

Comparison Evaluation of Bone Mineral Density in Patients with Ankylosing Spondylitis Before Treatment and One Year After Treatment with Alendronate

MOHSEN SOROUGH¹, MOHAMMAD MIRTALEBI¹ and ARMAN AHMADZADE^{2*}

¹Rheumatology Section, Department of Internal Medicine,
AJA University of Medical Sciences, Tehran, Iran.

²Rheumatology Ward , Loghman Hakim Hospital,
Shahid Beheshti University of Medical Sciences (SBMU), Tehran, Iran.

*Corresponding author E-mail : arman319@yahoo.com

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ABSTRACT

Ankylosing spondylitis (AS) is an inflammatory disease with an unknown cause, which primarily affects the axial skeleton. It usually appears during the second or third decade and its prevalence among *men is almost three times that of women*. Osteoporosis is known as a common finding in AS. Bone cytokines produced in the peripheral and axial joints in chronic inflammatory disease is responsible for systemic and local osteopenic activity. Considering the prevalence and importance of osteoporosis in patients with AS and the high costs of treatment and its dangerous and serious side effects such as fractures in patients with AS, it is necessary to evaluate the efficacy of drug agents in the patients. The purpose of this study is to evaluate the effectiveness of alendronate in patients with AS and comparison of them with standard treatment group. Total patients studied were 57. Of these, 8 cases were females and 49 cases were male. Of the 57 patients, 28 patients received the standard treatment of AS and 29 patients received Alendronate in addition to standard therapy. The average t-score and t-score mean difference of lumbar spine before and after the treatment in one-year period were calculated in both standard treatment receiving group and the group receiving standard treatment plus Alendronate. In addition to the lumbar spine, the average t-score and t-score mean difference of femoral neck were calculated for both groups. The densitometry of two groups showed that the T-score of patients in both groups were recovered after treatment compared to before therapy and the rate was more remarkable in the group treated with Alendronate. Oral bisphosphonate can be a proper substitute for the treatment of osteoporosis in this spectrum of patients.

Key words: Ankylosing spondylitis, osteoporosis, Alendronate.

INTRODUCTION

Spondyloarthropathies are a group of diseases with similar clinical characteristics that are associated with HLA-B27 allele, including Ankylosing Spondylitis¹. Ankylosing spondylitis (AS) is an inflammatory disease with an unknown cause, which primarily affects the axial skeleton². This disease usually presents in the second or third decade its incidence in men is almost three times that of women¹. Also in AS patients the rate of

depression is increased about 80% in female and 50% in male³.

There is a significant correlation between ankylosing spondylitis and histocompatibility antigen HLA-B27. The disease occurs worldwide, approximately proportional to the frequency of the antigen. These antigens are inherited in more than 90% of patients with ankylosing spondylitis. It seems that Enthesitis, *bone-ligament junction*, is the first place of occurring pathologic changes in AS,

especially in lesions around the hip and spine. Enthesitis is associated with an obvious edema in adjacent bone marrow characterized by erosive lesions that eventually leads to ossification¹. There is no laboratory test for the direct detection of AS⁴. In severe cases, it may be high levels of alkaline phosphatase and serum IgA⁵. AS diagnosis is important *before* they progress to an irreversible deformity. Osteoporosis is a common finding in patients with AS first described in 1877^{6,7}. Before the appearance of a significant immobilization at an early stage of the disease, the bone mineral density in the spinal column and proximal femur decreases significantly⁸⁻¹⁰. Bone cytokines produced in the peripheral and axial joints in chronic inflammatory disease are responsible for systemic and local osteopenic activity^{11,12}. Other possible mechanisms of osteoporosis caused by AS are genetic predisposition, impaired intestinal absorption of Calcium and Vitamin D associated with chronic inflammatory lesions and Lesions and Nonsteroidal anti-inflammatory Drugs NSAIDs¹³⁻¹⁵. Many drugs can reduce BMD T-score (the comparison of patient's condition with his PBM) and Z-score (the comparison of patient's condition with normal peer), and therefore increase the fracture risk¹⁶. Glucocorticoid effects on bone formation and its through multiple ways, however, it seems that the most important effect is the direct inhibition of bone formation^{17,18}.

Osteoporosis in AS is associated with increased bone resorption^{19,20}. In the interpretation of bone density in patients with AS some points should be considered such as negative & false positive of the increased bone mass due to the formation of large osteophytes and bamboo spine¹⁶.

