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ORIGINAL RESEARCH

Effect of Zoledronic Acid On Bone Mineral Density In Patients With Fragility Fracture

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ABSTRACT

Background: Osteoporotic fractures are common - it has been estimated that one in two women and one in five men aged over 50 years will sustain at least one low trauma fracture in their lifetime. **Objective:** To determine the effect of Zoledronic acid on BMD in patients with fragility fracture. **Methods**: This Prospective single arm, Observational Cohort Study was conducted among Patients above the age of 40 years of either sex presenting with osteoporotic fracture to Department of orthopedics St. Martha's Hospital, Nrupathunga road ,Bengaluru. Duration of Study was December 2015 to December 2017. **Results:** 46 % of the study population was between 71-80 years mainly from sedentary lifestyle. 96 %were postmenopausal women. 46 % of patients had fracture around hip, 40 % of patients had vertebral compression fractures and 14 % with distal radius fracture. Most of them were also noted to have additional vitamin D deficiency **Conclusions:** It was concluded that there is significant increase in BMD at 1 year of injection ZA. The Average BMD at the initial visit was- 0.65 gm/cm^2, Average BMD 1 year later – 0.66 gm/cm^2.

Keywords*:* Zoledronic Acid, Bone Mineral Density, Fragility Fracture

INTRODUCTION

Osteoporosis is defined as a reduction in bone mineral mass, makes the bone more fragile and more prone to increased bone fragility and increased fracture risk[1]. Osteoporosis may have no signs and symptoms until a fragility fracture occurs. It is detected on the basis of bone mineral density assessment. According to the WHO criteria, osteoporosis is defined as a BMD that lies 2.5 standard deviations or more below the average value for young healthy 30 year individual(a T- score of < - 2.5 SD)[2]. This definition only includes postmenopausal women evaluated by the total body dual energy X ray absorptiometry(DEXA) scanning technique. No similar definition exists for young women or men.

It can also be defined as reduction in bone per unit volume. The total amount of bone tissue is decreased. Despite thinning of bone trabeculae and loss of fine trabaculation, histological evidence shows a normal degree of calcification but with marked reduction in the number of cells. These anatomical changes are accompanied by normal levels of serum calcium, serum phosphorous and serum alkaline phosphatase. [4,5]

A fragility fracture is a type of fracture that occurs during normal activity, i.e fall from standing height or less. Osteoporotic fractures are defined as fractures associated with a low BMD and include those of the spine, forearm, hip and shoulder. Osteoporotic fragility fracture can cause substantial pain and disability, leading to a reduced quality of life, a hip fracture permanently disables 50 % and fewer recover fully. [6]

Bisphos phonates are the current standard of care for the treatment of osteoporosis. Oral preparations are associated with poor absorption and gastric side effects, leading to poor compliance.ZA 5mg once yearly IV Bisphosp honate is approved for the treatment and prevention of postmenopausal osteoporosis and for increasing bone mass in men with osteoporosis. It also is associated with better adherence being a once yearly treatment.

The objective of this study is to assess the improvement in the osteoporotic status (with BMD) of patients suffering from osteoporotic fragility

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fractures after a period of one year of ZA therapy. Also to assess the patients clinical outcomes like pain relief and functional outcome.

Indications for BMD: Women aged > 65 years and men aged >70 years
Postmenopausal women and men aged 50–69 years based on risk factor profile
All patients with a fragility fracture
National Osteoporosis Foundation: Clinician's Guide to Prevention and Treatment of Osteoporosis. 2015

MATERIALS AND METHODS

This Prospective single arm, Observational Cohort Study was conducted among Patients above the age of 40 years of either sex presenting with osteoporotic fracture to Department of orthopedics St. Martha's Hospital, Nrupathunga road, Bengaluru. Duration of study was December 2015 to December 2017.

Sample size: It is a hospital based study of 50 cases or more who are fulfilling the Inclusion/Exclusion criteria.

Inclusion criteria: Patients of Osteoporotic fragility fracture either sex aged 40 years and above.
All Patients with BMD T score less than -2.5.

