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ORIGINAL RESEARCH

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Clinical effectiveness of calcitriol and calcium gluconate in treating older male patients with osteoporosis

Jinchun Zhang[1], Zhihua Li[2,*], Lin Shen[3], Xilin Zhou[2]

[1]Department of Internal Medicine-Cardiovascular, Chongming Hospital affiliated to shanghai University of Medicine and Health Sciences, 202150 Shanghai, China
[2]Department of Geriatrics, Chongming Hospital affiliated to shanghai University of Medicine and Health Sciences, 202150 Shanghai, China
[3]Outpatient Convenience Service Center, Chongming Hospital affiliated to shanghai University of Medicine and Health Sciences, 202150 Shanghai, China

***Correspondence**
zh_li009@163.com
(Zhihua Li)

Abstract

Clinical studies on calcitriol in osteoporosis (OP) have been mostly conducted in postmenopausal women, with limited research reported in elderly male patients. In this study, we investigated the effects of combining calcitriol with calcium gluconate for treating OP in elderly men and compared it with calcium gluconate monotherapy to provide insights into the clinical treatment options for OP. A total of 86 elderly male OP patients were included in this study and randomly assigned to control or observation groups in a 1:1 ratio. The control group was given oral calcium gluconate (1.0 g, three times daily), while the observation group was given oral calcitriol capsule (0.25 μg twice daily) and oral calcium gluconate (1.0 g three times daily). The results indicated that treatment with single calcium gluconate for 6 months had minimal impact on the bone mineral density (BMD) of the lumbar spine, total hip and femoral neck, and balance function. In contrast, the combination of calcium gluconate and calcitriol significantly increased BMD and improved patients' balance function. Both single calcium gluconate treatment and the combination of calcium gluconate and calcitriol affected various bone metabolism and turnover markers to varying degrees, including a decrease in the level of tartrate-resistant acid phosphatase-5b (TRAP-5b) and an increase in the levels of osteocalcin and calcium. Both calcium gluconate and calcitriol affect patients' bone metabolism and turnover markers to varying degrees. Importantly, the combination of calcium gluconate and calcitriol had a significant effect on these markers compared to calcium gluconate monotherapy, and no significant difference in the incidence of adverse reactions was observed between the two groups during treatment. Calcium gluconate in combination with calcitriol in elderly male patients with OP may increase bone mineral density, improve bone metabolism, enhance bone turnover and maintain a high safety profile.

Keywords

Calcium gluconate; Calcitriol; Older men; Osteoporosis; Bone density

1. Introduction

Osteoporosis (OP) is a prevalent metabolic bone disorder characterized by decreased bone mass and density [1]. It is initially asymptomatic, but as it progresses, it is characterized by symptoms such as joint and bone weakness and pain, leading to a decline in bone density, which can result in spinal curvature, thoracic deformities and even fractures following minor traumas or routine activities. As the aging population increases, these fractures contribute significantly to elevated mortality and disability rates among the elderly, negatively impacting their quality of life and imposing substantial financial burdens on families and society [2, 3]. Therefore, enhancing bone density in the elderly, along with improving neuromuscular coordination, balance and fall prevention strategies, remains a pressing challenge.

Currently, there is no specific treatment for individuals with OP, and the commonly used drugs include teriparatide, calcitonin, calcium, sodium alendronate and Chinese patent medicines [4]. Calcium is an important element in bone composition, forming the foundational material for normal bone growth and development and is closely linked to bone maturation and aging. In traditional OP treatment, calcium supplementation is considered a direct and reliable approach as inadequate calcium intake can lead to reduced blood calcium levels, prompting the body to utilize bone calcium to maintain a proper blood calcium concentration, ultimately resulting in bone loss. Although calcium alone is instrumental in preserving bone mass associated with the aging process, the absorption of calcium in the small intestine relies on binding proteins, with the synthesis of these calcium-binding proteins regulated by the vitamin D3 metabolite, $1,25(OH)_2D_3$ and has generated interest in the utilization of calcitriol for OP therapy. Over the years, calcitriol has gradually emerged as the primary

pharmacological choice for OP treatment in clinical practice [5]. It is a significant active metabolite of vitamin D and can restore normal intestinal calcium absorption. When used with phosphorus preparations, calcitriol simultaneously facilitates bone development and corrects low blood calcium levels, elevated blood alkaline phosphatase levels, and blood parathyroid hormone concentrations [6]. However, OP is a multifaceted condition for which single-drug therapies have limited efficacy. Moreover, most clinical investigations on active vitamin D for OP have centered around postmenopausal women [1, 7], with fewer studies focusing on elderly male patients.

In this study, we administered a combination of calcitriol and calcium gluconate for the treatment of OP in elderly men and compared its effectiveness to calcium gluconate monotherapy to provide guidance for the selection of clinical treatment approaches for OP.