In a study in Florida by Eric Orwell, the Alendronate effect in Osteoporosis treatment in men was evaluated. The results showed that men who have received Alendronate had $7.1 \pm 0.3\%$ increase in BMD at the lumbar spine, $2.5 \pm 0.4\%$ at the femoral neck and $2 \pm 0.2\%$ at total body. In contrast, the group receiving placebo had $1.8 \pm 0.5\%$ increase in BMD at the lumbar spine with no significant changes in the density of femoral neck and total body. On the other hand, the incidence of vertebral fractures was lower in the group receiving Alendronate than the placebo group (0.8% vs

7.1%)²¹. In a randomized trial study conducted by Lyles KW, venous bisphosphonate, for more than 23 months, reduced the overall rate of clinical fractures and mortality, but did not change the rate of hip fractures²². Also the effect of one-year treatment with the oral Bisphosphonate Osteoporosis in men with primary and secondary

Osteoporosis led to an increased BMD at the lumbar spine and proximal femur and reduced radiographic fracture risk^{9,23}. AS treatment with bisphosphonates showed that amino-bisphosphonates Pamidronate has the effect of clinical and radiological improvement in AS, while the improvement is slight and transient^{24,25}. Since given that densitometry has no major side effects in patients with AS and citing the fact that the main complication of a vertebral column is vertebral fractures the aim of this study is evaluation of Alendronate on osteoporosis inhibition and comparison between standard treatment with Alendronate administrator patients in improvement of osteoporosis

METHODS

This study is a cross-sectional study on 57 patients with AS admitted to 501 Hospital and a private clinic. Patients were visited by a specialist rheumatology and the diagnosis of AS was confirmed by New York based diagnostic criteria. All personal information is protected in this study and an informed consent was taken from patients before entering the study. On the other hand, prescription was not harmful to patients' health.

Personal information, clinical findings, laboratory tests, imaging findings and the patient's medications were collected by questionnaire and the initial BMD was taken. Before laboratory tests, bone densitometry were done for all patients. The patients were treated by standard treatment of disease. 29 patients received Alendronate for one year along with the treatment. From these patient 14 person received glucocorticoid for evaluation of its effect. After the completion of therapy, BMD were retaken and the results were analyzed and compared by SPSS-16 software and according to the descriptive indices and also paired student's T-test Independent T-test, Kolmogorov-smirnov.

RESULTS

In this study, 57 patients were studied with a mean age of 10.83 ± 35.91 and a gender distribution of 49 males (86%) and 8 females (14%). The HLA-B27 investigation showed 34 positive cases (59.6%), 7 negative cases (12.3%) and 16 patients (28.1%) without HLAB-27. Of the 57 patients studied 28 patients (49.1%) received the standard treatment of AS, 29 patients (50.9%) received Alendronate in addition to standard therapy.

Statistical analysis showed that items including mean age, gender distribution, the mean

duration of disease, HLA-B27, mean morning stiffness, the average distance of head to the wall, the average distance of hand to the ground, the average of Lateral Bending limitation, the average of Hb, the average of platelet count, the average of ESR, the average of CRP, the average of serum levels of Ca, the average of serum levels of ALK, Lumbar Spine and SI Joint had a P-Value over standard and showed no significant difference between two treatment groups of the standard method and the Alendronate acceptor in addition to standard method.

The results obtained from densitometry in the patients in both groups for the average t-score

Table 1: The average t-score and t-score mean difference for the lumbar spine before and after the treatment. Group 1 received Alendronate in addition to common treatment and group 2 received the common treatment

P-Value	-2.26±1.69	Group 1	Pre-treatment	The average t-score of the lumbar spine
0.00	-1.14±1.12	Group 2		
P-Value	-1.67±1.74	Group 1	Post-treatment	t-score mean difference for the lumbar spine before and after the treatment
0.04	-0.96±1.48	Group 2		
P-Value	-0.59±0.38	Group 1		
0.04	-0.18±1.17	Group 2		

Table 2: The average t-score and t-score mean difference for the femoral neck before and after the treatment. Group 1 received Alendronate in addition to common treatment and group 2 received the common treatment

P-Value	-1.6±1.23	Group 1	Pre-treatment	the average t-score of the femoral neck
0.00	0.69±0.9	Group 2		
P-Value	-0.97±1.29	Group 1	Post-treatment	
0.02	0.77±0.95	Group 2		
P-Value	-0.62±0.68	Group 1		t-score mean difference for the femoral neck before and after the treatment
0.00	0.08±0.69	Group 2		

Table 3: The average t-score and t-score mean difference for the lumbar vertebra before and after the treatment. Group 1 received Alendronate in addition to common treatment and group 2 received the common treatment

P-Value	-1.74±2.03	Group 1	Pre-treatment	the average t-score of the lumbar vertebra
0.11	-2.75±1.12	Group 2		
P-Value	-1.3±2.16	Group 1	Post-treatment	
0.03	-1.95±1.25	Group 2		
P-Value	-0.37±0.29	Group 1		t-score mean difference for the lumbar vertebra before and after the treatment
0.00	-0.8±0.34	Group 2		

and t-score mean difference for the lumbar spine before and after the treatment can be seen in Table 1.