Exclusion criteria:

1. Patients with renal disease
2. Patients with severe cardiac disease
3. Patients on hormone replacement therapy, oral bisphosphonates or any other active management except calcium and vitamin D.
4. Patients with Clinically detectable underlying causes for back pain like primary and or secondary tumors of bone, disc Prolapse, infection, other hormonal abnormalities.
5. Patients with clinically detectable abdominal visceral malignancy

Investigations

1. Complete blood count
2. Bleeding and clotting times
3. Random Blood Sugar
4. Serum Creatinine and Urea
5. Electrocardiogram
6. Serum calcium and phosphate
7. X ray of area of interest.
8. Bone Mineral Density using DXA AP spine and Lateral vertebral analysis.

Method of collection of data:

Patients presenting with fractures in compliance with the criterion of the study population were selected. Informed consent was taken from the patients who agree to be part of the study. Demographic data, History, Clinical examination and details of investigations were recorded in the study Proforma. The assessment tools used are the routine blood investigations, serum calcium, serum alkaline phosphatase, radiographs, USG abdomen, DXA and MRI (only in select cases), severity of pain was recorded as per VAS score. The BMD measurements for the diagnosis of osteoporosis are considered according to WHO and the National Osteoporosis Foundation (NOF) guidelines 2013.The patients who turned out to be osteoporotic were advised to take sufficient oral fluids for hydration. Later they were given 5mg of ZA IV over a minimum period of 15 min after taking consent and observed for allergic and other reactions for a day. They were advised prophylactic antipyretic medications with paracetamol along with other management for their fracture, along with calcium and vitamin D supplements. They were assessed after 12 weeks/3 months, 24 weeks/6 months, and one year clinically, radiologically and DEXA scan for BMD at the end of one year. The data were interpreted.

Visit 1/ Day1/ Initial or baseline assessment-
Screening for inclusion of study and taking informed written consent.
Details of patient's demographic characteristics, and medical histories, concomitant medications and detailed physical/clinical evaluation were recorded .
Routine investigations like Complete blood picture, Renal function tests, serum calcium, phosphate, alkaline phosphatase, radiograph , Bone mineral density using DXA were recorded, VAS score was recorded.
Eligible patients were administered 5mg intravenous ZA with their consent.
They were observed for any acute reactions for one day, either on OPD basis or in patient if needed
Visit 2/ Week 12-
Assessment of pain by VAS scale
All observed or spontaneously volunteered adverse events were recorded.
Pulse rate and blood pressure were recorded.
Visit 3/ Week 24 -
Patients improvement with respect to pain were assessed using VAS scale
All observed or spontaneously volunteered adverse events were recorded.
Pulse rate and blood pressure were recorded.
Visit 4/ 1 year-
Patients improvement with respect to pain were assessed using VAS scale
All observed adverse events were recorded.
Pulse rate and blood pressure were recorded.
Patients improvement with respect to Bone mineral density were recorded using DXA.
Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean± SD (Min-Max) and results on categorical measurements are presented in Numbers (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1.Dependent variables should be

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normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent

Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale with in each group.

Significant figures

- Suggestive significance (P value: 0.05 - P <0.10)
- Moderately significant (P value:0.0l - P < 0.05)
- Strongly significant (P value : P 0.0l)

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, Med Calc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

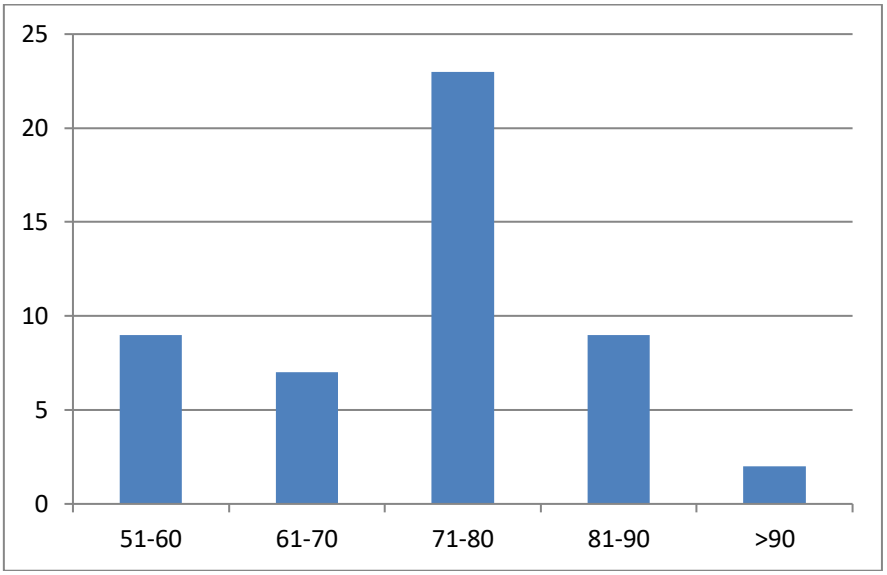
RESULTS

Table 1: WHO Definition of normal Bone Mineral Density, Osteopenia, Osteoporosis and Established or Severe Osteoporosis[3]

