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Original Research Article

Effect of anti-osteoporotic drugs in reducing risk of refracture after percutaneous vertebroplasty

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Abstract

Purpose: *To investigate the effectiveness of anti-osteoporotic drugs in lowering risk of refracture after percutaneous vertebroplasty.*
Methods: *The study involved 80 patients who underwent percutaneous vertebroplasty in The First Affiliated Hospital and College of Clinical Medicine of Henan University of Science and Technology, Luoyang, China between August 2020 and July 2022. The study group (n = 40) received postoperative rehabilitation in addition to anti-osteoporotic drugs for 6 months), while the control group (n = 40) received routine postoperative rehabilitation from the time of surgery completion to 3 months postoperative. Visual Analogue Scale (VAS) and Oswestry Disability Index (ODI) scores were compared before surgery, 3 days, 3 months, and 6 months postoperative. Changes in the middle height of the vertebral body and bone density T-score of the surgical and adjacent vertebrae before and at end of follow-up, and refracture rates were compared.*
Results: *The study group showed significantly lower VAS and ODI scores at 3 and 6 months after surgery compared to control group ($p < 0.05$). Both groups showed significant increase in vertebral body height before surgery ($p < 0.05$), with no significant difference at last follow-up ($p > 0.05$). Also, the study group showed significant increase in bone density in the surgical and adjacent vertebrae compared to control group at last follow-up ($p < 0.05$). Refracture rate was significantly lower in study group than in the control group ($p < 0.05$).*
Conclusion: *Administering anti-osteoporotic drugs after percutaneous vertebroplasty significantly alleviates pain, improves vertebral bone density, and reduces risk of refracture. However, a large-sample, multicenter, randomized prospective study to validate these findings is recommended.*

Keywords: *Anti-osteoporotic drugs, Percutaneous vertebroplasty, Pain, Bone density, Refracture rate*

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INTRODUCTION

Due to the continuous development of industrial construction and transportation projects in China, the likelihood of various types of spinal injuries has increased steadily among which thoracolumbar vertebral fractures are the most common, accounting for approximately 10 - 20 % of spinal traumas [1]. Studies have indicated that patients who have experienced spinal fractures often suffer from compromised spinal stability, resulting in a relatively elevated disability rate. As a result, surgical treatment is recommended to improve the stability of the fractured vertebral

bodies and restore living ability [2,3]. Common treatment modalities for patients with spinal fractures include percutaneous vertebroplasty (a technique to strengthen the vertebral body by injecting bone cement into the affected vertebral body) and balloon kyphoplasty (a procedure involving the insertion of an inflatable bone tamp into the vertebral body followed by injection of bone cement into the cavity, thereby restoring vertebral height and strength). These interventions improve recovery from pains while promoting restoration of vertebral height, enhancement of vertebral rigidity and strength, and restoration of spinal physiological curvature to improve quality of life [4,5]. However, with increasing adoption of procedures such as percutaneous vertebroplasty and balloon kyphoplasty, the shortcomings of these procedures have gradually come to the fore. For instance, some patients who have undergone percutaneous vertebroplasty have a high rate of secondary vertebral fractures during long-term follow-up, and most of them occur in the vertebrae adjacent to the injured vertebrae, which may be attributed to low bone density, cement leakage, and changes in vertebral height [6,7]. Wang *et al* [8] conducted a follow-up study of 183 patients with osteoporotic vertebral fractures and discovered that nearly 9.84 % of the patients experienced secondary vertebral fractures at 8-month follow-up. Li *et al* [5] also indicated through the establishment of nomogram, that patients suffering from osteoporotic vertebral compression fractures exhibit a heightened risk of developing new vertebral compression fractures and cement leakage following percutaneous vertebroplasty. Consequently, it becomes imperative to implement active follow-up interventions for such patients. Large-scale controlled clinical trials to reduce refracture rate in patients undergoing vertebroplasty are limited. Several studies have pointed out that osteoporosis may be associated with refracture after percutaneous vertebroplasty, and anti-osteoporotic drugs inhibit bone resorption and promote bone formation [6,8] which reduces refracture rate in patients undergoing percutaneous vertebroplasty. Therefore, this study was aimed at investigating the effect of anti-osteoporotic drugs in reducing risk of refracture after percutaneous vertebroplasty.

