effective in increasing the BMD among individuals suffering from osteopenia and osteoporosis.

Keywords: Bisphosphonates, Bone mineral density, Osteopenia, Osteoporosis, T score, zoledronic acid

INTRODUCTION

Osteoporosis is a skeletal disease that is characterized by compromised bone strength predisposing a person to an increased risk of fracture.[1] Overall, it is estimated that 50% of post-menopausal women and 25% of men aged more than 50 years will have osteoporosis-related fracture in their lifetime.[2] Bone strength is a combination of bone density and bone quality. Overall bone strength is difficult to measure in the clinical setting. In the absence of fragility fracture, bone, bone mineral density (BMD) is a proxy measure that accounts for up to 70% of bone strength. BMD is clinical tool used to diagnose osteoporosis. According to the classification of the World Health Organization, BMD of 2.5 standard deviations or more below the mean BMD of a young adult reference population, this is a T-score of -2.5 or less, qualifies for the diagnosis of osteoporosis.[3] As BMD decreases, fracture risk increases4. Therefore, BMD is considered as a useful indicator to assess the fracture risk among patients with osteoporosis.

Fractures associated with osteoporosis are a major cause of morbidity, disability, mortality, and costs.[5] Zoledronic acid is a bisphosphonate which has a high affinity for mineralized bone and especially for sites of high bone

turnover.[6] Zoledronic acid is an anti-resorptive agent that acts by slowing down osteoclast medicated bone resorption, thereby increasing bone density and decreasing the amount of calcium released from the bones into the blood stream. Zoledronic acid is used to prevent or treat osteoporosis in men and post-menopausal women, patients on glucocorticoids, and in Paget's disease of bone. It is also given as a supplement for cancer chemotherapy.[7] Annual intravenous injection of zoledronic acid 5 mg has been approved by the Food and Drug Administrative for the treatment of postmenopausal osteoporosis, treatment of male osteoporosis, and treatment and prevention of glucocorticoid-induced osteoporosis as a once – yearly infusion.[8] However, the clinical evidence of the effect of zoledronic acid on osteoporosis and its complication is conflicting. So, this study was conducted to determine the increase in bone mineral density among patients treated with zoledronic acid using dual X-ray absorbtiometry to track and document improvement. This study was carried out to estimate the prevalence of osteoporosis among adults and to evaluate the effects of intravenous injection of zoledronic acid 5 mg on bone mineral density.

METHODS

Study setting and participants

This study was carried out as a record based cross sectional study among adult patients who visited the outpatient department of Orthopedics of our Trichy SRM Medical College Hospital and Research Centre institution for management of osteoporosis with zoledronic acid. The study was carried out for a period of two years from August 2013 to July 2015

Inclusive criteria

Patients aged between 45-85 years, both male and female, those who have preliminary bone mineral density (BMD) with T-score ≤-1.5 and preliminary bone mineral density (BMD) with T-score ≤-2.5 with or without evidence of existing fractures were included.

Exclusive criteria

Patients with any systemic illness, secondary diseases such as diabetes mellitus, hypertension etc were excluded.

Sample size and sampling procedure

Based on the available literature, the expected mean difference in the BMD was 0.05 g/cm^2 with a standard deviation of 0.756 g/cm^2.[9] Assuming a 95% significance level and 80% power, the required sample size was calculated to be 28 and was rounded off to 30. All the case records from the medical records department were sequentially arranged for the duration from August 2013 to July 2015. The required sample of 30 cases was selected by simple random sampling.

Ethical approval

Approval was obtained from the Institutional Ethics Committee prior to the commencement of the study.

Data collection

Data regarding the demographic profile and risk factors for osteoporosis were elicited from the hospital records. Anthropometric parameters like body mass index (BMI) were documented. Bone mineral density (BMD) parameters assessed using DEXA scan were also documented. The parameters included bone mineral content (grams), projected bone area (square centimeters), and the derived areal BMD measurements (grams per square centimeters) at the LS spine and proximal femur. LS measurements of L2-L4 (Lunar Corp) or L1-L4 (Hologic, Inc.) were obtained.

Documentation of intervention with single dose of zoledronic acid 5 mg by intravenous infusion was verified and noted. The primary study outcome was change in BMD at the LS between baseline and at six months.

Data analysis

Data was entered and analyzed using statistical package for social sciences (SPSS) version 15 software. Results are expressed as proportions with 95% confidence interval. Univariate analysis was carried out using chi square test.