Diagnostic category	Definition	BMD T- score
Normal bone mass	BMD> 1 SD below average young and adult value	>-1
Osteopenia	BMD 1-2.5 SD below average young adult value	-1 to -2.5
Osteoporosis	BMD >2.5 SD below average young adult value	>-2.5
Severe osteoporosis	BMD >2.5 SD below the average young adult value and at least one osteoporotic fracture	> -2.5

Table 2: Age distribution of patients studied

Age in years	No. of patients	%
51-60	9	18
61-70	7	14
71-80	23	46
81-90	9	18
>90	2	4
Total	50	100



Graph 1: Age distribution of patients studied

Table 3: Gender distribution of patients studied

Gender	No. of patients	%
Female	**48**	**96**
Male	**2**	**4**
Total	**50**	**100**

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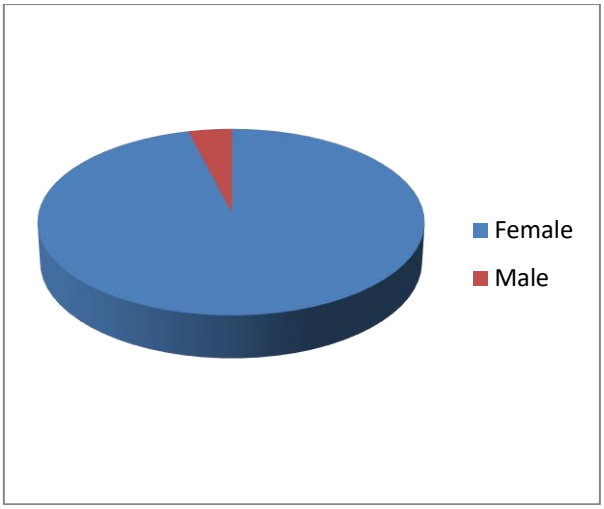
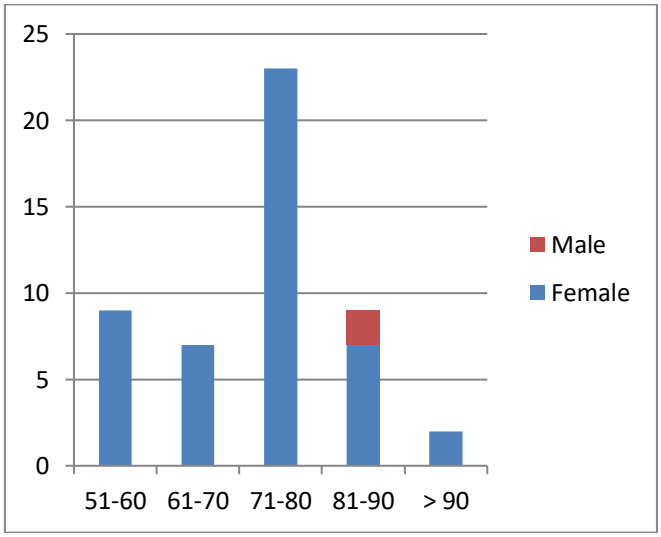


Graph 2: Gender distribution of patients studied

Table 4: Gender specific Age distribution of patients studied

Age in years	Gender		Total
	Female	Male	
51-60	9(18.75%)	0	**9(18%)**
61-70	7(14.58%)	0	**7(14%)**
71-80	23(47.91%)	0	**23(46%)**
81-90	7(14.58%)	2(100%)	**9(18%)**
>90	2(4.16%)	0	**2(4%)**
Total	**48(100%)**	**2(100%)**	**50(100%)**



Graph 3: Gender specific Age distribution of patients studied

Table 5: Site of fracture in patients studied

Fracture site	No of patients	Percentage (%)
Vertebral compression fracture	20	40 %
Fractures around hip	23	46 %
Distal radius fracture	7	14 %
Total	**50**	**100 %**

