

Original Article
Orthopaedics

**STUDY OF EFFECT
OF ZOLEDRONIC
ACID IN PATIENTS
WITH LOW BACK
PAIN ASSOCIATED
WITH VERTEBRAL
OSTEOPOROSIS**

Ramalingaiah A¹, Sridhar R²

¹ - Professor, Department of Orthopaedics, BMCRI, Bangalore

² - Junior Resident, Department of Orthopaedics, BMCRI, Bangalore

Corresponding Author:

Dr. Sridhar R
No. 517,
BMCRI PG Hostel for Men
Shivajinagar, Bangalore 560002.
Mobile: 9738413062

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Abstract:

Low back pain is the third most common orthopaedic problem. Most of the times it is overlooked and underdiagnosed and consequently undertreated. Vertebral osteoporosis is a common cause of low back pain and its early detection and prompt treatment prevents the complications of osteoporosis. Zoledronic acid a bisphosphonate class of Drug has excellent compliance due to its yearly dosage and there are early reports stating its analgesic properties. This study is done to note the same with respect to low back pain. The study concluded zoledronic acid has significant pain reducing effect in patients with low back pain due to vertebral osteoporosis.

Key-words: *Low back pain, vertebral osteoporosis, Zoedronic acid*

Introduction:

Osteoporosis, a condition characterized by decreased bone strength, is prevalent among postmenopausal women but also occurs in men and women with underlying conditions or major risk factors associated with bone demineralization. Its chief clinical manifestations are vertebral and hip fractures, although fractures can occur at any skeletal site. Osteoporosis affects >10 million individuals in the United States, but only a small proportion are diagnosed and treated.¹

70% of patients with symptomatic vertebral fracture complain of difficulty in standing and 65% of difficulty in bending, and 41% complain of constant pain.² Presence of one vertebral compression fracture increases the incidence of new vertebral compression fractures as stated by Klotzbuecher et al.³

Zoledronic acid being antiresorptive drug reduces the rate of bone resorption. There are several studies indicating zoledronic acid with few of the other bisphosphonates also have analgesic effect though the mechanism is poorly understood.⁴⁻¹⁰ This study evaluates the functional effect of yearly infusion of zoledronic acid in vertebral osteoporosis.

Materials and methods:

Patients of both the sexes presenting with low back pain for more than 4 weeks duration were screened.

Inclusion criteria: patients more than 40 years, symptoms more than 4 weeks, no known malignancy, no prior trauma / surgery, no known abdominal cause for low back pain.

Exclusion criteria: Less than 40 years, symptoms less than 4 weeks duration, prior trauma / surgery, patients presenting with features

of radiculopathy, impaired renal clearance, detectable abdominal cause for pain, females with features of pelvic inflammatory disease, who are already on hormonal replacement therapy.

Thorough history and clinical examinations were carried out. Routine investigations were done.

The patients were diagnosed to be osteoporotic according to WHO guidelines.¹¹

The patients after matching with the inclusion criteria were subjected to Bone mineral density assessment using GE lunar enCORE-based X-ray Bone Densitometer using enCORE software version 13.0. Both AP and Lateral vertebral analysis was carried out. Patients who had morphological features of vertebral bodies and those who turned out to be osteoporotic on AP assessment of lumbar vertebrae were infused 5 mg of iv Zoledronic acid after proper hydration of the patient. Infusion was over a period of 15 to 20 minutes. The patient was observed for a day for any adverse reactions. They were advised antipyretic medications for febrile reaction and only topical application was advised in case of episodes of increased back pain.

The patients were put on calcium and vitamin D3 and were assessed at 12 weeks, 24 weeks and at 1 year for functional improvement using VAS and Oswestry Low back pain questionnaire. At the end of 1 year a repeat DXA scan was done to note and change in the BMD of lumbar spine.

