

Original Article

Alendronate sodium demonstrates significant clinical advantages in treating osteoporosis secondary to severe fractures

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Abstract: Objective: To investigate the clinical efficacy of alendronate sodium in patients with osteoporosis secondary to severe fractures. Methods: A total of 102 patients with post-fracture osteoporosis were retrospectively included in this study. The control group (n=45) received standard treatment, while the research group (n=57) was additionally administered alendronate sodium. Bone metabolism markers, pain intensity (assessed by Visual Analogue Scale [VAS]), bone mineral density (BMD), and overall therapeutic efficacy were compared between the two groups. Multivariate logistic regression was performed to identify predictors of therapeutic efficacy. Results: Compared with the control group, the research group demonstrated significantly greater improvements in bone metabolism markers, VAS scores, BMD, and overall efficacy. Univariate and multivariate logistic regression analyses further identified smoking history, alcohol abuse, and treatment modality as independent risk factors for treatment failure, while elevated serum bone Gla protein (BGP) levels were identified as a protective factor. Conclusion: Alendronate sodium significantly improves clinical outcomes in treating patients with osteoporosis secondary to severe fractures.

Keywords: Alendronate sodium, severe fractures, osteoporosis, bone metabolism, pain, treatment efficacy

Introduction

Fractures resulting from traumatic injuries to the musculoskeletal system are prevalent and are characterized by partial or complete disruptions of bone integrity [1]. These injuries impose a substantial socioeconomic burden and are associated with elevated morbidity and mortality rates [2]. Most patients present with single-site fractures, whereas multiple fractures are less frequent. Severe fractures, however, are often associated with a more critical clinical condition, manifested by intense pain and significant functional impairment, potentially leading to paralysis or even death [3-5].

Secondary osteoporosis refers to bone loss caused by pathological conditions or medications other than aging or menopause. This results in progressive bone mass reduction and substantially increases the risk of fractures [6]. Statistically, secondary osteoporosis affects up to 30.0% of post-menopausal

women, at least 50% of pre-menopausal women, and 50%-80% of men [7]. Patients with severe fractures are particularly susceptible to secondary osteoporosis, primarily attributed to their restricted ambulatory capacity and decreased physical activities, which accelerate bone resorption and loss [8]. Additionally, certain medications used during treatment may impair calcium absorption. Inadequate nutritional intake, including deficits in protein and vitamins, can further disrupt the bone metabolism, exacerbating bone loss [9].

Pharmacotherapy remains the cornerstone in the management of osteoporosis secondary to severe fractures. Conventional medications, such as vitamin D-calcium supplements, calcitriol, calcitonin, and denosumab, are frequently employed. Nevertheless, their therapeutic efficacy remains suboptimal, necessitating improved treatment strategies to enhance clinical outcomes [10].

Alendronate sodium, a nitrogen-containing bisphosphonate developed in the 1970s, inhibits osteoclast-mediated bone resorption and thereby exerts anti-osteoporotic effects [11, 12]. Moreover, it plays a crucial role in augmenting bone mineral density (BMD) and reducing the risk of vertebral, non-vertebral, and hip fractures by 55.0%, 64.0%, and 47.0%, respectively [13, 14]. In a study by Li M et al. [15], alendronate sodium significantly increase the lumbar spine BMD in Chinese postmenopausal women with osteoporosis and exhibited milder side effects compared to teriparatide. Despite these benefits, studies on the application of alendronate sodium in patients with osteoporosis secondary to severe fractures remain limited. Therefore, this study was designed to conduct a comprehensive evaluation, aiming to provide novel perspectives and valuable insights into the treatment and management of this high-risk population.

Materials and methods

Case selection

This retrospective study was approved by the Ethics Committee of Xinrui Hospital of Xinwu District. A total of 102 patients diagnosed with osteoporosis secondary to severe fractures and admitted between March 2022 and October 2024 were included. Based on the treatment regimen, 45 patients received standard therapy that were allocated to the control group, and the remaining 57 patients treated with additional alendronate sodium were classified into the research group.