2. Materials and methods

2.1 Patients

Based on the required sample size for comparing two sample rates, with a significance level (α) of 0.05, and setting the minimum estimated overall rate (Π_{min}) at 0.75 and the maximum estimated overall rate (Π_{max}) at 0.98, the minimum number of cases needed in each group was determined to be 40 cases. In addition, to account for potential factors such as dropouts, missed visits, and non-compliance with prescribed medication, a total of 120 cases were selected for inclusion in the study. These participants were drawn from elderly male patients diagnosed with primary OP who sought care at the Osteoporosis Department of Chongming Hospital, affiliated with shanghai University of Medicine and Health Sciences. Eligibility was assessed based on bone mineral density (BMD) testing, medical history review, and clinical examination. All cases met the WHO diagnostic criteria for OP, which includes having a history of fragility fractures and a BMD T value of ≤ -2.5 at the 2nd to 4th lumbar spine (L2–L4) or femoral neck.

The study exclusion criteria were patients with chronic hepatic, renal, gastroduodenal ulcer disease and various endocrine disorders, as well as those with psychiatric disorders, dementia, recent cardiac infarction, tumors or immunodeficiency. Additionally, individuals who had received treatment with statins, bisphosphonates or glucocorticoids within the past 3 months were also excluded. In total, 92 patients fulfilled the inclusion criteria and were subsequently randomized (Fig. 1).

2.2 Randomization and intervention

Patients were allocated to two groups, the control group and the observation group, in a 1:1 ratio. The control group received oral calcium gluconate (Southwest Pharmaceutical Co., Chongqing, China; # H50020034) at a dosage of 1.0 g three times daily. The observation group was administered oral calcitriol capsules (CP Pharmaceutical, Qingdao, China; #H20030491) at a dosage of 0.25 μg twice daily, in addition to oral calcium gluconate at the same dosage of 1.0 g three times daily. The treatment course for both groups spanned a duration of 6 months.

2.3 Observation indicators

(1) Bone mineral density (BMD) Evaluation: Lumbar spine L1–4 (LS), total hip (TH), and femoral neck (FN) BMD measurements were conducted using the NORLAND-XR-46 dual-energy X-ray bone densitometer before and after treatment. (2) Biochemical indices: Fasting venous blood samples were collected from patients both before and after treatment. Serum bone turnover and bone metabolism-related markers, specifically tartrate-resistant acid phosphatase-5b (TRAP-5b) and Osteocalcin were quantified *via* enzyme-linked immunosorbent assays employing appropriate kits. Additionally, serum calcium (Ca), phosphorus (P), and bone alkaline phosphatase (Bone-ALP) levels were determined using an automated biochemical analyzer. (3) Balance function measurement: Before and after treatment, the patient's balance was assessed using the Berg balance scale (BBS), in which 0 indicates the need for the most amount of help to maintain body balance; <21 indicates the need for support to maintain body balance; 21–40 indicates the ability to maintain balance without support, but unable to resist balance disturbances and shift the center of gravity in all directions; 41–56 indicates the ability to maintain balance without support, can accomplish limited shifting of the body's center of gravity in all directions, and can resist moderate balance disturbances, and; >56 indicates the ability to maintain balance without support, can accomplish shifting the center of gravity in all directions and resist balance disturbances. (4) Follow-up. The patients were followed up by telephone every month during the course of treatment to record the occurrence of fragility fractures. (5) Adverse reactions. The occurrence of adverse reactions such as fever, rash, headache and allergy in the two groups was recorded.

2.4 Statistical analysis

The normal distribution of all outcomes was assessed using the Kolmogorov-Smirnov test. Continuous variables that exhibited a normal distribution are presented as mean $\pm$ standard deviation and analyzed using the independent samples *t*-test. Categorical data were analyzed using the χ^2 test or Fisher's exact probability method. A significance level of $p < 0.05$ was considered statistically significant. Statistical assessments were conducted using the SPSS software version 23.0 (IBM Corp., SPSS Statistics, Armonk, NY, USA).

3. Results

3.1 Baseline characteristics

A total of 86 elderly male OP patients were included in this study, among whom 42 were in the control group and 44 in the observation group (Fig. 1). Data analysis indicated no significant differences in age, BMI, BBS score, BMD or biochemical indicators between the two groups ($p > 0.05$, Table 1).

3.2 Bone mineral density

The assessment of BMD at the anterior and posterior lumbar spine and femoral neck was conducted after 6 months of treatment and observed no significant changes in LS BMD,