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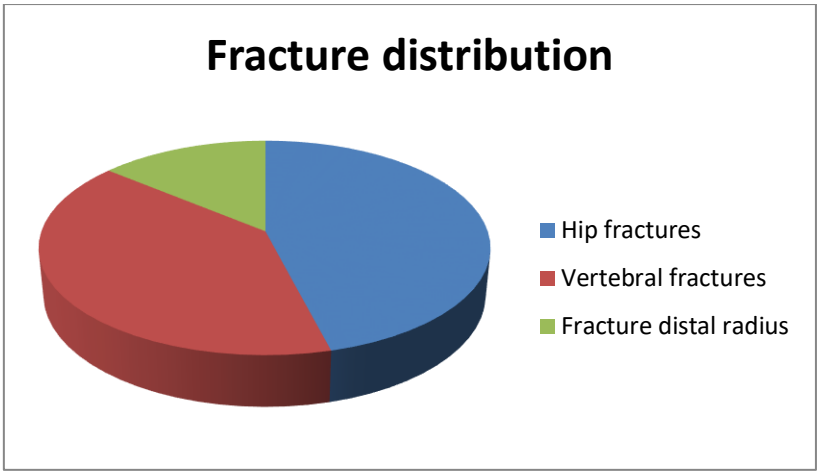
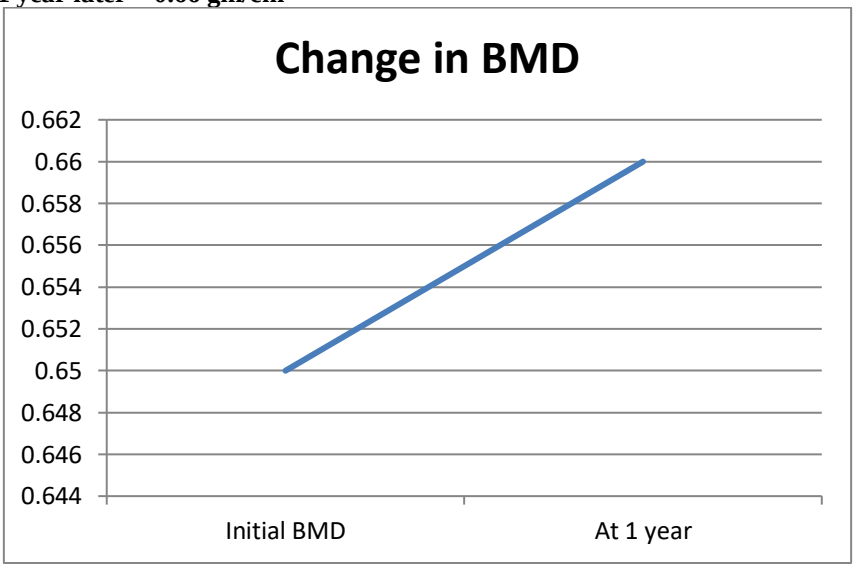


Graph 4: Distribution of fracture sites in the patients studied.

DXA (Average BMD) The Average BMD at the initial visit was- 0.65 gm/cm^2
Average BMD 1 year later – 0.66 gm/cm^2



Graph 5: DEXA (Average BMD)

DISCUSSION

46 % of the study population was between 71-80 years mainly from sedentary lifestyle. 96 %were postmenopausal women. 46 % of patients had fracture around hip, 40 % of patients had vertebral compression fractures and 14 % with distal radius fracture. Most of them were also noted to have additional vitamin D deficiency. Their compliance with calcium and vitamin D improved as they were kept under regular follow-up. One patient with Inter trochanteric fracture sustained fracture of IT fracture on the other side within 6 months.

None of the 40 % 0f patients with VCF in the study developed new vertebral osteoporotic fracture. This indicates the pain relief with ZA infusion specially in patients coming with chronic back pain associated with VCF may be due to prevention of new VCF along with its analgesic effect. Also, ZA had minor improvement in the T scores of BMD in the affected vertebrae. With a single yearly IV infusion, ZA in the treatment of osteoporosis overcomes compliance problems as with other oral agents.

CONCLUSION

It was concluded that there is significant increase in BMD at 1 year of injection ZA. The Average BMD at the initial visit was- 0.65 gm/cm^{2,} Average BMD 1 year later – 0.66 gm/cm^2

Being an antiresorptive drug, it improves bone mineral density of the patients, and is effective in preventing the occurance of new VCF in patients already having VCF.

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