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A retrospective study of alendronate for the treatment of ankylosing spondylitis

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Abstract

This retrospective study assessed the effect of alendronate for treating patients with ankylosing spondylitis (AS).

Eighty-six patients with AS were included in this retrospective study, and were divided into 2 groups. Forty-six patients in the intervention group received alendronate plus vitamin D (400 mg/day) and calcium (500 mg/day), while 40 patients in the control group received vitamin D and calcium only, the same dose as the intervention group. The primary outcome included bone densitometry. The secondary outcomes consisted of quality of life, measured by Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire, disease activity, measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and functional status, measured by Bath Ankylosing Spondylitis Functional Index (BASFI), as well as the adverse events (AEs).

At the end of 6-month treatment, patients in the intervention group were not superior to the patients in the control group in bone densitometry (hip, $P = .47$; lumbar, $P = .53$), quality of life ($P = .32$), disease activity ($P = .39$), and functional status ($P = .41$). Moreover, no significant differences in AEs were found between 2 groups.

The results of the present study showed that alendronate can neither be used to treat bone loss, nor to enhance the quality of life, disease activity, and functional status.

Abbreviations: AEs = adverse events, AS = ankylosing spondylitis, ASQoL = Ankylosing Spondylitis Quality of Life, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, BASFI = Bath Ankylosing Spondylitis Functional Index, BMD = bone mineral density.

Keywords: adverse event, alendronate, ankylosing spondylitis, effect, retrospective study

1. Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic condition.[1,2] It often affects sacroiliac, spine, and pelvic limb joints, which can lead to deformity and ankylosis of these joints, and poor quality of life.[3,4] The symptoms often manifest as the pain, limitation of spinal mobility, stiffness and function.[5,6] A study reported that its onset occurs mostly between 20 and 30 years old adults.[7] Unfortunately, such condition is often being diagnosis 5 to 6 years delay.[7] The incidence of AS varies from 0.2% to 1% of the adult population.[8] Additionally, males are more likely to suffer from such condition than females by 2 to 3 times.[9] Its prevalence rate ranges from 7.4 to 31.9 per 10,000 populations.[10]

Presently, no medication can cure such condition. Fortunately, several therapies are available to relive the symptoms, and to slow down its progression. These interventions include supplemental and physical therapies, as well as medication.[11–19] However, all of them have efficacious limitations.

Since bone loss and osteoporosis are reported as the most common complications of AS.[10] Thus, prevention of bone loss in patients with AS is very important. Calcium and vitamin D supplementation are reported to treat such condition with increasing bone mineral density (BMD) by 0.5% to 2% after 2 to 3 years treatment, although limited data available to support this therapy.[20] Several medications including pamidronate, denosumab, and alendronate are reported to enhance BMD in patients with AS, especially for alendronate.[21–25] However, its conclusion is still inconsistent.[22–24]

In this retrospective study, we evaluated the effect and safety of alendronate for the treatment of patients with AS among Chinese population.

2. Methods

2.1. Ethics

It was approved by the Medical Ethical Committee of The Affiliated Hongqi Hospital of Mudanjiang Medical University. All patients have provided the signed informed consent.

2.2. Design

This work was designed as a retrospective study. It was conducted between January 2015 and December 2017. All 86

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Table 1

Patients characteristic values before study.

Characteristics	Intervention group (n = 46)	Control group (n = 40)	P
Mean age, y	35.6 (7.1)	34.8 (7.3)	.61
Gender			
Male	32 (69.6)	27 (67.5)	.84
Female	14 (30.4)	13 (32.5)	.84
BMI, kg/m^2	22.5 (1.7)	22.8 (1.8)	.43
Disease duration, y	5.9 (2.7)	5.7 (2.6)	.73
Marital status			
Married	42 (91.3)	37 (92.5)	.83
Single	4 (8.7)	3 (7.5)	.83
ASQoL	9.8 (4.1)	10.1 (4.3)	.74
BASDAI	6.4 (2.1)	6.5 (2.2)	.83
BASFI	5.1 (2.0)	4.9 (2.0)	.64
Hip BMD, mg/cm^2	0.84 (0.17)	0.82 (0.16)	.57
Lumbar BMD, mg/cm^2	1.00 (0.08)	0.99 (0.09)	.59

Note: Data are present as mean ± standard deviation or number (%).
ASQoL = Ankylosing Spondylitis Quality of Life (0–18), BASDAI = Bath Ankylosing Spondylitis Disease Activity Index (0–10), BASFI = Bath Ankylosing Spondylitis Functional Index (0–10), BMD = bone mineral density, BMI = body mass index.

eligible patients were included and were divided into an intervention group and a treatment group according to the different interventions they received. All patients in both groups received supplemental treatment with vitamin D and calcium. In addition, patients in the intervention group also underwent alendronate. All the treatments were applied for a total of 6 months.

2.3. Eligibility

All eligible patients were 18 to 65 years old. They were all conformed diagnosis of AS according to the modified New York criteria for AS with spinal pain intensity,[26,27] measured by Numerical Rating Scale ≥4. Patients were excluded if they received supplemental treatment with vitamin D and calcium, and alendronate therapy 1 month before this study. Additionally, patients were also excluded if they were pregnancy or breastfeeding, severe organ diseases, and abnormal liver and kidney functions.

2.4. Treatment schedule

All patients were administered supplemental treatment with vitamin D (400 mg/day) and calcium (500 mg/day), 1 session daily, 5 sessions weekly for a total of 6 months. Additionally, patients in the intervention group also underwent oral alendronate 70 mg once weekly for a total of 6-month treatment.