METHODS

Patients

A total of 80 patients who underwent percutaneous vertebroplasty in The First Affiliated Hospital and College of Clinical Medicine of Henan University of Science and Technology, New District Hospital, Luoyang, China from August 2020 to July 2022 were randomized equally (n = 40 each) into study and control groups. Study group received postoperative rehabilitation combined with anti-osteoporotic drugs, while control group received routine postoperative rehabilitation. This study was approved by the Ethics Committee of The First Affiliated Hospital and College of Clinical Medicine of Henan University of Science and Technology, New District Hospital (approval no. 2023 Review (049)) and conducted in accordance with the guidelines of Declaration of Helsinki [9].

Inclusion criteria

Patients diagnosed with spinal fracture by imaging test, had low back and lumbar pain, with the typical symptoms such as pressing pain and percussion pain at the fracture site on examination; examination showed intact posterior wall of the injured vertebrae, no neurological symptoms in the lower limbs, tolerance to undergo surgical treatment, complete data, and treated by percutaneous vertebroplasty in the hospital.

Exclusion criteria

Patients with other causes of low back pain, participation in other unfinished studies, coagulation disorders, allergies to surgical materials or bone cement, incomplete posterior vertebral wall or concomitant spinal stenosis, concomitant malignant tumors and psychiatric disorders, presence of communication disorders that may affect results of follow-up, concomitant spinal space occupying lesions; and patients whose imaging examinations showed old fractures.

Interventions

Enrolled patients all underwent percutaneous vertebroplasty. After lumbar medication administration, patients maintained a prone position. The C-shaped arm was used to confirm the surgical site which was marked before proceeding with the surgical intervention. Sterile dressings were applied after the procedure [8]. Control group underwent routine postoperative interventions, including close postoperative electrocardiogram monitoring, antibiotic treatment, wound drainage, limb movement, muscular tension check. Intervention measures continued till after discharge. Upon discharge, patients were advised to engage in joint and muscle training on a regular basis, such as

walking, lifting the lower limbs, and jogging, but were not treated with anti-osteoporotic drugs after discharge. In addition to the intervention measures administered to control group, study group was treated with anti-osteoporotic drugs which include; intranasal Calcitonin Salmon nasal spray (Novartis Pharma Schweiz AG, Switzerland; Specification: 2 mL/4400 IU; no. H20080148) at a dose of one spray once daily; Alendronate Sodium tablets (MSD Pharma (Singapore) Pte Ltd; Specification: 70 mg/tablet; no. J20130085) at 70 mg once weekly; Calcitriol Soft Capsules (Roche Pharma Ltd; specification: 0.25 μg/capsule; no. J20100056, Basel, Switzerland) at 0.25 μg, once daily; Calcium Carbonate and Vitamin D3 Granules (Beijing Kangyuan Pharmaceutical Co. Ltd; Specification: 0.5 g/sachet; no. H20090334, Beijing, China) at 0.5 g sachet twice daily for 6 months.

Evaluation of parameters/indices

Pain intensity and joint function

Differences in visual analogue scale [10] (VAS) and Oswestry Disability index [11] (ODI) scores were compared between the two groups preoperative, 3 days, 3 months and 6 months postoperative. For the VAS score, a 0-10 cm straight line was employed to denote pain intensity, with 0 signifying absence of pain and 10 signifying severe pain. Based on personal pain levels, a specific point on this scale was selected to represent pain intensity. The ODI rating was employed to evaluate daily functional activities and activity-related disorders. This scale comprised 10 items, each offering 6 options, corresponding to a scale of 0-5 points. The total score is computed as the sum of individual item scores, divided by 50.

Postoperative follow-up of vertebral height and bone density

Difference in middle height of vertebral body was compared between the two groups preoperative and 6 months postoperative. Bone density of the surgical and adjacent vertebrae were compared between the two groups preoperatively and 6 months postoperative. Bone density measurements were performed using a QDR4500 dual-energy X-ray bone densitometer [4].

Postoperative follow-up of refracture rate

A follow-up was conducted 6 months after surgery to analyze and compare differences in refracture rates between the two groups.

