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Original Research Article

Effect of total hip arthroplasty combined with alendronate sodium for the treatment of geriatric patients with femoral neck fracture

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Abstract

Purpose: *To study the effect of total hip arthroplasty (THA) combined with alendronate sodium for the treatment of geriatric patients with femoral neck fracture (FNF).*
Methods: *A retrospective analysis was conducted on 100 geriatric patients with FNF treated at Heilongjiang Provincial Hospital, Harbin, China from August 2020 to August 2022. The patients were divided into control (n = 45) and study groups (n = 55). Control group received THA, while the study group received THA plus oral alendronate sodium (10 mg daily for three months). Bone mineral density (BMD), tartrate-resistant acid phosphatase (TRAP), serum osteosclerosis (SOST) and insulin-like growth factor 1 (IGF-1) levels were compared between groups before and 3 months after treatment.*
Results: *Study group exhibited significantly higher total effective rate compared to control group ($p < 0.05$). After treatment, the study group exhibited significantly increased BMD and IGF-1 levels and decreased SOST and TRAP levels compared to control group ($p < 0.05$). Both groups showed significant changes in SOST and IGF-1 levels, with a decrease in SOST and an increase in IGF-1 ($p < 0.05$). Furthermore, the study group demonstrated significant increase in BMD but a decrease in TRAP level after treatment ($p < 0.05$).*
Conclusion: *The combination of THA and alendronate sodium significantly enhances BMD and promotes healing in geriatric patients with FNF. Additional studies should address the challenge of small sample size to improve reliability and generalizability of these findings.*

Keywords: *Total hip arthroplasty, Alendronate sodium, Femoral neck fracture, Efficacy*

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INTRODUCTION

A femoral neck fracture (FNF) is a common fracture type, predominantly affecting middle-aged and elderly individuals especially those with osteoporosis. Osteoporosis, a condition marked by reduced bone density and increased fracture susceptibility, significantly contributes to the risk of FNF. While FNFs constitute only 3 % of all fractures, they account for over 40 % of all hip fractures [1]. Annually, approximately 1.6 million individuals worldwide experience hip fractures annually, with over 800,000 cases in the U.S. among those aged 65 or older, indicating an age-related increase in incidence [2]. In China, hip fracture incidence has declined in those aged 65

and above, but it remained stable in younger groups, with a fourfold rise in total hip fractures among those aged 55 and above [3].

At present, FNFs are treated either conservatively or surgically. Total hip arthroplasty (THA), is a commonly performed surgical procedure for severe hip injuries, including FNF. However, its efficacy may be compromised in osteoporotic geriatric patients due to weakened bone structure. Alendronate sodium binds to bone inhibits bone resorption and stimulates new bone formation, thus ameliorating osteoporosis symptoms and reducing fracture risks [4]. Therefore, this study was aimed at investigating the effectiveness of combining THA and alendronate sodium for treating FNF in geriatric patients to provide relevant treatment information.

METHODS

Patient data

A retrospective analysis was conducted on 100 geriatric patients with FNF treated at Heilongjiang Provincial Hospital, Harbin, China from August 2020 to August 2022. Patients were divided into control (n = 45) and study groups (n = 55). Control group received THA, while the study group received THA plus oral alendronate sodium (10 mg daily for three months). Ethical approval was obtained from the Medical Ethics Committee of Heilongjiang Provincial Hospital (approval no. SYYLLBA202377) and conducted in accordance with the guidelines of Helsinki Declaration [5].

Inclusion criteria

Patients diagnosed with FNF using imaging techniques [6], 55 years or older, patients with a clear history of trauma suitable for THA and willing to undergo surgery as well as detailed medical records.

Exclusion criteria

Patients with pathological fractures or non-FNF types, osteoarthritis, contraindications for surgery, drug allergies relevant to this study, bone metabolism affecting medication use within 6 months, poor treatment compliance, significant cardiac, hepatic, or renal impairments, and psychiatric disorders.

