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The effect of Jintiange capsules on pain in patients with primary osteoporosis: a systematic review and meta-analysis

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Abstract

Background To evaluate the effectiveness of Jintiange capsules (JTG) in relieving pain in patients with primary osteoporosis (POP).

Methods A systematic review of the literature was conducted through seven databases, including PubMed, Web of Science, Cochrane Library, Embase, Chinese National Knowledge Infrastructure, Wanfang Database and SinoMed, from inception to October 2023. The control group was given conventional anti-osteoporosis drug therapy such as Alfacalcidol soft capsules, Alendronate sodium tablets, Caltrate D3, etc. The experimental group was treated with JTG alone or in combination with JTG on the basis of the drugs used in the control group. The primary outcome measure was the visual analog scale (VAS). Stata SE-64 software was used to conduct meta-analyses of the final included studies.

Results A total of 2916 participants were included in 21 articles. The results of meta-analysis showed that JTG relieved pain (WMD: -2.51; 95% CI: -3.30, -1.71; $p < 0.05$), improved the bone mineral density (BMD) of femoral neck (WMD: 0.83; 95% CI: 0.33, 1.33; $p < 0.05$) and lumbar (WMD: 1.14; 95% CI: 0.67, 1.62; $p < 0.05$), improved oswestry disability index (ODI) (WMD: -1.79; 95% CI: -3.05, -0.54; $p < 0.05$), enhanced timed up and go test (TUG) (WMD: -2.61; 95% CI: -4.60, -0.62; $p < 0.05$) and decreased fracture incidence (WMD: 0.37; 95% CI: 0.15, 0.93; $p < 0.05$).

Conclusion In terms of relieving pain, improving BMD, improving activity function, and improving gait and preventing fracture, JTG is a good choice for patients with osteoporosis (OP).

Keywords Primary osteoporosis, Jintiange capsules, Systematic review, Meta-analysis

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Introduction

Reduced bone mineral density (BMD) and the microstructure of the bone are the hallmarks of primary osteoporosis (POP), a chronic bone disease that weakens bones and increases their vulnerability to fracture., including postmenopausal osteoporosis (PMOP) and senile osteoporosis (SOP) [1]. According to an epidemiological survey of osteoporosis (OP) in China, the prevalence of OP in men and women is 20.73% and 38.05%, respectively, and the prevalence of osteoporotic fracture in elderly individuals is 18.9% [2, 3]. POP is an easily overlooked but widespread public health problem.

Pain is one of the most common symptoms in patients with POP and usually occurs noticeably during turning, sitting up and prolonged walking. The pain not only severely affects the patient's mood and quality of life, but also further exacerbates bone loss. Studies have shown that the chronic pain rate of POP patients is 58%, of which low back pain accounts for 70% to 80% [4]. Another study showed that the average visual analogue scale (VAS) score of pain in POP patients before vertebral compression fracture was 4.33, which affected the patients'daily life [5]. The aggravation of pain affected the patients'balance and mobility, and both balance and mobility tended to decrease as the pain score increased [6]. When a patient's balance and flexibility decrease, the risk of falling increases, which can lead to fractures. In addition, pain-induced adverse effects such as anxiety and sleep disturbances seriously affect patients'quality of life, so the main complaint of most patients is to relieve pain [7]. Although the improvement of BMD and the reduction of fracture risk are important indicators for evaluating the efficacy of anti-OP drugs, pain as a major symptom of POP should not be ignored. Pain relief greatly improves the subjective feeling and quality of life of patients, which is conducive to improving the adherence of POP patients.