Statistical analysis

Data were analyzed using Statistical Package for Social Science (SPSS) 18.0 (IBM, Armonk, NY, USA). Student t-test was adopted to compare differences in VAS scores, ODI scores, bone density, and middle height of vertebral body between the two groups. Additionally, chi-squared test was employed to compare refracture rates in both groups. $P < 0.05$ was considered statistically significant.

RESULTS

Baseline data

There was no significant difference in baseline data (gender, age, weight, body mass index (BMI), cause of injury, fracture segment, operative time, intraoperative bleeding) between study and control groups ($p > 0.05$; Table 1).

Table 1: Baseline clinical data (N, %, mean ± SD); n = 40

General data		Study	Control	t/X^2	P-value
Gender	Male	19(47.50)	20(50.00)	0.005	0.945
	Female	21(52.50)	20(50.00)		
Average age (years)		51.11±3.28	51.21±3.34	0.106	0.781
Average body weight (kg)		65.18±3.91	65.31±3.77	0.119	0.780
Average BMI (kg/m^2)		22.19±2.19	21.98±2.28	0.331	0.724
Cause of injury	Traffic accident	15(37.50)	14(35.00)	0.889	0.231
	Injury due to fall from height	14(35.00)	13(32.50)		
	Injuries from heavy objects	7(17.50)	10(25.00)		
	Fall-related injury	4(10.00)	3(7.50)		
Fracture segment	T11	8(20.00)	7(17.50)	0.891	0.221
	T12	9(22.50)	8(20.00)		
	L1	7(17.50)	10(25.00)		
	L2	10(25.00)	10(25.00)		
	L3	6(15.00)	5(12.50)		
Operative time (min)		30.20±5.16	29.65±5.81	0.448	0.656
Intraoperative bleeding (mL)		10.63±3.56	11.02±2.98	0.523	0.602

Pain intensity

There was no statistically significant difference in preoperative and 3 days postoperative VAS scores between the two groups ($p > 0.05$). At 3 and 6 months postoperative, study group (SG) exhibited significantly lower VAS scores compared to control group (CG) ($p < 0.05$; Figure 1).

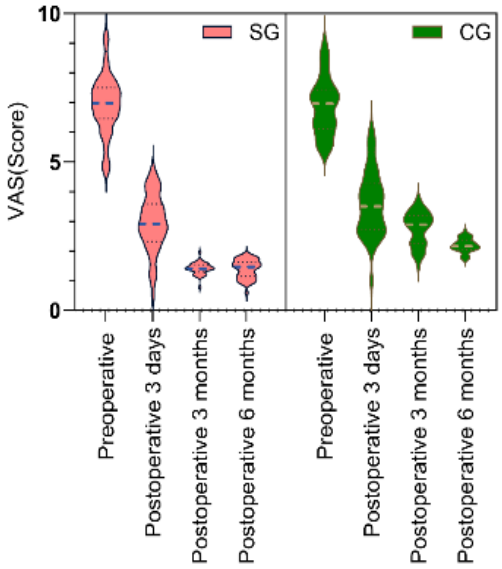

Figure 1: Preoperative and postoperative pain intensity**.** At 3 months and 6 months postoperative, study group (SG) showed significantly lower VAS scores compared to the control group (CG; $p < 0.05$)

Oswestry disability index (ODI) scores

There was no significant difference in preoperative and 3 days postoperative ODI scores between the two groups ($p > 0.05$). At 3 and 6 months postoperative, study group (SG) showed significantly lower ODI scores compared to control group (CG; $p < 0.05$; Figure 2).

Middle height of vertebral body

There was no significant difference in preoperative middle height of vertebral body between the two groups ($p > 0.05$). At the end of follow-up, there was a significant increase in middle height of vertebral body compared to preoperative period ($p < 0.05$). Also, there was no significant difference in middle height of vertebral body between study and control groups 6 months postoperative ($p > 0.05$; Figure 3).