RESULTS

A total of 30 medical records were taken up for analysis. Majority of the participants belonged to the age group pf 61-70 years (40%) and were females (56.7%). About 30% of the participants were unemployed and were educated up to primary school level. Majority of the participants (56.7%) had a normal body mass index (BMI).Most of the women (64.7%) had attained menopause and 26.5% of the participants were alcoholics (Table 1).

Based on the T-scores, the bone mineral density (BMD) was calculated and tabulated (Table 2). Majority of the participants were categorized as osteopenia (43.3%) while osteoporosis was prevalent in 20% of the participants.

It was observed that osteopenia was increasingly prevalent in all age groups, while osteoporosis was highest in the age group of 51-50 years (30%). Similarly, osteopenia was more prevalent among the males (61.5%) compared to the females, who had increased prevalence of osteoporosis (35.3%). In addition, participants who

were underweight had an increased risk of osteoporosis (42.9%) compared to those who were overweight / obese (33.3%) (Table 3).

The impact of zoledronic acid on BMD measured at femoral neck and lumbar spine is given in Table 4. It was observed that there was a significant difference in the mean scores for both femoral neck and lumbar spine with respect to BMD values and T-score values between baseline parameters and values measured after 6 months of zoledronic acid infusion. The difference was statistically significant ($p<0.05$) (Table 4).

Table 1: Background characteristics of the study participants (n=30).

Characteristics	Frequency (N)	Percentage (%)
Age (years)		
41-50	**7**	23.3
51-60	10	33.3
61-70	12	40.0
>70	1	3.4
Gender		
Male	13	43.3
Female	17	56.7
Occupation		
Professional	1	3.3
Skilled worker	7	23.3
Semi-skilled worker	5	16.7
Un skilled worker	8	26.7
Un employed	9	30.0
Education of the participant		
Graduate/ post graduate	5	16.7
High school certificate	6	20.0
Middle school certificate	4	13.3
Primary school	9	30.0
Illiterate	6	20.0
Socio economic status		
Upper	2	6.7
Upper middle	8	26.7
Lower middle	4	13.3
Upper lower	9	30.0
Lower	7	23.3
BMI		
<18.5	7	23.3
18.5 to 24.99	14	56.7
≥25.0	9	30
Personal habits		
Smoking	5	16.7
Alcoholism	8	26.7
No habits	17	56.6
T- score values		
Normal (T-score ≥-1.5)	11	36.7
Osteoporosis (T-score -2.5 to -1.5)	13	43.3
Osteoporosis	6	20.0

Table 2: Prevalence and categorization of osteoporosis among the study participants (n=30).

T score	Frequency (N)	Percentage (%)
Normal (T-score ≥-1.5)	11	36.7
Osteopenia (T-Score -2.5 to -1.5)	13	43.3
Osteoporosis	6	20.0

Table 3: Distribution of characteristics of risk factors of osteoporosis

Characteristics	Total	Normal	Osteopenia	Osteoporosis
		N (%)	N (%)	N (%)
Age (years)				
41-50	7	4 (57.1)	3 (42.9)	0
51-60	10	3 (30.0)	4 (40.0)	3 (30.0)
61-70	12	4 (33.3)	5 (41.7)	3 (25.0)
>70	1	0 (0.0)	1 (100.0)	0
Gender				
Male	13	5 (38.5)	8 (61.5)	0
Female	17	6 (35.3)	5 (29.4)	6 (35.3)
Time since menopause (years)				
<5	7	2 (28.6)	2 (28.6)	3 (42.8)
>5	4	0	1 (25.0)	3 (75.0)
BMI				
<18	7	3 (42.8)	1 (14.3)	3 (42.9)
18-24.99	14	4 (28.6)	10 (71.4)	0
≥25	9	4 (44.5)	2 (22.2)	3 (33.3)
Socio economic status				
Upper	2	1 (50.0)	1 (50.0)	0
Upper middle	8	4 (50.0)	4 (50.0)	0
Lower middle	4	1 (25.0)	2 (50.0)	1 (25.0)
Upper lower	9	3 (33.3)	2 (22.2)	4 (44.4)
Lower	7	2 (28.57)	4 (57.14)	1 (14.26)

Table 4: Impact of zoledronic acid infusion on the BMD.

Characteristics	Base line values	After 6 months of zoledronic acid infusion	P value
BMD femoral neck	0.53±0.064	0.77±0.09	<0.0001
BMD lumber spine	0.79±0.140	1.32±0.06	<0.0001
T-score femoral neck	-2.367±0.87	-1.488±0.06	0.0287
T-score femoral spine	-0.835±0.07	0.453±0.04	0.0343

DISCUSSION

Osteoporosis is a skeletal disease that is characterized by compromised bone strength predisposing a person to an increased risk of fracture. Annual intravenous injection of zoledronic acid 5 mg has been approved by the Food and Drug Administration for the treatment of postmenopausal osteoporosis and treatment of male osteoporosis. This study was conducted to establish the increase in bone mineral density (BMD) among patients treated with zoledronic acid using Dual X-ray absorbtiometry (DEXA).