Therapeutic protocols

In both groups, patients underwent THA after preoperative examination. Under general anesthesia, the patients were positioned laterally. The modified Hardinge approach was employed to expose the femoral neck [7]. The surgical procedure involved sequential incision through tissue layers, removal of the femoral head, and femoral neck truncation 1.5 cm above the head to expose the acetabulum [8].

After acetabular exposure and osteophyte removal, the true acetabular margin was identified. Acetabular reaming and polishing were followed by the selection and fitting of the acetabular prosthesis and metal cup to the correct angle. The metal socket cup was implanted, and the femoral stem was prepared and inserted after reaming. Post-implantation, hip joint reduction was checked for stability and range of motion. The surgical site was then irrigated, a drainage tube inserted, and the incision closed in layers. Postoperative management included antibiotics for 24 h and analgesics for three days [9]. After surgery, control group received calcium carbonate and vitamin D3 (600 mg/tablet, Wyeth Pharmaceutical Co., LTD., SFDA approval no. H10950029) plus calcium twice daily for 3 months.

Study group received alendronate sodium (10 mg/tablet, Shijiazhuang Pharma Group Ouyi Pharmaceutical Co., Ltd., SFDA approval no. H10980109) once daily for 3 months in addition to the regimen of the control group.

Evaluation of parameters/indices

Bone mineral density and tartrate-resistant acid phosphatase

Blood samples (5 mL) were collected from fasting participants before treatment and three months after treatment, centrifuged at 3500 rpm for 10 min, and the supernatant was stored in a refrigerator for analysis. Bone mineral density (BMD) of the femur and tartrate-resistant acid phosphatase (TRAP) levels were measured by a CM-200 bone density meter (Furuno) and an Infinete M200 multifunctional enzyme marker (TECAN) [10]. Changes in BMD and TRAP levels were compared between study and control groups before and after treatment.

Serum osteosclerosis and Immunoglobulin levels

Serum osteosclerosis (SOST) levels were determined by an immunomagnetic bead flow cytometry assay [11] while insulin-like growth factor 1 (IGF-1) levels were determined using enzyme-linked immunosorbent assay [12]. The

SOST and IGF-1 levels were compared between study and control groups before and after three months of treatment using data from the biomarker analysis. Adverse effects and complications after treatment were monitored and compared between the groups.

Harris hip score

After 3 months of treatment, patient outcomes were assessed using the Harris hip score focusing on joint motion, function, and pain. Scores were classified as follows excellent (≥ 90), good (80 – 89), fair (70 – 79), and poor (≤ 70) [13]. Total effective rate (TR) was calculated using Eq 1.

$$TR = \{(ME+E)/N)\}100 \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Where ME is markedly effective, E is effective and N is total number of cases.

Statistical analysis

Data were visualized using GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA) and analyzed with SPSS 20.0 (SPSS Inc., Chicago, IL, USA). Categorical data were presented as percentages (%) and analyzed using chi-squared test (χ^2). Continuous data following normal distribution were examined using t-test. Paired t-test was used to compare differences within a group, while inter-group differences were compared using independent sample t-tests. $P < 0.05$ was considered statistically significant.

RESULTS

Baseline data

There was no significant difference in gender, fracture site, age, Garden's classification, nation, body mass index and place of residence between the two groups ($p > 0.05$; Table 1).

Efficacy

Study group demonstrated a significantly higher total efficacy rate compared to control group ($p < 0.05$; Table 2).

SOST and IGF-1 levels

Before treatment, there was no significant difference in SOST and IGF-1 levels in both groups ($p > 0.05$). However, after treatment, study group showed a significant decrease in SOST and an increase in IGF-1 levels compared to control group ($p < 0.05$). Both groups experienced a significant decrease in SOST and an increase in IGF-1 levels after treatment ($p < 0.05$; Figure 1).