Inclusion and exclusion criteria

Inclusion criteria: 1) Diagnosis of osteoporosis secondary to severe fractures; 2) Age between 18 and 80 years; 3) Fracture occurrence within 3 months before enrollment; 4) Normal serum calcium, phosphorus, and parathyroid hormone levels; 5) Ability to comply strictly with the prescribed medication protocol; 6) No use of any anti-osteoporosis medications in the past six months; 7) First-time treatment for osteoporosis; 8) Normal cognitive function and ability to cooperate with the study protocol.

Exclusion criteria: 1) Vitamin D deficiency; 2) Concurrent malignancy; 3) Motor dysfunction or sacroiliac inflammatory disorders; 4) History of allergic constitution; 5) Severe cardiac, pul-

monary, or renal insufficiency; 6) Use of medications affecting bone metabolism or BMD in the past three months; 7) Presence of metabolic bone diseases, including hyperparathyroidism, Paget's disease, or osteogenesis imperfecta; 8) Prior use of bisphosphonate (oral or intravenous); 9) Active upper gastrointestinal disorders (e.g., reflux esophagitis, Barrett's esophagus), delayed esophageal emptying, hypocalcemia (defined as serum calcium < 2.1 mmol/L), or severe vitamin D deficiency (25(OH) D < 20 ng/mL despite adequate supplementation); 10) Women in pregnancy or with planned pregnancy; 11) Prolonged bed confinement (> 50% of waking hours) or complete immobilization.

Intervention methods

Patients in the control group received conventional treatment. Specifically, patients were advised to follow a regular diet and given lifestyle guidance in the first three months post-fracture. Pharmacologically, they were prescribed oral vitamin D-calcium chewable tablets (one tablet three times daily; Haeon (Suzhou) Pharmaceutical Co., Ltd., H10950029) and calcitriol soft capsules (0.25 µg twice daily; Catalent Germany Eberbach GmbH, H20000065).

In the research group, patients received alendronate sodium tablets (one tablet once daily; Hangzhou Minsheng Binjiang Pharmaceutical Co., Ltd., H20203221) in addition to the conventional treatment described above. Both groups were continuously treated for three months.

Based on oral medications, all patients were guided to engage in rehabilitation exercises. Exercise type, intensity, and duration were consistent across both groups. The rehabilitation protocol included isometric quadriceps contractions, straight-leg raises, and joint flexion-extension exercises. Quadriceps massage was performed for one hour per session, three times a day. On the second day after the operation, continuous passive knee joint flexion-extension exercises were initiated under the supervision of trained nurses. The range of motion was carefully adjusted according to each patient's pain tolerance, gradually increasing from a range of 0 to 50°. Each session lasted for one hour and was repeated twice daily. Starting on day five, the joint range of

Table 1. Comparison of baseline characteristics between the two groups

Indicators	Control group (n=45)	Research group (n=57)	χ^2/t	P
Age (years old)	56.20±7.82	55.47±9.35	0.420	0.675
Gender			0.221	0.638
Male	20 (44.44)	28 (49.12)		
Female	25 (55.56)	29 (50.88)		
Body mass index (kg/m ²)	23.16±2.32	22.26±2.35	1.931	0.056
Smoking history			1.978	0.160
No	23 (51.11)	37 (64.91)		
Yes	22 (48.89)	20 (35.09)		
Alcohol abuse history			0.027	0.868
No	26 (57.78)	32 (56.14)		
Yes	19 (42.22)	25 (43.86)		

pain alleviation, notably enhanced activity capacity, and a 1%-2% increase in BMD; Ineffective: Failure to meet the above criteria. The total effective rate was calculated as the percentage of cases rated as markedly effective and effective in relation to the total number of cases.

The primary outcome measures included CTX-I, NTX-I, BGP levels, VAS scores, and treatment efficacy. BMD was assessed as a secondary indicator.

motion was increased by 10° per day, maintaining a session duration of one hour. Upon initiation of ambulation, patients were instructed to wear a lumbar support brace and avoid forward bending. These ambulatory sessions were limited to 30 minutes per time, three times a day.