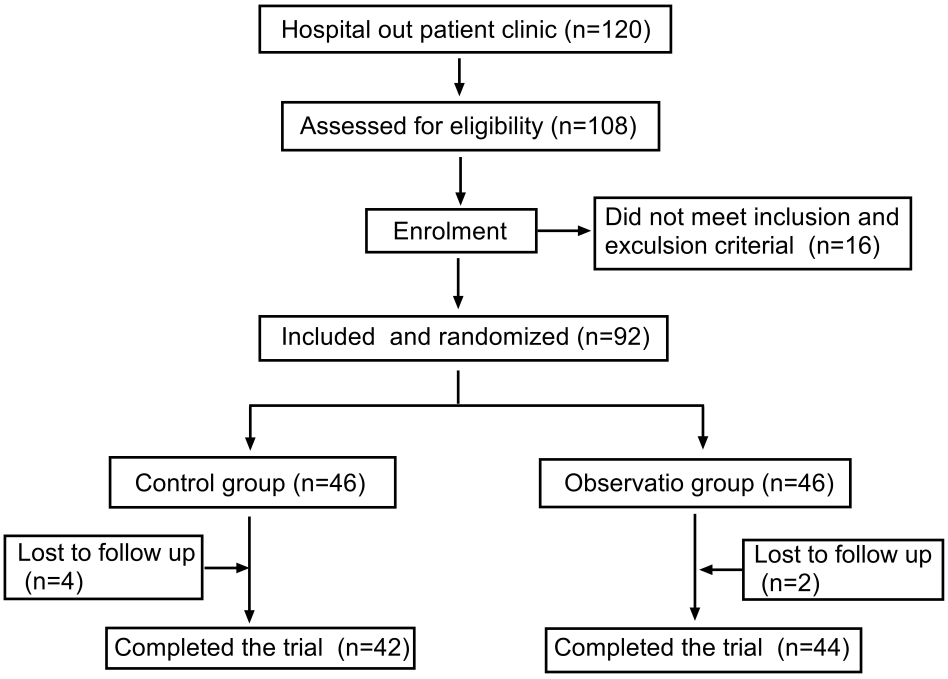

FIGURE 1. Diagram for participant flow.

TABLE 1. Characteristics of patients at baseline.

Variable	Control group (n = 42)	Observation group (n = 44)	*p*
Age (years)	67.40 ± 6.22	67.16 ± 6.67	0.868
Body mass index (kg/m^2)	24.20 ± 1.46	24.44 ± 1.69	0.470
HbA1C (%)	8.71 ± 2.52	9.10 ± 2.69	0.490
SBP (mmHg)	135.71 ± 13.22	140.55 ± 17.25	0.149
DBP (mmHg)	78.25 ± 6.68	78.57 ± 6.17	0.816
Creatine (μmol/L)	86.62 ± 26.17	83.88 ± 24.05	0.614
Glucose (mg/dL)	109.77 ± 19.78	113.01 ± 25.95	0.518
Triglycerides (mg/dL)	145.87 ± 42.55	138.11 ± 35.52	0.360
HDL (mg/dL)	58.19 ± 14.97	59.12 ± 15.92	0.782
LDL (mg/dL)	123.17 ± 31.19	119.59 ± 25.34	0.559
BBS score	45.09 ± 6.32	47.20 ± 5.77	0.109
LS BMD (g/cm^2)	0.76 ± 0.15	0.72 ± 0.15	0.189
TH BMD (g/cm^2)	0.81 ± 0.15	0.80 ± 0.13	0.823
FN BMD (g/cm^2)	0.71 ± 0.12	0.70 ± 0.11	0.695
TRAP-5b (U/L)	15.92 ± 0.63	16.04 ± 0.66	0.394
Bone-ALP (μg/L)	10.71 ± 2.80	10.92 ± 2.52	0.714
Osteocalcin (ng/mL)	8.75 ± 1.49	8.78 ± 1.45	0.913
Ca (mmol/L)	2.14 ± 0.37	2.13 ± 0.40	0.922
P (mmol/L)	1.52 ± 0.13	1.51 ± 0.13	0.755

SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoproteins; LDL, low-density lipoproteins; LS, lumbar spine; TH, total hip; FN, femoral neck; BMD, bone mineral density; TRAP-5b, tartrate-resistant acid phosphatase-5b; ALP, alkaline phosphatase; BBS, Berg balance scale; Ca, calcium; P, phosphorus. HbA1C: Glycosylated Hemoglobin, Type A1C.

TH BMD and FN BMD between baseline and 6 months in the control group ($p > 0.05$, Table 2, Fig. 2A). However, in the observation group, significant improvements were observed: LS BMD increased significantly from 0.72 ± 0.15 at baseline to 0.86 ± 0.14 at 6 months ($p < 0.05$); TH BMD increased significantly from 0.80 ± 0.13 at baseline to 0.95 ± 0.15 at 6 months ($p < 0.05$, Fig. 2B); FN BMD increased significantly from 0.70 ± 0.11 at baseline to 0.86 ± 0.13 at 6 months ($p < 0.05$, Table 2, Fig. 2C). In addition, after the 6-month treatment period, the observation group exhibited significantly higher LS BMD, TH BMD and FN BMD compared to the control group ($p < 0.05$, Table 2).

3.3 Bone metabolism and bone turnover indexes

Compared to baseline values, both the control and observation groups exhibited a significant reduction in TRAP-5b levels after treatment and significant increases in osteocalcin and calcium levels ($p < 0.05$, Table 3, Fig. 3). Furthermore, after 6 months of treatment, the observation group demonstrated a substantial decrease in TRAP-5b compared to the control group, and there were significant increases in bone-ALP, Osteocalcin, Ca and P in the observation group ($p < 0.05$, Table 3, Fig. 3).