This record based study was taken up on 30 individuals who underwent treatment with zoledronic acid for osteoporosis to evaluate the change in the BMD levels pre-and post-intervention. All individuals both males and females, aged more than 45 years were included in the study. The mean age of the participants was 54.6±4.33 years. It is evident that as age advances, so does the prevalence of osteopenia and osteoporosis. It is interesting to note in this study that there is a large prevalence of osteopenia with advancing age. Similar findings were observed in studies conducted by Jothi Unni et al and Gandhi et al.[10,12] In our study osteopenia and osteoporosis were prevalent in 29.4% and 35.3% of the females respectively. Among the males, osteopenia was prevalent in 61.5% while none of them showed signs of osteoporosis. Similar findings were seen in a study done by Anburajan et al with a prevalence of osteoporosis of 31.8% among females.[12] Moreover, osteoporosis was prevalent in 75% of the post-menopausal women.

The mean BMD of lumbar spine increased significantly from pre-intervention value of 0.75695 g/cm^2 to post-infusion of 0.80216 g/cm^2. The T-score also increased from pre-infusion value of -3.567±0.77 to -3.158±0.08 in 12 months following the infusion (P<0.01). The increase is 5.026% higher than pre infusion values. After the menopause, the incidence of both osteopenia and osteoporosis rose significantly and the time since menopause was found to be major risk factor in this regard. In a study done by Rakel et al in men, the zoledronic infusion was shown to be non-inferior to weekly alendronate for the percentage change in lumbar

spine BMD at month 24 relative to baseline (Zol 6.1% vs alendronate 6.2%).[13] Similar observations were documented among the Bangladeshi women in a study done by Hossain M et al.[9]

The mean BMI among the study participants was 23.04 kg/m^2. BMD was higher in obese women, and it is evident that low BMI leads to increased osteoporosis and osteopenia when compared to normal BMI. Similar findings were seen in a study done by Unni et al and Acha et al.[10,14] They found that each one-unit increase in BMI was associated with 9% decreased risk of hip fracture. Therefore, the findings of this study show an inverse relationship between BMI and BMD.

The mean BMD of lumbar spine increased significantly from pre-infusion value of 0.79 g/cm^2 to post-infusion of 1.32 g/cm^2. The T-Score also increased from pre-infusion value of -2.367±0.87 to -1.488±0.06 in 6 months following the infusion. The increase was 37.13% higher than pre infusion values. There was a statistically significant improvement in the BMD values 6 months after infusion of zoledronic acid. Similarly, the mean BMD of femoral neck also increased significantly from pre-infusion value of 0.53 g/cm^2 to post-infusion of 0.77 g/cm^2. The T-Score also increased from pre-infusion value of -2.368±0.87 to -1.488±0.06 in 6 months following the infusion which was statistically significant (p value <0.0001 and 0.0287 respectively).

Machao et al observed that the BMD values statistically increased at femoral neck and total hip among patients infused with zoledronic acid over three years, compared to the controls.[2] A previous clinical HORIZON trial with 107 patients indicated that intravenous zoledronate therapy significantly increased BMD of lumbar spine over 3 years.[15] A study done by Doggrell et al documented 70% reduction in vertebral fracture rate observed with zoledronic acid.[16-18] The health outcomes and reduced incidence with zoledronic acid once yearly (HORIZON) Extension trail, used a design with a shorter treatment period (3 years of treatment followed by 3 years of placebo or active extension) and observed that zoledronic acid administered once-yearly significantly prevented non-vertebral Osteoporosis Fractures.[19] Jun Zhang et al in his meta-analysis had documented that longer term intervention, more than 12 months interventions, could gain a better prevention effect for osteoporosis (OR, 95% CI for BMD was 3.35, 2.77-3.92; for fracture was 0.67, 0.54-0.82).[20] They concluded that zoledronic acid could be effective approach in the prevention of osteoporosis, and could increase the bone mineral density and reduce the risk of fracture.

CONCLUSION

Our study conducted among individuals aged more than 45 years has found that proportion of osteopenia and osteoporosis among study population were 13 (43.33%) and 6 (20.0%) respectively (according to WHO classification of Osteoporosis). Single dose of zoledronic acid 5 mg by intravenous infusion was found to be effective in increasing the BMD among individuals suffering from osteopenia and osteoporosis. There was a statistically significant improvement in the BMD values and T-score measured at femoral neck and lumbar spine 6 months after infusion of zoledronic acid. Over a short term period, the study concludes that zoledronic acid has positive benefit in enhancing the T-score values in osteoporosis and osteoporotic patients.