The results obtained from densitometry in the patients in both groups for the average t-score and t-score mean difference for the femoral neck before and after the treatment can be seen in Table 2.

Of the 29 AS patients who received standard treatment with Alendronate, 14 patients

received glucocorticoids as a part of standard treatment and 15 patients did not. Data from the statistical analysis of treatment process for these patients are shown in the following tables. Table 3 shows the investigation of lumbar vertebra.

Table 4 also shows the densitometry study of patients receiving Alendronate and glucocorticoids and receiving only Alendronate for the femoral neck.

Table 4: The average t-score and t-score mean difference for the femoral neck before and after the treatment. Group 1 received Alendronate and glucocorticoids in addition to common treatment and group 2 received the Alendronate treatment

P-Value	-1.61±1.46	Group 1	Pre-treatment	the average t-score of the femoral neck
0.95	-1.58±1.02	Group 2		
P-Value	-0.93±1.51	Group 1	Post-treatment	
0.04		Group 2		
P-Value	-0.67±0.82	Group 1	t-score mean difference for the femoral neck before and after	the treatment
0.04	-0.56±0.53	Group 2		

DISCUSSION

Ankylosing spondylitis (AS) is a chronic inflammatory disease which is characterized by an inflammation in the spine and peripheral skeleton, and may lead to a focal bone erosions or Osteoporosis in the early stages. Pathogenesis of AS is not fully understood but it is certainly mediated by immunity. None of the laboratory tests are diagnostic for AS.

Osteoporosis is a common finding in AS. Osteoporosis reasons in AS is a multi-factorial. Bone cytokines produced in the peripheral and axial joints in this inflammatory disease is responsible for systemic and local osteopenic activity. Other possible mechanisms in AS-induced Osteoporosis include genetic predisposition, impaired intestinal absorption of Ca and Vitamin D associated with chronic intestinal inflammatory lesions and certain medications such as glucocorticoids in these patients.

In a study in Florida by Eric Orwell, the Alendronate effect in Osteoporosis treatment in men

was evaluated. The results showed that men who have received Alendronate had $7.1 \pm 0.3\%$ increase in BMD at the lumbar spine, $2.5 \pm 0.4\%$ at the femoral neck and $2 \pm 0.2\%$ at total body. In contrast, the group receiving placebo had $1.8 \pm 0.5\%$ increase in BMD at the lumbar spine with no significant changes in the density of femoral neck and total body. On the other hand, the incidence of vertebral fractures was lower in the group receiving Alendronate than the placebo group (0.8% vs 7.1%)²¹. In a randomized trial study conducted by Lyles KW, venous bisphosphonate, for more than 23 months, reduced the overall rate of clinical fractures and mortality, but did not change the rate of hip fractures²². Also the effect of one-year treatment with the oral Bisphosphonate Osteoporosis in men with primary and secondary

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In this study, evaluation of markers determining the disease severity including age, disease duration, morning stiffness, the distance of head to the wall, the distance of hand to the ground, Skeletal limitation, the amount of ESR, CRP, and ALK, showed no significant difference between two treatment groups receiving the Alendronate and the standard method.

The densitometry of two groups showed that the lumbar spine T-score of patients in both groups were improved after treatment compared to before therapy and the rate was more remarkable in the group treated with Alendronate.

On the other hand, using this treatments the inflammatory processes in these patients have been treated and so led to density improvement in patient. But with the densitometry of femoral neck in the two groups of patients, we have reached the conclusion that the standard treatment alone cannot improve the bone density in these patients. Natural process of the disease and other possible factors worsen the density of the femoral neck in these

patients, while the treatment with Alendronate improves the density of femoral neck. In fact, Alendronate has a positive impact on improving the bone densitometry in both the lumbar spine and the femoral neck. Glucocorticoids have some effect on bone formation via several routes. One of the most important route is direct inhibition of bone formation. However, as previous studies, glucocorticoids also cause a deterioration of bone densitometry in these patients.

CONCLUSION

The results obtained in this study are similar to previous studies, with the difference that all previous studies were on the effects of venous bisphosphonate such as pamidronate and etc. This is the first study on the effect of oral bisphosphonate (Alendronate) in the treatment of osteoporosis in AS patients, and due to the comfortable consumption (weekly), being cheaper and more accessible in Iran, the oral bisphosphonate can be a proper substitute for the treatment of osteoporosis in this spectrum of patients.

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