Figure 1. 75 years old female with low back pain for 5 months. Lumbar spine BMD -3.4

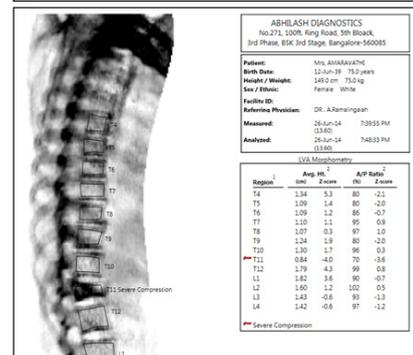
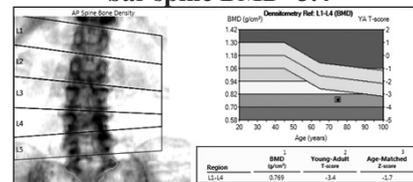


Figure 2. Same patient as above. Showing LVS morphological characteristics of spine

Results:

A total of 120 patients were screened and 50 patients included in the study who were found to be osteoporotic. Of them, 30 (60%) were females and 20 (40%) were male patients. Mean age was 51.5 years. Mean duration of pain was 6 weeks. Average BMD at initial visit was 0.75262 gm / cm². Initial mean VAS score was 7.46 and Oswestry score was 42.28. Mean VAS was 7.46 and ODI 42.48.

All the patients were followed at 12 weeks and 24 weeks. None lost to follow up. At 12 weeks intervals patients had improvement in their functional status as shown by the VAS and Oswestry scores. Mean VAS was 6.41 and Oswestry scores were 41.20. All the patients showed improvement at 24 weeks follow up also.

The change in the mean VAS scores at 12 weeks and 24 weeks were significant compared to the initial visit (p value at 12 weeks <0.001 and 24 weeks <0.001). Similar change in

the Oswestry scores were observed (p value at 12 weeks 0.006 and at 24 weeks <0.001) However at the end of 1 year, VAS and Oswestry scores were increased but below the initial values. The changes at 1 year were insignificant (for VAS score p value 0.019 and ODI p value 0.108) There was no significant change in BMD at lumbar spine of these patients

Of 120 patients who presented with idiopathic low back pain, 50 were osteoporotic in their lumbar spine.

Infusion of Zoledronic acid showed improvement in the functional status of the patient at 12 weeks and 24 weeks. However a single dose is insufficient to prevent recurrence of pain at 1 year. Only febrile reactions were observed in the initial 1 week after infusion. No severe adverse reactions were noted in the study

Discussion:

Some osteoporotic vertebral fractures go unnoticed and are discovered during routine radiography. Others cause severe pain, requiring hospitalisation of the patient. Our patients suffered from particularly painful compression, which, in most cases, was refractory to ambulatory treatment.

Zoledronic acid is an approved drug for use in Osteoporosis. It is given IV once a yearly dose has excellent compliance compared to other oral bisphosphonates due to their GI irritability and daily dose / once a month regimen.

It acts by inhibiting osteoclastic activity and preventing further decrease in BMD.

There are several studies indicating analgesic properties of bisphosphonates.

An animal based experimental study conducted by A. Bonabella

et al, Indicated that clodronate and pamidronate present a central and peripheral anti nociceptive effect in mice model study. However, the main mechanism cannot be determined from their data. The findings suggested a pharmacological role of the bisphosphonates in the modulation of anti-nociception even in acute conditions not related to accelerate osteolytic and inflammatory response, with a possible clinical application to control pain.³

Jane A Cauley et al conducted a randomized controlled HORIZON pivotal fracture study of Once yearly Zoledronic acid to determine the effect of once-yearly zoledronic acid on the number of days of back pain and the number of days of disability. This was done across 27 countries and was a three year multicentric trial and concluded that in women with postmenopausal osteoporosis, a once-yearly infusion with zoledronic acid over a 3-year period significantly reduced the number of days that patients reported back pain, limited activity owing to back pain, and limited activity and bed rest owing to a fracture.⁴

This study showed significant improvement in pain and subjective increase in working duration in the study group. Also the study noted that there were no new vertebral compression fractures at the end of 1 year as shown by the LVS analysis. Zoledronic acid might be effective in preventing new osteoporotic compression fractures thereby the indirectly providing analgesic effect. However the mode of analgesic effect still needs to be evaluated.

In the present study, there were significant functional improvements in pain scales in the initial 6 months following Zoledronic acid infusion.

Our study correlates well with the HORIZON pivotal study in terms of results though the study period was less.

Conclusion:

Patients above 40 years of age presenting with low back pain can be due vertebral osteoporosis and needs to be evaluated. Zoledronic acid 5 mg IV once a year has excellent compliance with minimal adverse effects and has shown to improve pain in the initial 6 months following infusion. Only modest improvement was noted in BMD with zoledronic acid.

Limitations of the study:

All patients were put on oral calcium and vitamin D. No control was done note their effect. Patients were advised only topical irritants for pain after infusion. There was no monitoring of patient compliance to topical applicants and no control group was created to note their effect.

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