Table 1: Comparison of baseline data

Parameter	Property	Control (n = 45)	Study (n = 55)	χ^2	*P*-value
Age (years)	≤65	26	22		
	>65	19	33	3.134	0.077
Gender	Male	19	25		
	Female	26	30	0.105	0.746
body mass index (kg/m^2)	≤21	20	24		
	>21	25	31	0.007	0.936
Fracture site	Left hip	18	24		
	Right hip	27	31	0.134	0.714
Garden's classification	Type III	29	34		
	Type IV	16	21	0.073	0.787
Nation	Han	34	43		
	Minority nationality	11	12	0.964	0.756
Place of residence	City	28	33		
	Rural	17	22	0.051	0.821

Table 2: Comparison of efficacy

Group	Excellent	Good	Fair	Poor	Total effective rate
Control (n = 45)	6(13.33)	23(51.11)	10(22.22)	6(13.33)	29(64.44)
Study (n = 55)	12(21.82)	37(67.27)	6(10.91)	0	49(89.09)
χ^2					8.761
P-value					0.003

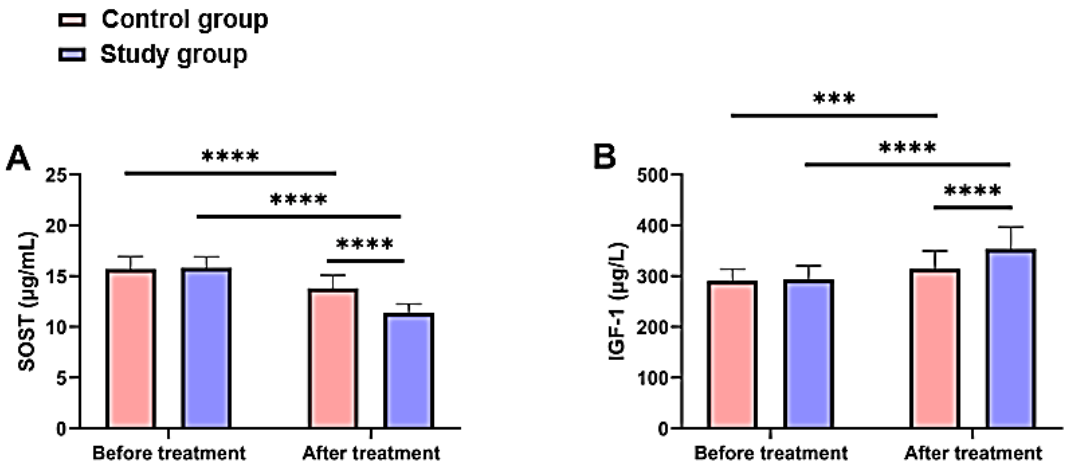

Figure 1: SOST and IGF-1 levels. (A) Changes in SOST level (B) Changes in serum IGF-1 level. ***P < 0.001, ****p < 0.0001. ***Key:*** SOST (osteosclerosis), IGF-1 (insulin-like growth factor 1)