Data collection

1. Bone metabolism assessment: Venous blood samples (3 mL) were collected from the elbow before treatment and at 3 months post-treatment. Following centrifugation, serum was isolated to quantify C-terminal telopeptide of type I collagen (CTX-I), N-terminal telopeptide of type I collagen (NTX-I), and osteocalcin (bone Gla protein, BGP) levels using enzyme-linked immunosorbent assay (ELISA; Shanghai Yuan-Mu Biological Technology Co., Ltd.).

2. Pain assessment: Pain intensity was evaluated before and after treatment using the Visual Analogue Scale (VAS; score range: 0-10), assessing pain during weight-bearing, turning over, joint flexion-extension, and at rest. Higher VAS scores indicated greater pain severity.

3. BMD measurement: BMD of the femoral neck was measured using dual-energy X-ray absorptiometry device (GE Lunar prodigy Advance).

4. Treatment efficacy evaluation: Treatment efficacy was classified based on the following criteria: markedly effective: Complete relief of chronic pain, unrestricted physical activities, and ≥ 2% increase in BMD; Effective: significant

Statistical analysis

Continuous variables were expressed as mean ± standard error of the mean (SEM). Comparisons between the two groups were performed using the independent samples t-test, while within-group comparisons before and after treatment were conducted using the paired t-test. Categorical variables were expressed as rates (percentages), and comparisons between groups were conducted using the chi-square (χ^2) test. All statistical analysis were performed using SPSS 21.0. Binary logistic regression analysis was used to identify factors influencing treatment efficacy in patients with osteoporosis secondary to severe fractures. A *P*-value < 0.05 was considered as statistically significant.

Results

Comparison of general characteristics between the two groups

Statistical analysis of patients' baseline characteristics, including age, body mass index (BMI), smoking history, and alcohol abuse history, revealed no significant inter-group differences (*P* > 0.05, **Table 1**), demonstrating clinical comparability.

Comparison of bone metabolism markers between the two groups before and after treatment

At baseline, there were no significant inter-group differences in serum levels of CTX-I,

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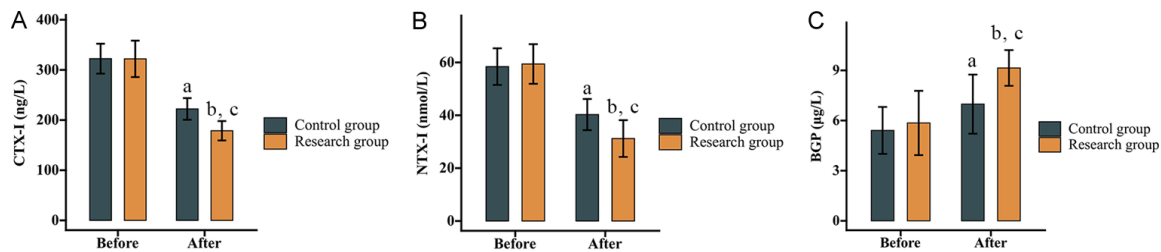


Figure 1. Comparison of bone metabolism markers between the two groups. A: Pre- and post-treatment CTX-I levels in the control and research groups. B: Pre- and post-treatment NTX-I levels in the control and research groups. C: Pre- and post-treatment BGP levels in the control and research groups. Notes: CTX-I, C-terminal telopeptide of type I collagen; NTX-I, N-terminal telopeptide of type I collagen; BGP, osteocalcin (bone Gla protein). ^aP < 0.05, ^bP < 0.01, in comparison with the pre-treatment level; ^cP < 0.05, when compared with the control group.