Pain can progress with bone loss, microstructural deterioration and other conditions, shifting from intermittent to constant pain and exacerbating the patient's discomfort. In addition to traumatic pain due to fragility fractures, OP can cause pain without evidence of fracture [8]. The results of a European survey revealed that severe chronic pain affects 19% of European adults [9]. Central sensitization is the earliest mechanism of osteoporosis-induced severe pain and is manifested by increased responsiveness of injurious neurons in the central nervous system to their normal or subthreshold afferent inputs [10]. This sensitization mechanism not only exacerbates pain manifestations, but also promotes the chronicity of pain symptoms. Activation of N-methyl-D-aspartate (NMDA) receptors and glial cells is the main cause of central sensitization [11, 12]. NMDA receptor activation amplifies pain in osteoporotic patients. The release of pro-inflammatory mediators from pathological changes such as ischemia, infection, and mechanical injury could activate microglia, leading to the onset of pain through pathologic changes in the nervous system. In addition, sympathetic nerves play an important role in the development of osteoporotic pain. Neuropeptides such as substance P and Calcitonin-Gene Related Peptide (CGRP), which are released from sympathetic nerve endings in bone tissue and are involved in the processes of local bone turnover, inflammatory response and angiogenesis, are also strongly implicated in osteoporotic pain [13–15]. In the skeletal system, sympathetic nerve fibers were involved in the regulation of bone formation and destruction, vasoconstriction and diastole, bone progenitor cell function, macrophage infiltration, etc. When the skeletal system is injured, sympathetic nerve fibers regulate the function of sensory nerve fibers, and thus sympathetic nerves play an important role in the development of osteoporotic pain. When osteoclasts are hyperactive, the process of bone resorption (BR) is accelerated, which leads to pathological changes in bone sensory nerve fibers causing pain. In addition, hyperactive osteoclasts transport H+ to the bone surface via specific transporter enzymes, and the resulting lower pH environment activates receptors such as acid-sensing ion channel-3 (ASIC-3) and transient receptor potential vanilloid 1 (TRPV1) to generate pain signals and cause inflammatory pain [16, 17]. Furthermore, patients with POP often experience long-term imbalance of force on the joint muscles of the spine, with adjacent joint surfaces rubbing against each other under stress, resulting in hyperplasia, necrosis, and other inflammatory reactions, ultimately leading to chronic pain [18]. OP patients have significant bone microstructure lesions, often accompanied by sarcopenia, leading to postural abnormalities, and the slightest external force can cause damage to the bone microstructure, so patients often suffer from low back pain, which is associated with activity and weight-bearing. When the body is in a POP state, bone brittleness increases, making bones more susceptible to uneven stresses on the articular surfaces [19]. Excessive muscle tension near the spinal joints, jamming of joint contents, and joint misalignment trigger low back pain and impaired mobility. Therefore, relieving pain, preventing falls, and reducing the risk of fracture are the primary therapeutic goals in the treatment of POP patients.

Currently, POP is mainly treated by drugs in clinical practice, including BR inhibitors, bone formation (BF) promoters, and other drugs. Anti-BR drugs mainly inhibit osteoclast BR, including bisphosphonates,

calcitonin, estrogen, and so on. Bisphosphonates can increase the level of bone metabolism (BM) and effectively reduce the risk of osteoporotic fracture [20, 21], but prolonged use of bisphosphonates increases the risk of osteonecrosis of the jaw and atypical femur fracture [22, 23], and long-term use is not recommended. A hormone that controls calcium levels called calcitonin has the ability to reduce osteoclasts'biological activity and bone loss, and alleviate bone pain, but there is a possibility that nasal spray salmon calcitonin may increase the risk of tumors, and the duration of use is limited [24]. Estrogen is effective in reducing bone loss and decreasing the risk of fracture in postmenopausal women, but it increases the risk of endometrial cancer and breast cancer [25, 26]. BF promoters mainly stimulate osteoblastic BF, including parathyroid hormone analogs, such as teriparatide. Teriparatide stimulates osteoblast activity, promotes BF, and increases BMD. However, studies have shown that there may be a risk of osteosarcoma, so the duration of treatment was limited [27, 28].

Other drugs refer to traditional Chinese medicine (TCM) treatments, commonly including Xianling Gubao capsules, Gushukang capsules, Jintiange capsules (JTG), etc. TCM has the advantages of being safe and inexpensive, so it is getting more and more attention in China. In recent years, more and more studies have demonstrated the effectiveness of TCM in the treatment of OP. In China, JTG is among the major proprietary Chinese medicines for the treatment of POP. The main ingredient in JTG is artificial tiger bone powder. The composition of artificial tiger bone powder contains collagen and various bone growth factors. JTG promoted osteogenesis as shown by changes in MC3 T3-E1 osteoblast proliferation, differentiation, and mineralization, decreased apoptosis, and enhanced autophagosome production and autophagy [29]. The study showed that JTG increased BMD and improved bone microarchitecture in rats after ovariectomy, increased osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) by up-regulating the expression of key proteins of the BMP and Wnt/β-catenin pathways, and inhibited osteoclastogenesis by inhibiting the NF-κB pathway for the treatment of OP [30]. During the 52-week treatment, Liang proved that JTG might successfully lower the risk of falls in patients with OP by improving muscle strength and balance [31]. JTG is one of the Chinese patent medicines for OP, which has been widely used and has remarkable clinical effects. At present, there are only systematic reviews and meta-analyses of JTG in the treatment of osteoporotic vertebral compression fractures after surgery, but no systematic reviews and meta-analyses of JTG in the treatment of POP [32, 33]. In this paper, we evaluated the pain relief of POP patients via the JTG through a meta-analysis to provide a reference basis for clinical practice.