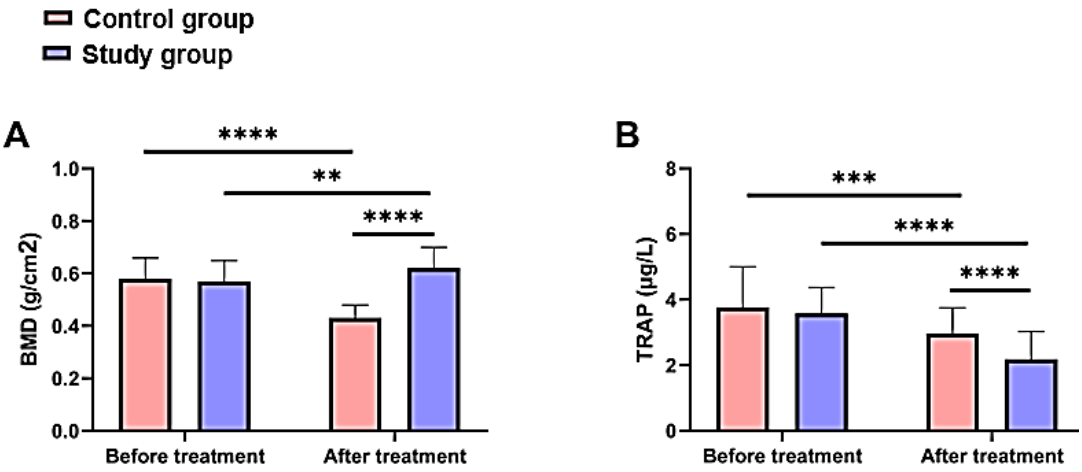

Figure 2: Serum BMD and TRAP levels. (A) Changes in BMD level (B) Changes in TRAP level. **P < 0.01, ***p < 0.001, ****p < 0.0001. ***Key:*** BMD (Bone mineral density), TRAP (tartrate-resistant acid phosphatase)

Serum BMD and TRAP levels

Before treatment, BMD and serum TRAP levels did not differ significantly between groups (p > 0.05). After treatment, study group displayed significant increase in BMD and decrease in TRAP levels compared to control group (p < 0.05). Intra-group analysis revealed significant BMD increase in study group and decrease in control group while TRAP levels decreased significantly in both groups after treatment (p < 0.05; Figure 2).

Incidence of adverse effects and complications

Adverse effects occurred in 4.44 % of control group and 7.27 % of study group (Table 3) while complications were reported for 11.11 % in control group and 3.64 % in study group (Table 4). These differences were not statistically significant (p > 0.05).

Table 3: Incidence of adverse effects

Group	Fever	Nausea	Gastrointestinal reaction	Rash	Total adverse events
Control (n = 45)	0	1(2.22)	1(2.22)	0	2(4.44)
Study (n = 55)	0	1(1.82)	2(3.64)	0	4(7.27)
χ^2					0.351
P-value					0.554

Table 4: Comparison of complications

Group	Displacement of fracture	Prosthesis loosening	Lower extremity deep vein thrombosis	Prosthesis dislocation	Total incidence rate
Control (n=45)	1(2.22)	2(4.44)	0	2(4.44)	5(11.11)
Study (n=55)	0	1(1.82)	0	1(1.82)	2(3.64)
χ^2					2.124
P-value					0.145

DISCUSSION

Osteoporosis, characterized by low bone mass and compromised microstructure of bone tissue, significantly increases bone fragility and fracture risk, particularly in geriatric individuals, impacting quality of life [14]. Femoral neck fractures (FNF), common in osteoporotic patients, are prone to occur due to weakened structures of the bone, leading to severe pain and mobility restrictions [15]. Such fractures result in complications like pressure ulcers, nonunion, avascular necrosis, urinary infections, malunion, pulmonary embolism, joint stiffness, deep vein thrombosis, and muscle weakness. Therefore, prevention and early treatment of FNF are crucial. Total hip arthroplasty (THA) is a commonly used surgical method that replaces a damaged or fractured hip with an artificial joint, often made of metal and plastic, to restore function and relieve pain [16].

Evidence supports the efficacy of THA in alleviating symptoms and enhancing limb function in patients with traumatic arthritis post-acetabular fracture [17]. However, THA involves risks like post-operative infections, thrombosis, osteolysis, aseptic prosthesis loosening, and peri-prosthetic fractures. Alendronate sodium, a bisphosphonate, mitigates bone loss and enhances BMD, potentially improving treatment success and effectiveness [18]. In this study, the results revealed a superior total effective rate in study group compared to control group. As a result, the treatment combination improves joint motion, function, and pain reduction. Other studies also revealed that THA with alendronate sodium expedited fracture healing, promoted bone restoration, and improved outcomes and life quality, consistent with our findings [19].

Serum osteosclerosis is a key bone cell-produced protein regulating bone metabolism [20]. Insulin-like growth factor 1 (IGF-1), produced by the liver and other tissues, promotes bone cell proliferation, differentiation and bone formation [21]. After treatment, the study group exhibited significantly lower SOST and higher IGF-1 levels compared to control group. These alterations suggest that combined treatment markedly improves SOST and IGF-1 levels in FNF patients. Reduced SOST overexpression enhances BMD and fracture resistance, while elevated IGF-1 aids bone matrix synthesis and mineralization, promoting bone growth and repair. These outcomes are consistent with the findings of Wan *et al* [22].