3.4 Balance function score

Compared to the baseline assessment, there were no significant changes in the BBS score of the control group after 6 months ($p > 0.05$), while the BBS score of the observation group increased significantly during the same period ($p < 0.05$, Fig. 4). After 6 months of treatment, it was observed that the BBS score of the observation group was significantly higher than that of the control group ($p < 0.05$, Fig. 4).

3.5 Follow-up and adverse effects

During the treatment period, 3 cases of fragility fractures were recorded in the control group, resulting in an incidence rate of 7.14%, while no fragility fractures were observed in the observation group ($\chi^2 = 1.480$, $p = 0.224$). In terms of adverse reactions, the control group experienced one case of nausea and vomiting, resulting in an adverse reaction incidence rate of 2.38%. In the observation group, there was one case of nausea and vomiting, one case of skin rash, and one case of headache, resulting in an adverse reaction incidence rate of 6.82%. No statistically significant difference was observed in the incidence rate of adverse reactions between the two groups ($\chi^2 = 0.216$, $p = 0.642$). As appropriate interventions were given to the patients, all adverse reactions were treated without drug therapy interruption.

TABLE 2. Comparison of bone mineral density.

Variables	Control group (n = 42)		Observation group (n = 44)	
	Baseline	6 months	Baseline	6 months
LS BMD (g/cm^2)	0.76 ± 0.15	0.79 ± 0.14	0.72 ± 0.15	0.86 ± 0.14*#
TH BMD (g/cm^2)	0.81 ± 0.15	0.82 ± 0.13	0.80 ± 0.13	0.95 ± 0.15*#
FN BMD (g/cm^2)	0.71 ± 0.12	0.75 ± 0.13	0.70 ± 0.11	0.86 ± 0.13*#

*LS, lumbar spine; TH, total hip; FN, femoral neck; BMD, bone mineral density. *$p < 0.05$ compared with Baseline; #$p < 0.05$ compared with Control group.*

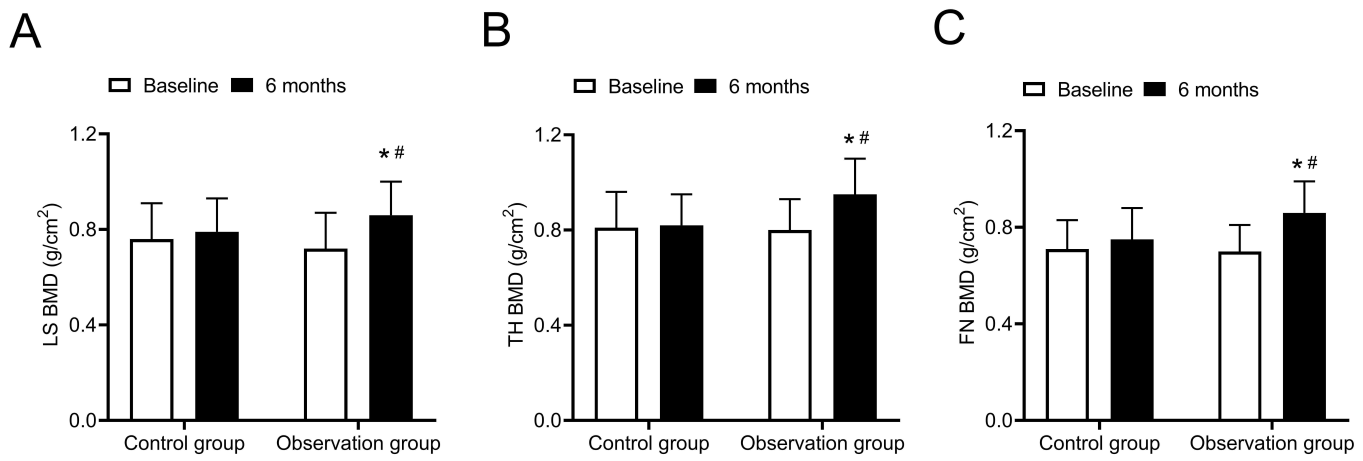

FIGURE 2. Comparison of bone mineral density between the two groups in the (A) lumbar spine, (B) total hip and (C) femoral neck. *$p < 0.05$ compared with Baseline; #$p < 0.05$ compared with Control group. LS, lumbar spine; TH, total hip; FN, femoral neck; BMD, bone mineral density.

TABLE 3. Comparison of bone metabolism and bone turnover indices.