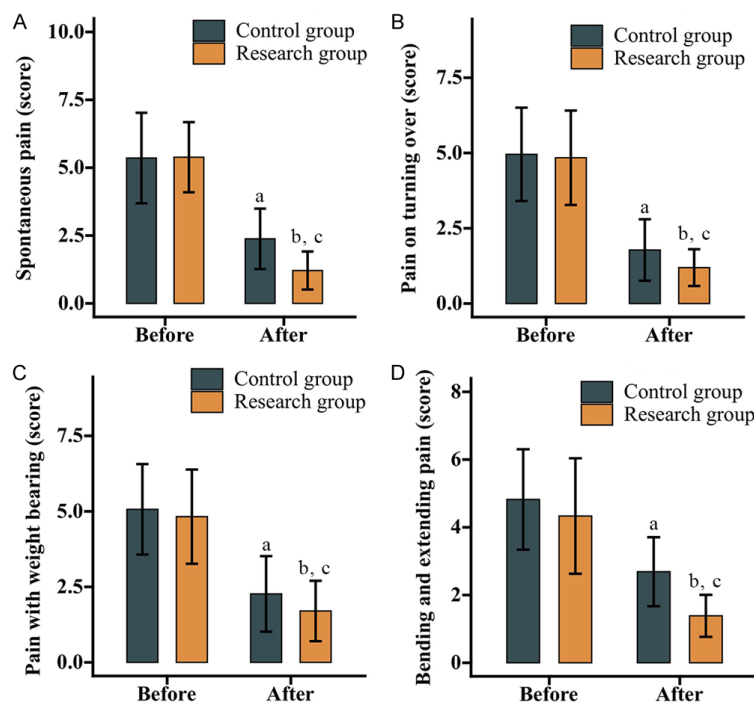


Figure 2. Comparison of pain intensity between the two groups. A: Pre- and post-treatment VAS scores for spontaneous pain in the control and research groups. B: Pre- and post-treatment VAS scores for pain during turning over in the control and research groups. C: Pre- and post-treatment VAS scores for pain during weight-bearing in the control and research groups. D: Pre- and post-treatment VAS scores for pain during flexion-extension in the control and research groups. Notes: VAS, Visual Analogue Scale. ^aP < 0.05, ^bP < 0.01, compared to pre-treatment levels; ^cP < 0.05, compared to the control group.

NTX-I, or BGP ($P > 0.05$). After treatment, both groups showed significant reduction in CTX-I and NTX-I levels, and a marked increase in BGP levels ($P < 0.05$). Notably, compared to the control group, the research group displayed significantly lower post-treatment CTX-I and NTX-I levels and notably higher BGP levels ($P < 0.05$).

BMD compared to the control group ($P < 0.05$, Table 2).

Comparison of treatment efficacy between the two groups

The research group exhibited a significantly higher total effective rate than the control

Detailed comparisons are illustrated in Figure 1.

Comparison of pain intensity between the two groups

No significant differences were observed in baseline VAS scores between the two groups ($P > 0.05$). After treatment, both groups demonstrated significant reductions in VAS scores across all categories ($P < 0.05$). Notably, the research group demonstrated significantly lower post-treatment VAS scores than the control group in all pain categories ($P < 0.05$). The details are shown in Figure 2.

Comparison of BMD between the two groups

The two groups were comparable in baseline BMD values ($P > 0.05$). Both groups showed a significant increase in BMD after treatment ($P < 0.05$). However, the research group demonstrated a significantly higher post-treatment

Table 2. Comparison of BMD between the two groups

Indicators	Control group (n=45)	Research group (n=57)	t	P
BMD (g/cm ²)				
Before treatment	0.70±0.18	0.77±0.21	1.779	0.078
After treatment	0.84±0.11 ^a	1.04±0.18 ^b	6.547	< 0.001

Notes: BMD, bone mineral density. ^aP < 0.05, ^bP < 0.01, compared to pre-treatment level.

Table 3. Comparison of treatment efficacy between the two groups

Indicators	Control group (n=45)	Research group (n=57)	χ ²	P
Markedly effective	13 (28.89)	22 (38.60)		
Effective	18 (40.00)	28 (49.12)		
Ineffective	14 (31.11)	7 (12.28)		
Total effective rate	31 (68.89)	50 (87.72)	5.454	0.020

Table 4. Univariate analysis of factors influencing treatment efficacy in patients with osteoporosis secondary to severe fractures