Bone mineral density (BMD) is an important indicator for assessing bone health and fracture risks [23]. Tartrate-resistant acid phosphatase (TRAP) is primarily found in macrophages and osteoclasts, playing a key role in bone resorption [24]. In this study, BMD was significantly higher and TRAP levels were lower in study group compared to control group after treatment. These results suggest that combination therapy effectively enhances BMD and lowers serum TRAP levels. The observed reduction in BMD in control group may result from surgical tissue damage and post-operative activity limitations. Hence, combining alendronate sodium with THA reduces BMD loss, and improves treatment success and outcomes of THA. Correspondingly, Wang et al [25] reported that combining alendronate sodium with InterTan for osteoporotic intertrochanteric femoral fractures increased BMD, promoted healing, and decreased fracture recurrence risk which is consistent with the findings of this present study. The study concluded with an analysis of adverse effects and complications, revealing no significant differences between the groups. This suggests that combining THA with alendronate sodium effectively heals fractures and restores hip function without increasing the incidence of adverse effects corroborating earlier findings of Axelsson *et al* [26].

Limitations of this study

The retrospective design and small sample size may introduce bias, affecting the results' validity. Additionally, the absence of long-term follow-up prevented the evaluation of sustained efficacy and patient prognosis.

CONCLUSION

The combination of THA with alendronate sodium offers an effective and safe treatment for

FNF, significantly enhancing (BMD) and facilitating fracture healing. Given its efficacy and safety, further studies should aim to address the limitations of small sample size to improve the reliability and generalizability of the results.

DECLARATIONS

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Ethical approval

Ethical approval was obtained from the Medical Ethics Committee of Heilongjiang Provincial Hospital (approval no. SYYLLBA202377).

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

We 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 the authors. Xuezhao Li and Fangqiu Tian conceived and designed the study, and drafted the manuscript. Xuezhao Li, Ming Fu, Xiang Liu, Zhiyin E and Cong Wang collected, analyzed and interpreted the experimental data. Ming Fu and Fangqiu Tian revised the manuscript for important intellectual content. All authors read and approved the final manuscript for publication.

REFERENCES

1. *Ren W, Wu R. Effect of general and sub-arachnoid anesthesia on the incidence of postoperative delirium and cognitive impairments in elderly Chinese patients. Trop J Pharm Res 2021; 20: 433-439.*
2. *Dou C, Li T, Yang S, Geng Q, Lu Q, Zhang Y, Yu J, Hu F, Ding J. Epidemiological status and risk factors of deep vein thrombosis in patients with femoral neck fracture. J Orthop Surg Res 2022; 17: 41.*
3. *Akcal MA, Eke I, Mutlu T. Femoral neck fractures in elderly patients with coxarthrosis and high dislocation: The application of conservative treatment. Cureus 2023; 15: e35805.*
4. *Abu-Dief AM, Salaheldeen M, El-Dabea T. Recent advances in development of gold nanoparticles for drug delivery systems. J Mod Nanotechnol 2021; 1(1): 1-14*
5. *World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013; 310: 2191-2194.*
6. *Florschutz AV, Langford JR, Haidukewych GJ, Koval KJ. Femoral neck fractures: current management. J Orthop Trauma 2015; 29: 121-129.*
7. *Petis S, Howard JL, Lanting BL, Vasarhelyi EM. Surgical approach in primary total hip arthroplasty: anatomy, technique and clinical outcomes. Can J Surg 2015; 58: 128-139.*
8. *Obada B, Iliescu DM, Popescu IA, Petcu LC, Iliescu MG, Georgeanu VA. Clinical outcomes of modified direct lateral approach of Hardinge for total hip arthroplasty. Acta Orthop Belg 2023; 89: 625-633.*
9. *Ahmed HE, Al-Dadah O. Total Hip Arthroplasty in fracture neck of femur: A review of the literature. Acta Orthop Belg 2023; 89: 29-36.*
10. *An J, Briggs TA, Dumax-Vorzet A, Alarcon-Riquelme ME, Belot A, Beresford M, Bruce IN, Carvalho C, Chaperot L, Frostegard J, et al. Tartrate-resistant acid phosphatase deficiency in the predisposition to systemic lupus erythematosus. Arthritis Rheumatol 2017; 69: 131-142.*
11. *Guanabens N, Mumm S, Gifre L, Ruiz-Gaspa S, Demertzis JL, Stolina M, Novack DV, Whyte MP. Idiopathic acquired osteosclerosis in a middle-aged woman with systemic lupus erythematosus. J Bone Miner Res 2016; 31: 1774-1782.*
12. *Bailes J, Soloviev M. Insulin-like growth factor-1 (IGF-1) and its monitoring in medical diagnostic and sports. Biomolecules 2021; 11(2): 217*
13. *Lara-Taranchenko Y, Pujol O, Gonzalez-Morgado D, Hernandez A, Barro V, Soza D. Validation of the Spanish version of the modified Harris score. Rev Esp Cir Ortop Traumatol 2023; 68(2): 121-127*
14. *Ensrud KE, Crandall CJ. Osteoporosis. Ann Intern Med 2017; 167: ITC17-ITC32.*