Bone density of the surgical and adjacent vertebrae

There was no significant difference in preoperative bone density of the surgical and adjacent vertebrae between the two groups ($p > 0.05$; Figure 4 A, 5 A). However, 6 months postoperative, study group (SG) showed significant increase in bone density of the surgical and adjacent vertebrae compared to control group (CG) (Figure 4 B, 5 B) ($p < 0.05$; Figure 4 and Figure 5).

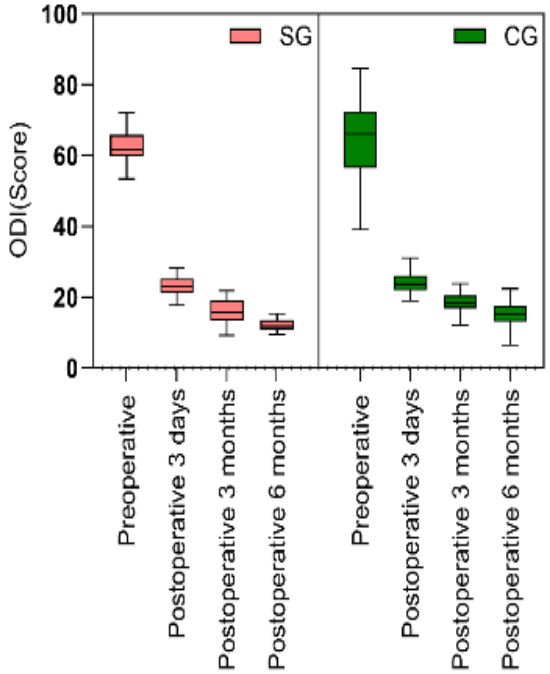

Figure 2: Preoperative and postoperative ODI scores. At 3 and 6 months postoperative, study group (SG) showed significantly lower ODI scores compared to control group (CG; $p < 0.05$)

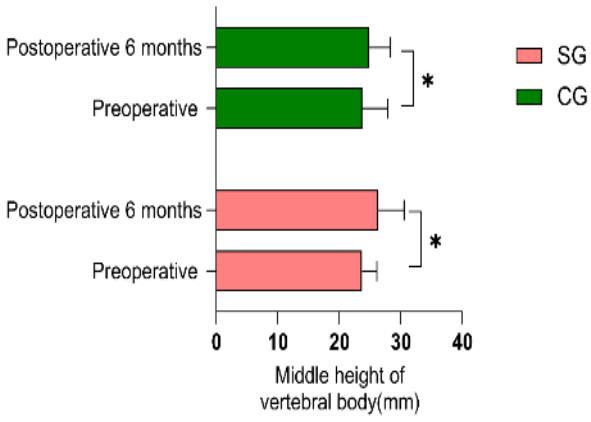

Figure 3: Preoperative and postoperative middle height of vertebral body. At 6 months postoperative, both groups exhibited significant increase in middle height of vertebral body compared to the preoperative period (*$p < 0.05$)