Indicators	Ineffective group (n=21)	Effective group (n=81)	χ ²	P
Age (years old)			0.132	0.717
< 55	10 (47.62)	35 (43.21)		
≥ 55	11 (52.38)	46 (56.79)		
Gender			4.081	0.043
Male	14 (66.67)	34 (41.98)		
Female	7 (33.33)	47 (58.02)		
Body mass index (kg/m ²)			0.398	0.528
< 22	8 (38.10)	25 (30.86)		
≥ 22	13 (61.90)	56 (69.14)		
Smoking history			9.992	0.002
No	6 (28.57)	54 (66.67)		
Yes	15 (71.43)	27 (33.33)		
Alcohol abuse history			5.969	0.015
No	7 (33.33)	51 (62.96)		
Yes	14 (66.67)	30 (37.04)		
Treatment modality			5.454	0.020
Alendronate sodium	7 (33.33)	50 (61.73)		
Conventional therapy	14 (66.67)	31 (38.27)		
CTX-I (ng/L)			6.840	0.009
< 330	6 (28.57)	49 (60.49)		
≥ 330	15 (71.43)	32 (39.51)		
NTX-I (nmol/L)			2.604	0.107
< 60	7 (33.33)	43 (53.09)		
≥ 60	14 (66.67)	38 (46.91)		
BGP (μg/L)			4.857	0.028
< 5.50	15 (71.43)	36 (44.44)		
≥ 5.50	6 (28.57)	45 (55.56)		

Notes: CTX-I, C-terminal telopeptide of type I collagen; NTX-I, N-terminal telopeptide of type I collagen; BGP, osteocalcin (bone Gla protein).

group (87.72% vs. 68.89%, P < 0.05). Refer to **Table 3** for further details.

Univariate and multivariate analysis of factors influencing treatment efficacy

Univariate analysis identified gender, smoking history, alcohol abuse history, treatment modality, CTX-I, and BGP as factors significantly associated with treatment efficacy (P < 0.05). These variables were incorporated into a binary logistic regression model, with treatment efficacy as the dependent variable. Appropriate values were assigned to each factor for further analysis. Multivariate analysis revealed that smoking history, alcohol abuse history, and treatment modality were independent risk factors for treatment failure in patients with osteoporosis secondary to severe fractures (P < 0.05). In contrast, BGP emerged as a protective factor (P < 0.05). Detailed results are presented in **Tables 4-6**.

Discussion

In this study, alendronate sodium significantly reduced CTX-I and NTX-I levels while increasing BGP levels in patients with osteoporosis secondary to severe fractures. These effects were markedly superior to those observed with conventional treatment, indicating that alendronate sodium can significantly improve the bone metabolic hemostasis in this patient population. CTX-I and NTX-I are key markers of bone resorption and are negatively correlated with BMD in females. Moreover, they are also recognized as crucial predictors of non-spinal and hip fractures [16-18]. A study by

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Table 5. Assignment table for variables included in the analysis

Indicators	Variables	Assignments
Gender	X1	Male =0, female =1
Smoking history	X2	None =0, yes =1
Alcohol abuse history	X3	None =0, yes =1
Treatment modality	X4	Alendronate sodium =0, conventional therapy =1
CTX-I (ng/L)	X5	< 330 ng/L =0, ≥ 330 ng/L =1
BGP (μg/L)	X6	< 5.50 μg/L =0, ≥ 5.50 μg/L =1
Efficacy	Y	Effective =0, ineffective =1

Notes: CTX-I, C-terminal telopeptide of type I collagen; BGP, osteocalcin (bone Gla protein).

Table 6. Multivariate analysis of factors influencing treatment efficacy in patients with osteoporosis secondary to severe fractures

Indicators	β	SE	Wald	P	Exp (β)	95% CI
Gender	-0.415	0.609	0.465	0.495	0.660	0.200-2.178
Smoking history	2.055	0.647	10.084	0.001	7.806	2.196-27.750
Alcohol abuse history	1.589	0.649	5.993	0.014	4.898	1.373-17.478
Treatment modality	1.486	0.630	5.563	0.018	4.420	1.286-15.196
CTX-I (ng/L)	1.057	0.633	2.789	0.095	2.876	0.832-9.939
BGP (μg/L)	-1.531	0.663	5.331	0.021	0.216	0.059-0.793

Notes: CTX-I, C-terminal telopeptide of type I collagen; BGP, osteocalcin (bone Gla protein).