Variables	Control group (n = 42)		Observation group (n = 44)	
	Baseline	6 months	Baseline	6 months
TRAP-5b (U/L)	15.92 ± 0.63	11.31 ± 0.80*	16.04 ± 0.66	10.21 ± 0.91*#
Bone-ALP (μg/L)	10.71 ± 2.80	11.66 ± 1.40	10.92 ± 2.52	13.75 ± 1.28*#
Osteocalcin (ng/mL)	8.75 ± 1.49	13.21 ± 1.72*	8.78 ± 1.45	15.27 ± 1.41*#
Ca (mmol/L)	2.14 ± 0.37	2.93 ± 0.46*	2.13 ± 0.40	3.85 ± 0.39*#
P (mmol/L)	1.52 ± 0.13	1.68 ± 0.51	1.51 ± 0.13	2.98 ± 0.76*#

TRAP-5b, tartrate-resistant acid phosphatase-5b; ALP, alkaline phosphatase; Ca, calcium; P, phosphorus. $^{*}p < 0.05$ *compared with Baseline;* $^{\#}p < 0.05$ *compared with Control group.*

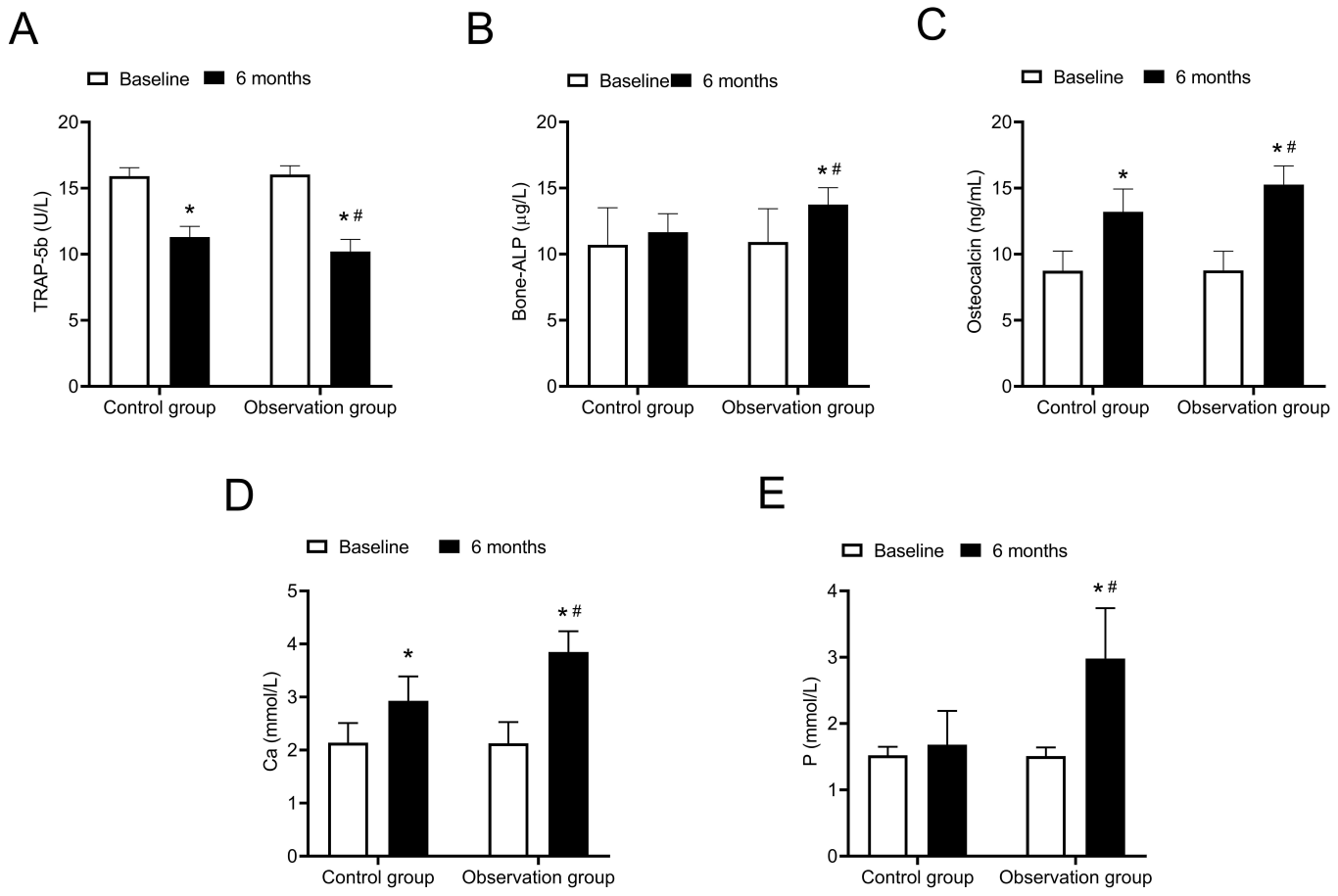

FIGURE 3. Comparison of bone metabolism and bone turnover indices in regard to the following markers. (A) tartrate-resistant acid phosphatase-5b. (B) bone alkaline phosphatase. (C) osteocalcin. (D) calcium. (E) P. $^{*}p < 0.05$ compared with Baseline; $^{\#}p < 0.05$ compared with Control group. TRAP-5b, tartrate-resistant acid phosphatase-5b; ALP, alkaline phosphatase; Ca, calcium; P, phosphorus.