15. Asadipooya K, Graves L, Greene LW. Transient osteoporosis of the hip: Review of the literature. Osteoporos Int 2017; 28: 1805-1816.
16. Meermans G, Konan S, Das R, Volpin A, Haddad FS. The direct anterior approach in total hip arthroplasty: A systematic review of the literature. Bone Joint J 2017; 99-B: 732-740.
17. Stibolt RD Jr., Patel HA, Huntley SR, Lehtonen EJ, Shah AB, Naranje SM. Total hip arthroplasty for posttraumatic osteoarthritis following acetabular fracture: A systematic review of characteristics, outcomes, and complications. Chin J Traumatol 2018; 21: 176-181.
18. Rancic N, Simic VD. Therapeutic drug monitoring: Is there anything new? J Mod Pharmacol Pathol, 2023; 1: 1.
19. Ouyang X, Ding Y, Yu L, Xin F, Yang X, Sha P, Tong S, Cheng Q, Xu YQ. Effects of hip replacement combined with alendronate sodium on postoperative healing of osteoporotic femoral neck fracture and levels of CTX-1 and BALP in patients. Exp Ther Med 2019; 18: 4583-4590.
20. Xie Y, Zhao N, Shen G. Anti-resorptive effects of cementocytes during orthodontic tooth movement. Trop J Pharm Res 2018; 17: 2291-2298.
21. Yan J, Herzog JW, Tsang K, Brennan CA, Bower MA, Garrett WS, Sartor BR, Aliprantis AO, Charles JF. Gut microbiota induce IGF-1 and promote bone formation and growth. Proc Natl Acad Sci USA 2016; 113: E7554-E7563.
22. Wan JM, Zhang JF, Huang K, Zhang PL, Zhu SY. Comparison of the clinical effects between Dihuang Decoction and alendronate sodium in the treatment of primary osteoporosis. Zhongguo Gu Shang 2019; 32: 535-538.
23. Bellver M, Del Rio L, Jovell E, Drobnic F, Trilla A. Bone mineral density and bone mineral content among female elite athletes. Bone 2019; 127: 393-400.
24. Nakamura M, Aoyama N, Yamaguchi S, Sasano Y. Expression of tartrate-resistant acid phosphatase and cathepsin K during osteoclast differentiation in developing mouse mandibles. Biomed Res 2021; 42: 13-21.
25. Wang KM, Wei SP, Yin XY, Meng QJ, Kong YM. Effects of alendronate sodium combined with InterTan on osteoporotic femoral intertrochanteric fractures and fracture recurrence. World J Clin Cases 2022; 10: 7324-7332.
26. Axelsson KF, Wallander M, Johansson H, Lundh D, Lorentzon M. Hip fracture risk and safety with alendronate treatment in the oldest-old. J Intern Med 2017; 282: 546-559.