Materials and methods

The study was carried out and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria [34] and was registered on PROSPERO (CRD42023483351).

Eligibility criteria

Inclusion criteria

P: The patient was diagnosed with POP (PMOP or SOP).

I: Treated with JTG alone or in combination with other therapies.

C: Any conventional anti-OP treatment, such as Alfacalcidol soft capsules, Alendronate sodium tablets, Caltrate D3, Alendronate sodium tablets, etc.

O: VAS, femoral neck BMD, lumbar BMD, ODI, TUG, and fracture incidence.

S: RCTs.

Exclusion criteria

(a): Duplicate studies.
(b): Unable to obtain the full text of the literature.
(c): Animal studies, reviews, meta-analyses, etc.
(d): The studies in which raw data were lacking or data couldn't be extracted.

Selection of participants

This meta-analysis included patients with POP. There were no preset restrictions on sex, age, or nationality. According to the relevant guidelines and the diagnostic criteria recommended by the WHO, patients with a BMD (T-value ≤ -2.5) according to dual-energy X-ray absorptiometry (DXA) were diagnosed with OP [35–38].

Types of interventions

The experimental group was treated with JTG alone or in combination with JTG on the basis of the drugs used in the control group. The therapeutic dose of JTG was 1 capsule to be taken three times daily, totaling 3 capsules per day. The control group was treated with conventional anti-OP drugs.

Types of outcome measures

The primary outcome measure of this meta-analysis was VAS. The secondary outcome measures were

femoral neck BMD, lumbar BMD, ODI, TUG, and fracture incidence.

Literature search strategy

To ascertain the efficacy of JTG in the treatment of POP, we conducted a systematic literature search. We searched seven databases: PubMed, Web of Science, Cochrane Library, Embase, Chinese National Knowledge Infrastructure (CNKI), Wanfang Database, and SinoMed. The time limit for searching was from the establishment of the databases to October 31, 2023. The search strategy was conducted using a combination of free words and MeSH terms. The relevant keywords for POP were "osteoporosis" OR "senile osteoporosis" OR "postmenopausal osteoporosis" OR "primary osteoporosis". The keywords of JTG, including "Jintiange" OR "Jintiange capsule" OR "artificial tiger bone". The search strategies were described in the supplementary document.

Quality assessment

The risk of bias was assessed by two authors in the included studies using the Physiotherapy Evidence Database (PEDro) scale. Discrepancies were resolved through discussion or arbitration by a third evaluator. The total PEDro score is obtained by summing the scores for items 2 through 11, with the total score ranging from 0 to 10. Higher scores indicate higher methodological quality. A score of <4 was considered 'poor', 4 to 5 was considered 'fair', 6 to 8 was considered 'good', and 9 to 10 was considered 'excellent' [39].

Study selection and data extraction

Firstly, two authors independently searched the databases and eliminated obvious duplicates. Subsequently, two other authors carefully read the titles and abstracts of the literature, eliminating animal experiments, reviews, etc. Then, the two authors checked their respective initial screening results and summarized them. After summarizing the literature, a full-text reading of the literature was done to screen the final required literature after eliminating those that did not meet the inclusion and exclusion criteria. Finally, We extracted the the basic characteristics and study characterization data into Excel by reading the full text of the included studies. The basic