4. Discussion

OP is a common systemic bone disease prevalent among the elderly, primarily attributed to age-related degenerative changes within the bones. Patients with OP often experience abnormal bone metabolism and increased bone resorption, resulting in reduced bone strength and an imbalance between bone formation and resorption, thereby elevating the risk of fragility fractures [8]. Clinical manifestations of OP typically include low back pain and spinal degeneration, which can significantly impair an individual's ability for self-care. The incidence of OP is closely associated with aging, with survey data revealing an age-standardized prevalence of spinal or hip OP at 6.46% for men and 29.13% for women aged 50 years and older, highlighting the societal urgency of addressing OP [9]. Currently, the primary goals in treating OP are increasing bone mass, enhancing bone quality, and reducing the incidence of fractures [8].

Calcium gluconate, a widely used calcium supplementation medication, can rapidly increase serum calcium levels due to its calcium carbonate content [10]. In addition, calcium gluconate effectively alleviates resting pain and percussion

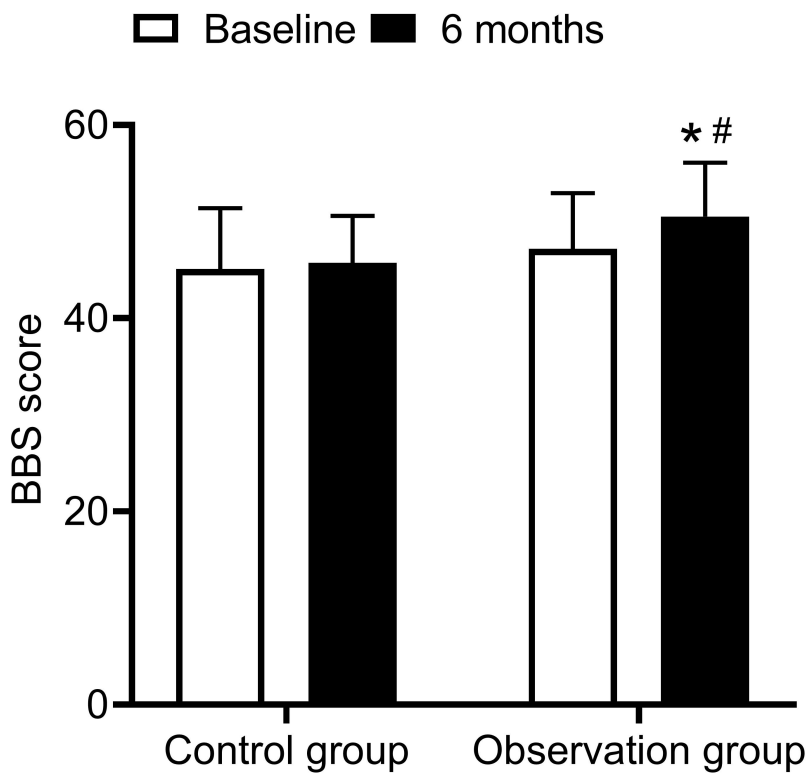

FIGURE 4. Comparison of balance function scores between the two groups. $^{*}p < 0.05$ compared with Baseline; $^{\#}p < 0.05$ compared with Control group. BBS, Berg balance scale.

pain in the lower back caused by OP while also enhancing bone density [11]. Although calcium is the most commonly used treatment for OP, any regimen for OP must be accompanied by calcium supplementation, as calcium supplementation alone does not impact bone mass or fracture incidence [12]. Therefore, the prevailing clinical approach for OP primarily involves calcium supplementation with vitamin D to enhance calcium absorption. Vitamin D plays a pivotal role in regulating calcium balance in the body, with its active metabolite, $1,25(OH)_2D_3$, also known as active vitamin D, holding significant importance in OP prevention and treatment. Related research has demonstrated that the combined use of calcium and vitamin D reduces the risk of vertebral fractures by 37% [13]. In this present study, we observed that treating elderly male OP patients with calcium gluconate supplementation supplemented by calcitriol led to improved bone mineral density, while the use of calcium gluconate alone had minimal impact on the patients' bone mineral density.

Studies have indicated that calcitriol can enhance neuromuscular coordination by regulating myoblast differentiation into myotubes and stimulating the synthesis of nerve growth factors [14, 15]. Furthermore, a meta-analysis has demonstrated the fall prevention and OP reduction effects of active vitamin D [16]. In our study, we not only observed the effectiveness of calcitriol in improving lumbar spine bone mass but also in enhancing balance coordination. In bone tissues, calcitriol exerts a bidirectional regulatory influence on both bone formation and bone resorption [17]. On the one hand, it interacts with the D hormone receptor in osteoblasts, increasing the production of transforming growth factor-β (TGF-β) and the number of insulin-like growth factor 1 (IGF-1) receptors in osteoblasts, which promotes the synthesis of alkaline phosphatase (ALP), osteocalcin, osteoblasts and collagen, thereby enhancing bone quality. On the other hand, although mature osteoclasts lack D hormone receptors, their precursor cells possess these receptors. Calcitriol facilitates the conversion of precursor osteoclasts into mature osteoclasts, leading to an increase in osteoclast numbers and, subsequently, bone resorption. Moreover, calcitriol, through its interaction with the D hormone receptor, enhances the activity of the dihydroxyvitamin D receptor in muscle and neural tissue, thereby increasing muscle strength and improving balance function.