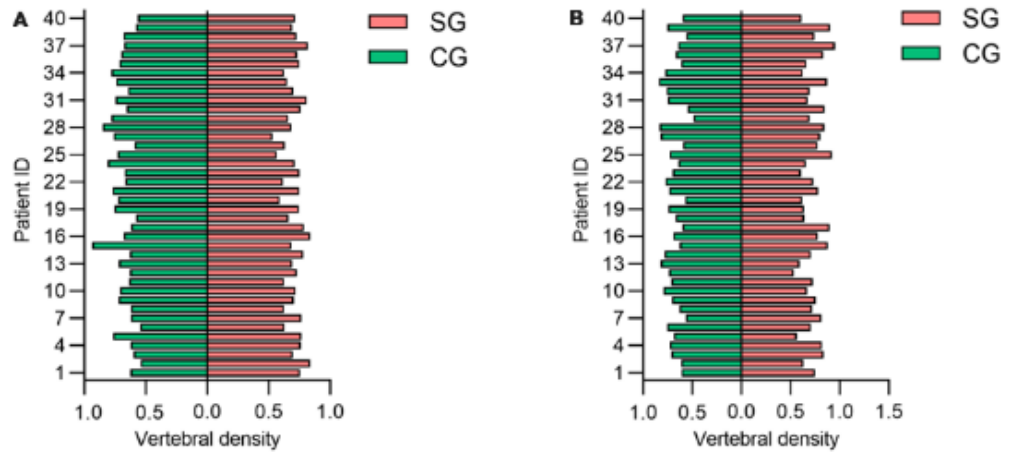

Figure 4: Preoperative and postoperative bone density of the surgical vertebrae

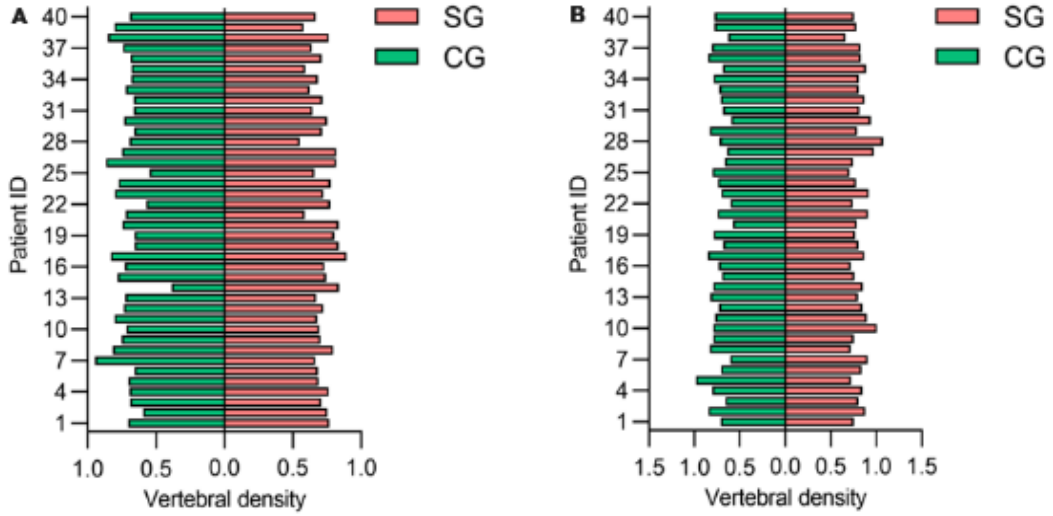

Figure 5: Preoperative and postoperative bone density of the surgical adjacent vertebrae

There was no significant difference in bone density of the surgical vertebrae between the groups ($p > 0.05$; Figure 4 A). Study group showed significantly higher bone density of the surgical vertebrae compared to control group ($p < 0.05$) (Figure 4 B).

There was no significant difference in preoperative bone density of the surgical adjacent vertebrae between the groups ($p > 0.05$; Figure 5 A). Study group showed significantly higher bone density of the surgical adjacent vertebrae compared to control group 6 months postoperative ($p < 0.05$; Figure 5 B).

Refracture rate

Study group showed significantly lower refracture rate 6 months postoperative compared to control group ($p < 0.05$) (Figure 6).

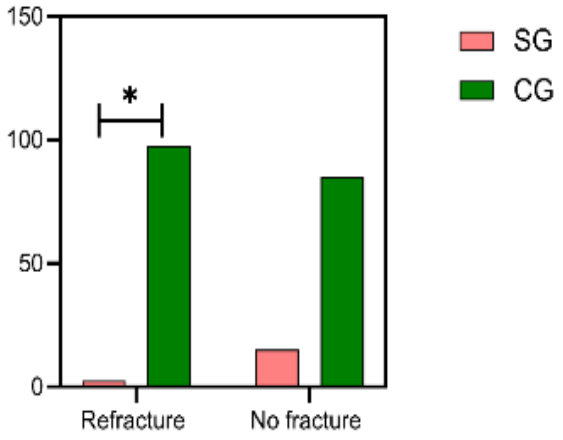

Figure 6: Refracture rates at postoperative follow-up. Study group showed significantly lower refracture rate (2.50 %) compared to control group (15.00 %; *$p < 0.05$)

DISCUSSION

In recent years, incidence of spinal fractures has persistently increase high. This may be attributed to a multitude of factors, including advancements in transportation and construction industry, as well as the evident trend towards an aging population. Spinal fractures significantly affect normal life and, in severe cases, may lead to disability. Therefore, it is imperative to proactively pursue surgical intervention for affected individuals [12,13]. Percutaneous vertebroplasty is certainly valuable in improving pain in patients with spinal fractures. However, follow-up has shown that even patients with spinal fractures who receive active surgical treatment continue to experience refractures, stiffness, and weakness of the back during long-term follow-up [14].