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REFERENCES

1. National Institute of Health Consensus Development Panel on Osteoporosis, Prevention, Diagnosis and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA. 2001;285(6):785-95.
2. National Osteoporosis Foundation. Fast facts on osteoporosis (fact sheet). [Online]. Available from: http://www.nof.org/osteoporosis/diseasefacts.htm. Accessed on 4 September 2019.
3. Genant HK, Cooper C, Poor G, Reid I, Ehrlich G, Kanis J, et al. Interim report and recommendations of the World Health Organization Task-Force for Osteoporosis. Osteoporos Int. 1999;10(4):259-64.
4. Johnell O, Kanis JA, Oden A, Johansson H, De Laet C, Delmas P, et al. Predictive value of BMD for hip and other fractures. J Bone Miner Res. 2005;20(7):1185-94.
5. Cauley JA, Thompson DE, Ensrud KC, Scott JC, Black D. Risk of mortality following clinical fractures. Osteoporos Int. 2000;11(7):556-61.
6. Lambrinoudaki I, Vlachou S. Once-yearly zoledronic acid in the prevention of osteoporotic bone fractures in postmenopausal women. Clin Interven Ageing. 2008;3(3):445-51.
7. Bonnick SL, Shulman L. Monitoring osteoporosis therapy: bone mineral density, bone turnover markers, or both? Am J Med. 2006;119:S25-31.
8. Package insert. Reclast injection. East Hanover: Novartis Pharmaceuticals Corp; 2010. Available from https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/reclast.pdf? Accessed on 4 September 2019.
9. Hossain M , Chowdhury IH, Emran MA, Habib AH, Asaduzzamnan AK, Alam M, et al. Effect of single dose intravenous zoledronic acid on bone mineral density in postmenopausal osteoporosis of Bangladeshi women. Bangladesh Med Res Counc Bull. 2010;36(3):747.
10. Unni J, Garg R, Pawar R. Bone mineral density in women above 40 years. J Midlife Health. 2010;1(1):19-22.

11. Gandhi A, Shukla A. Evaluation of BMD of women above 40 years of age. J Obstet Gynaecol India. 2005;55:265-7.
12. Anburajan M, Kumar DA, Sapthagirivasan V. Evaluation of Osteoporosis in Indian Women and Men using Peripheral Dual Energy X-ray Absorptiometry (pDXA). IACSIT Press, Singapore. 2011;5:470-4.
13. Räkel A, Boucher A, Louis, Ste-Marie G. Role of Zoledronic acid in the prevention and treatment of osteoporosis. Clin Interven Ageing. 2011:6:89-99.
14. Acha AA, Ostir GV, Markides KS, Ottenbacher KJ. Cognitive status, body mass index and hip fracture in hispanic older adults. J Am Geriatr Soc. 2006;54:1251-5.
15. Popp AW, Guler S, Lamy O, Senn C, Buffat H, Perrelet R, et al. Effects of zoledronate versus placebo on spine bone mineral density and microarchitecture assessed by the trabecular bone score in postmenopausal women with osteoporosis: a three-year study. J Bone Miner Res. 2013;28:449-54.
16. Doggrell SA. Zoledronic Acid Once-yearly: What Role in the prevention of non-vertebral Osteoporotic Fractures? Clinical Medicine Insights: Therapeutics. 2010;2:539-47.
17. Black DM, Bauer DC, Schwartz AV, Cummings SR, Rosen CJ. Continuing Bisphosphonate Treatment for Osteoporosis — For Whom and for How Long? N Engl J Med. 366;22:2051-3.
18. Black DM, Delmas PD. Once-Yearly Zoledronic Acid for Treatment of Postmenopausal Osteoporosis. N Engl J Med. 2007;356:1809-22.
19. Black DM, Reid IR, Boonen S, Bucci-Rechtweg C, Cauley JA, Cosman F et al. The effect of 3 versus 6 years of zoledronic acid treatment in osteoporosis: a randomized extension to the HORIZONPivotal Fracture Trial (PFT). J Bone Miner Res. 2012;27(2):243-54.
20. Zhang J, Wang R, Zhao YL, Sun XH, Zhao HX, Lu T, et al. Efficacy of intravenous zoledronic acid in the prevention and treatment of osteoporosis: A meta-analysis. Asian Pacific J Trop Med. 2012;5(9):743-8.

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