TRAP-5b, originating in osteoblasts, is a robust indicator of bone resorption and osteoclast activity and is a highly specific and sensitive marker of bone metabolic response [18]. Conversely, bone-ALP and osteocalcin exert opposing effects on TRAP-5b and form a distinct group of indicators highly specific to bone formation and osteoblast activity [19, 20]. Bone-ALP, an extracellular enzyme produced by osteoblasts, primarily functions in the hydrolysis of phosphatase during osteogenesis, supplying essential phosphate required for hydroxyapatite deposition. Additionally, it acts on pyrophosphate hydrolysis, alleviating its inhibitory influence on bone salt formation and facilitating the osteogenic process. Since bone-ALP originates from osteoblasts and remains unaffected by liver, kidney, intestinal and other diseases, it represents a specific and sensitive marker reflecting osteoblast activity and bone formation [21]. The quantitative assessment of serum bone-ALP as an indicator of abnormal bone metabolism has gained increasing clinical prominence. Clinical studies

have shown that bone-ALP is significantly correlated with age, and bone-ALP is elevated in patients with osteopenia and OP [22]. Osteocalcin, a hormone-like peptide synthesized and secreted by osteoblasts, functions as a specific indicator reflecting bone renewal status and the process of bone formation [23]. Variations in serum osteocalcin levels have been associated with osteoblast activity and serve as specific indicators of osteoblast function and bone mineralization, thus establishing their gradual clinical utilization as bone turnover markers [24]. Notably, the absorption of calcium necessitates the presence of calcitriol. By stimulating the production of calcium-binding proteins and enhancing Ca^{2+}-ATPase activity, calcitriol facilitates the *in vivo* conversion that enhances calcium and phosphorus absorption by mucosal cells within the small intestine [25]. Furthermore, calcitriol contributes to calcium salt replenishment, new bone formation, increased calcium and phosphorus reabsorption by renal tubular cells, and reduced urinary excretion [26]. A pivotal target of calcitriol is osteoblasts, in which it prompts the synthesis of matrix and proteins, playing a critical role in bone mineralization, function and metabolism [27–29]. Importantly, calcium supplementation alone is insufficient to address bone loss and treat OP. In this study, we observed that compared to the calcitriol treatment only, the combination of calcium gluconate and calcitriol resulted in reduced serum TRAP-5b levels and increased calcium, phosphorus, bone-ALP and osteocalcin levels in OP patients, highlighting the potential of the calcium gluconate and calcitriol combination in regulating bone metabolism, bone turnover and the delivery of essential trace elements such as calcium and phosphorus into the bloodstream, which can ultimately improve patient symptoms and therapeutic outcomes.

However, there were some limitations that should be acknowledged in this study. First, the sample size was relatively small, which might have influenced the study results. Second, the follow-up period was relatively short to facilitate timely adjustments to the treatment regimen. Future research could focus on large-scale, multicenter studies with extended follow-up periods to establish the clinical efficacy of diverse treatment strategies.

5. Conclusions

In summary, the use of calcium gluconate with calcitriol in OP patients enhanced bone mineral density, improved bone metabolism and regulated bone turnover while maintaining a favorable safety profile. Despite the intricate mechanisms underlying the enhancement of muscle strength, balance, reflex sensitivity and mobility through drug intervention, it is important to acknowledge the significance of optimizing calcium and active vitamin D supplementation in elderly male OP patients to reduce the risk of falls and fractures.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