A study involving 200 cases of osteoporotic thoracolumbar vertebral fractures treated with percutaneous vertebroplasty revealed that over a 2- to 3-year follow-up period, 28 % (56/200) experienced postoperative adjacent vertebral refractures, and a significant association between patient age, bone density, vertebral height restoration, and bone cement leakage [15]. Keaveny *et al* [16] have pointed out that biomechanical computed tomography analysis indicates a higher likelihood of refractures within five years postoperative for patients with osteoporotic spinal fractures (11.1 %). While these studies revealed a high rate of postoperative refracture, none of them provided clarity on how to reduce refracture rate in patients with spinal fractures.

This study investigated the effect of anti-osteoporotic drugs in preventing refracture in patients undergoing percutaneous vertebroplasty. The results revealed that the study group showed significantly lower postoperative VAS scores at 3 and 6 months compared to control group. Pain is a common postoperative complication in patients undergoing percutaneous vertebroplasty, which may be due to nociceptive sensitivity of nerve endings in the vertebral body leading to higher pain perception, vertebral fracture which stimulates peripheral nerve roots, prolonged tensing around muscles of the injured vertebrae leading to muscle spasms, influence of gravity which causes compression of the injured vertebra, and the unstable injured vertebrae (even after reconstruction), causing neuromuscular damage [3,17]. Pain affects normal life and causes limited limb movement and intractable low back pain, thus necessitating the implementation of active interventions [18,19]. Alendronate sodium tablets administered to study group inhibits osteoclast activity, decreases bone conversion, and inhibits bone resorption, ultimately improving bone pain, while calcitonin is effective in inhibiting secretion of prostaglandins, thus regulating pain sensation of the central nervous system, which also reduce pain intensity [8].

The findings in this study showed that postoperative ODI scores were significantly lower in study group compared to control group which suggested that patients in the study group had milder postoperative articular dyskinesia. Percutaneous vertebroplasty is mainly used to correct spinal deformity by injecting bone cement into the injured vertebrae to restore height of the injured vertebrae as much as possible [20,21]. This helps to improve symptoms of spinal dysfunction, but there is also the problem of cement leakage, leading to height loss of the injured vertebrae ultimately affecting postoperative recovery.

In this study, calcitonin was administered to slow down bone resorption by inhibiting osteoclasts, promoting uptake of blood calcium by the bone, and osteogenesis, thereby serving as an effective means of calcium retention. This is a major contributory factor in increasing bone density of the injured vertebrae and adjacent vertebrae during follow-up compared to control group [22]. Meanwhile, calcitriol facilitates calcium absorption in the intestinal tract, augments muscular strength, and improves coordination of neuromuscular functions thereby reducing incidence of postoperative fall [23].

Furthermore, this study revealed that study group showed lower refracture rate at follow-up compared to control group. This suggests that proactive anti-osteoporotic drug therapy reduces postoperative refracture rates. This is due to enhanced bone density, effectively delaying progression of osteoporosis, and reducing incidence of fractures [24]. Also, medicinal intervention improves the muscular-neurological coordination of patients, reducing fall incidence and refractures due to hazardous activities [25]. Furthermore, pain intensity is reduced, enhancing compliance to rehabilitation exercises. This is also a significant factor in improving physical activity and reducing fracture rates.

Limitations of this study

This study has some limitations which include the small sample size and single-center approach which may have exerted certain influence on the findings.

CONCLUSION

Postoperative application of anti-osteoporotic drugs ameliorates pain, enhances vertebral bone density, and reduces refracture rate. There is a need for a large-sample, multicenter, randomized prospective study to validate these findings.

DECLARATIONS

Acknowledgement

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Funding

None provided.

Ethical approval

This study was approved by the Ethics Committee of The First Affiliated Hospital and College of Clinical Medicine of Henan University of Science and Technology, New District Hospital, China (049).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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