Chailurkit LO et al. [19] revealed that alendronate sodium significantly decreased CTX-I and NTX-I levels in postmenopausal women with osteoporosis in Thailand, corroborating our findings. Yang Y et al. [20] also indicated that alendronate sodium could prominently up-regulate serum levels of alkaline phosphatase (ALP), 25-hydroxyvitamin D (25-OH-VD), and calcium, while decreasing bone resorption markers like CTX-I in postmenopausal women with osteoporosis, consistent with current study findings.

Additionally, patients receiving alendronate sodium showed significantly lower VAS scores across multiple pain dimensions, including spontaneous pain, pain during turning, weight-bearing, and flexion-extension, compared to those receiving conventional therapy. This evidence strongly suggests a alendronate sodium is highly effective in pain relief. Bai Z et al. [21] also found that a therapeutic regimen combining alendronate sodium, pamidronate disodium, and calcium significantly reduced pain levels in elderly patients with osteoporosis at both 6 and 12 months after treatment, further supporting our conclusions.

Alendronate sodium treatment also yielded a more remarkable elevation in BMD than con-

ventional therapy, indicating that alendronate sodium promotes bone mass gain possibly attributed to improved bone metabolism and pain relief. Adesina OO et al. [22] reported that alendronate sodium stabilized lumbar spine BMD in adult patients with sickle cell disease and osteoporosis over five years, with only mild adverse effects. Similarly, Wang KM et al. [23] found that the combined use of alendronate sodium and InterTan improved BMD, hip joint function, fracture healing, and reduced recurrence risk in patients with osteoporotic intertrochanteric fractures.

Moreover, the overall treatment efficacy in the alendronate sodium group was significantly higher compared to the conventional therapy group, suggesting that alendronate sodium can maximize therapeutic outcomes in patients with osteoporosis secondary to severe fractures possibly by stabilizing bone metabolism, alleviating pain, and increasing BMD, all of which contribute to the amelioration of disease-related symptoms, thereby facilitating the smooth recovery process of patients.

Univariate analysis identified gender, smoking history, alcohol abuse history, treatment modality, CTX-I, and BGP as factors significantly correlated with therapeutic efficacy. Binary

Logistic regression analysis further confirmed that a history of smoking, an alcohol abuse history, and conventional treatment approaches were independent risk factors for treatment failure, whereas elevated BGP served as a protective factor. Specifically, smoking adversely affects bone metabolism through multiple mechanisms. Nicotine and other noxious components in tobacco smoke can suppress osteoblast activity and enhance osteoclast activity, thereby impairing bone formation and promoting bone resorption. Such alterations in the bone-remodeling process can potentially undermine the effectiveness of alendronate sodium treatment. Alcohol abuse can impair liver function, disrupting vitamin D metabolism and calcium absorption, thereby compromising treatment efficacy of alendronate sodium. In contrast, elevated BGP reflects enhanced osteoblast activity and active bone formation, which is conducive to therapeutic efficacy and clinical improvement [24-26].

This study has several limitations that warrant attention in subsequent research. First, the absence of long-term follow-up data limits the assessment of sustained treatment effects. Future studies should incorporate extended follow-up periods to assess long-term therapeutic impact and prognosis. Second, fracture types were not stratified in the analysis. Given potential variations in treatment response across different fracture sites (e.g., vertebral, hip, or radial fractures), further subgroup analyses are needed to elucidate site-specific efficacy. Third, dynamic imaging assessments were not included. Incorporating longitudinal imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI) could facilitate quantitative monitoring of fracture healing and its correlation with BMD improvements. Addressing these limitations in future research will enhance the robustness and clinical relevance of the findings.

Conclusion

Alendronate sodium significantly improves bone metabolism, alleviates pain across diverse dimensions, and increases BMD in patients with osteoporosis secondary to severe fractures, thereby enhancing overall therapeutic efficacy. For patients with a history of smoking or alcohol abuse, those undergoing conven-

tional therapy, or those with low BGP levels, intensified clinical monitoring is recommended. Additionally, comprehensive rehabilitation and nursing interventions, including smoking and alcohol cessation guidance, and the promotion of healthy lifestyle habits, should be implemented to further optimize treatment outcomes.

Disclosure of conflict of interest

None.

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