JCZ, ZHL—designed the study and carried them out, prepared the manuscript for publication and reviewed the draft of the manuscript; JCZ, ZHL, LS and XLZ—supervised the data collection, analyzed the data, interpreted the data. All authors have read and approved the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Chongming Hospital affiliated to shanghai University of Medicine and Health Sciences (Approval no. LLWYH-2018-09). Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Brown JP. Long-term treatment of postmenopausal osteoporosis. Endocrinology and Metabolism. 2021; 36: 544–552.
[2] Johnston CB, Dagar M. Osteoporosis in older adults. Medical Clinics of North America. 2020; 104: 873–884.
[3] Coughlan T, Dockery F. Osteoporosis and fracture risk in older people. Clinical Medicine. 2014; 14: 187–191.
[4] Muñoz M, Robinson K, Shibli-Rahhal A. Bone health and osteoporosis prevention and treatment. Clinical Obstetrics & Gynecology. 2020; 63: 770–787.
[5] Lung BE, Mowery ML, Komatsu DEE. Calcitriol. StatPearls Publishing: Treasure Island (FL). 2024.
[6] Ringe JD. Plain vitamin D or active vitamin D in the treatment of osteoporosis: where do we stand today? Archives of Osteoporosis. 2020; 15: 182.
[7] Dechant KL, Goa KL. Calcitriol. A review of its use in the treatment of postmenopausal osteoporosis and its potential in corticosteroid-induced osteoporosis. Drugs & Aging. 1994; 5: 300–317.
[8] Aspray TJ, Hill TR. Osteoporosis and the ageing skeleton. Subcellular Biochemistry. 2019; 12: 453–476.
[9] Zeng Q, Li N, Wang Q, Feng J, Sun D, Zhang Q, *et al*. The prevalence of osteoporosis in China, a nationwide, multicenter DXA survey. Journal of Bone and Mineral Research. 2019; 34: 1789–1797.
[10] Chakraborty A, Can AS. Calcium gluconate. StatPearls Publishing: Treasure Island (FL). 2022.
[11] Li R, Wang X, Luan J, Zhang T. Effects of salmon calcitonin combined with calcium gluconate on bone metabolism in senile osteoporosis patients. Chinese Journal of Osteoporosis. 2012; 18: 3.
[12] Yong E, Logan S. Menopausal osteoporosis: screening, prevention and treatment. Singapore Medical Journal. 2021; 62: 159–166.
[13] Capozzi A, Scambia G, Lello S. Calcium, vitamin D, vitamin K2, and

magnesium supplementation and skeletal health. Maturitas. 2020; 140: 55–63.

[14] Gradilone A, Ribuffo D, Silvestri I, Cigna E, Gazzaniga P, Nofroni I, *et al*. Detection of melanoma cells in sentinel lymph nodes by reverse transcriptase-polymerase chain reaction: prognostic significance. Annals of Surgical Oncology. 2004; 11: 983–987.

[15] Yang R, Chen J, Zhang J, Qin R, Wang R, Qiu Y, *et al*. 1,25-Dihydroxyvitamin D protects against age-related osteoporosis by a novel VDR-Ezh2-p16 signal axis. Aging Cell. 2020; 19: e13095.

[16] Tilyard MW, Spears GFS, Thomson J, Dovey S. Treatment of post-menopausal osteoporosis with calcitriol or calcium. New England Journal of Medicine. 1992; 326: 357–362.

[17] Avenell A, Mak JC, O'Connell D. Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. Cochrane Database of Systematic Reviews. 2014; 2014: CD000227.

[18] Williams C, Sapra A. Osteoporosis markers. StatPearls Publishing: Treasure Island (FL). 2023.

[19] Eastell R, Szulc P. Use of bone turnover markers in postmenopausal osteoporosis. The Lancet Diabetes & Endocrinology. 2017; 5: 908–923.

[20] Szulc P. Bone turnover: biology and assessment tools. Best Practice & Research Clinical Endocrinology & Metabolism. 2018; 32: 725–738.

[21] Riancho JA. Diagnostic approach to patients with low serum alkaline phosphatase. Calcified Tissue International. 2023; 112: 289–296.

[22] Tourkova IL, Larrouture QC, Onwuka KM, Liu S, Luo J, Schlesinger PH, *et al*. Age-related decline in bone mineral transport and bone matrix proteins in osteoblasts from stromal stem cells. American Journal of Physiology-Cell Physiology. 2023; 325: C613–C622.

[23] Parveen B, Parveen A, Vohora D. Biomarkers of osteoporosis: an update. Endocrine, Metabolic & Immune Disorders-Drug Targets. 2019; 19: 895–912.

[24] Brown JP, Don-Wauchope A, Douville P, Albert C, Vasikaran SD. Current use of bone turnover markers in the management of osteoporosis. Clinical Biochemistry. 2022; 109–110: 1–10.

[25] Wang D, Song J, Ma H. An *in vitro* experimental insight into the osteoblast responses to vitamin D3 and its metabolites. Pharmacology. 2018; 101: 225–235.

[26] Gram J. Dose-response effect of short-term calcitriol treatment on bone and mineral metabolism in normal males. Bone. 1996; 18: 539–544.

[27] Ryan BA, McGregor NE, Kirby BJ, Al-Tilissi A, Poulton IJ, Sims NA, *et al*. Calcitriol-dependent and -independent regulation of intestinal calcium absorption, osteoblast function, and skeletal mineralization during lactation and recovery in mice. Journal of Bone and Mineral Research. 2020; 37: 2483–2497.

[28] Kassem M, Kveiborg M, Eriksen EF. Production and action of transforming growth factor-beta in human osteoblast cultures: dependence on cell differentiation and modulation by calcitriol. European Journal of Clinical Investigation. 2000; 30: 429–437.

[29] Turner AG, Hanrath MA, Morris HA, Atkins GJ, Anderson PH. The local production of $1,25(OH)_2D_3$ promotes osteoblast and osteocyte maturation. The Journal of Steroid Biochemistry and Molecular Biology. 2014; 144: 114–118.

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