2.5. Outcome measurements

The primary outcome included bone densitometry, measured by the Hologic QDR model instrument (Hologic, Inc., Waltham, MA). The secondary outcomes included quality of life, measured by Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire[28,29]; disease activity, measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[28,30]; and functional status, measured by Bath Ankylosing Spondylitis Functional Index (BASFI)[28,31]; as well as the adverse events (AEs). All outcome measurements were performed before and at the end of 6-month treatment.

2.6. Statistical analysis

SAS version 8.3 (SAS Institute, Inc., Cary, NC) was used to analyze all the outcome data and characteristic values. Of those data, categorical data was analyzed by Chi-square tests, and continuous data was analyzed by *t* test or Mann–Whitney *U* test. Statistical significance level was defined as $P < .05$.

3. Results

The characteristics of all included patients are listed in Table 1. No significant differences in all of the characteristic values were found before the study between 2 groups.

The results for the effect measurements at the end of 6-month treatment are summarized in Tables 2 and 3. Supplemental treatment of vitamin D and calcium cannot improve BMD for patients with AS (hip, $P = .47$; lumbar, $P = .53$; Table 2). Moreover, it neither can enhance the quality of life, measured by ASQoL ($P = .32$, Table 3), nor can improve the disease activity, measured by BASDAI ($P = .39$, Table 3), and functional status, measured by BASFI ($P = .41$, Table 3).

Table 2

Change of BMD at the end of the 6-month treatment (change from baseline).

BMD	Intervention group (n = 46)	Control group (n = 40)	Difference	P
Hip, mg/cm^2	0.01 (−0.01, 0.02)	−0.01 (−0.01, 0.01)	0.02 (0.01, 0.03)	.47
Lumbar, mg/cm^2	0.02 (0.01, 0.03)	0.01 (0.01, 0.02)	0.01 (0.01, 0.02)	.53

Note: Data are present as mean ± standard deviation.
BMD = bone mineral density.

Table 3

Outcome measurements at the end of the 6-month treatment (change from baseline).

Outcome measurements	Intervention group (n = 46)	Control group (n = 40)	Difference	P
ASQoL	−1.7 (−2.4, −1.1)	−1.0 (−1.6, −0.5)	−0.6 (−1.0, −0.2)	.32
BASDAI	−1.5 (−2.2, −0.9)	−0.8 (−1.3, −0.2)	−0.7 (−1.1, −0.3)	.39
BASFI	−0.9 (−1.3, −0.4)	−0.5 (−0.8, −0.1)	−0.4 (−0.7, −0.2)	.41

Note: Data are present as mean ± standard deviation.
ASQoL = Ankylosing Spondylitis Quality of Life (0–18), BASDAI = Bath Ankylosing Spondylitis Disease Activity Index (0–10), BASFI = Bath Ankylosing Spondylitis Functional Index (0–10).

Table 4

Adverse events between 2 groups.

Adverse events	Intervention group (n = 46)	Control group (n = 40)	P
Heartburn	4 (8.7)	1 (2.5)	.25
Bloating	3 (6.5)	0 (0)	.22
Nausea/vomiting	4 (8.7)	2 (5.0)	.51
Stomach pain	2 (4.3)	0 (0)	.33
Diarrhea	3 (6.5)	0 (0)	.22
Constipation	2 (4.3)	1 (2.5)	.65
Joint pain	3 (6.5)	1 (2.5)	.39
Joint swelling	2 (4.3)	0 (0)	.33
Dizziness	3 (6.5)	0 (0)	.22
Eye pain	2 (4.3)	0 (0)	.33
Headache	3 (6.5)	1 (2.5)	.39

Note: Data are present as number (%).

Several mild AEs were recorded in this study (Table 4). The most frequency AEs included heartburn, nausea/vomiting, bloating, diarrhea, joint pain, dizziness, and headache in this study. No significant differences regarding any kinds of AEs were found between 2 groups. Moreover, no severe AEs occurred; and no treatment-related deaths were found in both groups.

4. Discussion

Presently, there is still inconsistent conclusion regarding the effect of alendronate for the treatment and the improvement of symptoms in patients with AS. Previous studies have found that alendronate can effectively be used to prevent bone loss after at least 1 year treatment.[22–24] However, recent studies reported that alendronate is ineffective for the treatment of bone loss even after 2 years treatment in patients with AS.[32,33]

The results of this retrospective study were partly consistent with the recent reported studies.[32,33] In our study, there were not significant differences regarding the bone loss, quality of life, disease activity, and functional status between 2 groups. All these outcomes were measured by bone densitometry, ASQoL questionnaire, BASDAI, and BASFI, respectively. The results indicate that alendronate is not efficacious for the treatment of patients with AS after 6 months treatment.

Three limitations exist in this study. First, this study included only 86 patients, and had a relative small sample size. Then, this study only consisted of 6-month intervention and no follow-up after the treatment. Compared with the previous studies of at least 1 year treatment period, our treatment duration is quite short. Finally, the observed effect was the result of the synergistic effect of supplemental treatment and alendronate, although the intervention was similar between 2 groups before the study. Therefore, the effect and safety of longer term treatment of alendronate should still be explored among Chinese population in the future study.

5. Conclusions

The results of this study demonstrated that alendronate can neither prevent bone loss, nor improve the quality of life, disease activity, and the functional status among Chinese population.

Author contributions

Conceptualization: Wei Zhao, Gang Li, Chang-an Lv, Li Tian, Lian-jin Jin.
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Writing – original draft: Wei Zhao, Gang Li, Chang-an Lv, Li Tian, Lian-jin Jin.
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