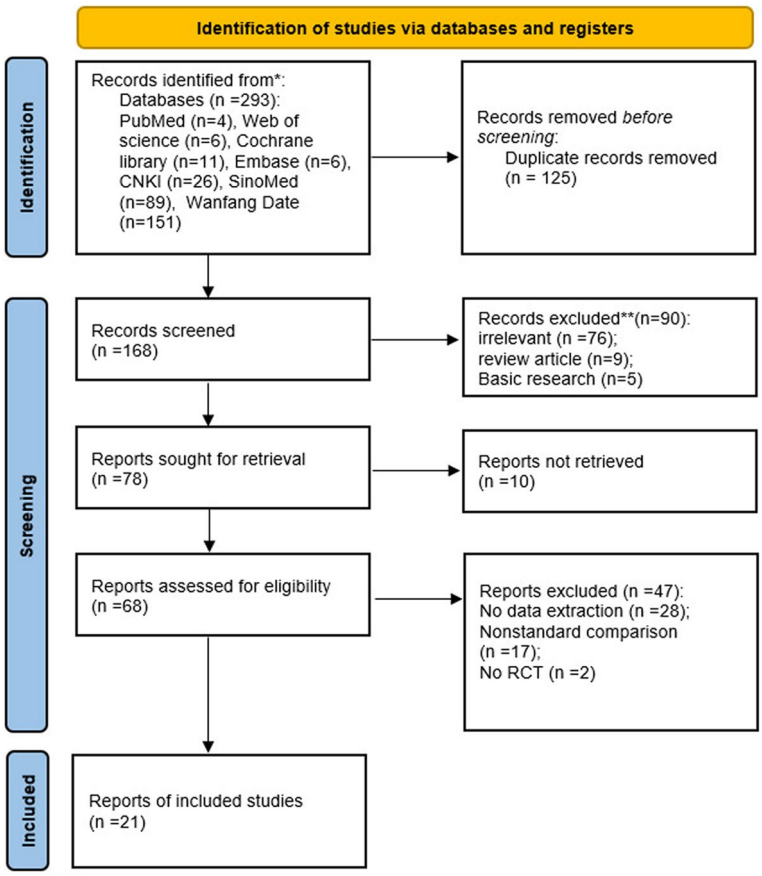

Fig. 1 Flowchart of the study selection process

Table 1 Basic characteristics of the included studies

References	Sample size	T/C (M/F)	Age(years)	Diagnosis standard	Intervention	Control	Treatment duration	Adverse effects reporting	Outcome measures
Cao Q et al. 2019 [40]	124	T:62 C:62	T:60.6 ± 2.9 C:60.1 ± 2.6	PMOP	Jintiange capsules + C	Alfacalcidol soft capsules	6 months	Y	a, c
Chen JR et al. 2019 [41]	160	T:80 C:80	T:65 ± 4 C:65 ± 4	PMOP	Jintiange capsules + C	Alendronate sodium tablets	8 months	N	a, b, c
Cheng JL et al. 2021 [42]	471	T:356 (46/310) C:115 (14/101)	T:67.48 ± 9.11 C:66.65 ± 8.74	POP	Jintiange capsules + Gushukang capsules placebo	Jintiange capsules placebo + Gushukang capsules	6 months	Y	b
Deng XJ 2022 [43]	80	T:40 (21/19) C:40 (23/17)	T:67.62 ± 2.87 C:67.52 ± 2.85	SOP	Jintiange capsules + C	Salmon calcitonin injection + Risedronate sodium tablets	3 months	N	a, c
Huang HL et al.2014 [44]	168	T:84 C:84	/	POP	Jintiange capsules + Diqiao vitamin D calcium chewable tablets	Alendronate sodium tablets + Diqiao vitamin D calcium chewable tablets	3 months	Y	b
Ji QX et al. 2021 [45]	120	T:60 (36/24) C:60 (33/27)	T:65.40 ± 2.55 C:65.48 ± 2.66	POP	Jintiange capsules + C	Caltrate D3 + Sodium Ibandronate Injection	6 months	Y	b, c, d, f
Kong HY et al. 2022 [46]	60	T:30 C:30	T:59.40 ± 2.95 C:58.90 ± 2.30	PMOP	Jintiange capsules + C	Alendronate sodium tablets + Caltrate D3	6 months	Y	c
Liang HT et al. 2022 [31]	399	T:199 (24/175) C:200 (29/171)	T:63.31 ± 7.02 C:62.88 ± 7.42	POP	Jintiange capsules + Caltrate D3 placebo + Alfacalcidol soft capsules	Caltrate D3 + Jintiange capsules placebo + Alfacalcidol soft capsules	13 months	N	a, c, e, f
Liu MY 2016 [47]	116	T:58 (22/36) C:58 (24/34)	T:71 ± 5 C:70 ± 6	SOP	Jintiange capsules + C	Alendronate sodium tablets + Caltrate D3	12 months	N	a, b, c, d
Liu ZY 2018 [48]	151	T:76 C:75	T:59.96 ± 9.24 C:59.48 ± 9.35	PMOP	Jintiange capsules + C	Risedronate sodium capsules	6 months	Y	c
Luo Q et al. 2016 [49]	112	T:56 C:56	/	SOP	Jintiange capsules + Alendronate sodium tablets	Alendronate sodium tablets + Caltrate D3	6 months	Y	a, c, f
Qi YJ et al. 2017 [50]	133	T:87 C:46	T:65.30 ± 10.90 C:63.90 ± 14.80	PMOP	Jintiange capsules + C	Alendronate sodium tablets + Caltrate D3	6 months	Y	a, b, c
Tian F et al. 2019 [51]	120	T:60 (27/33) C:60 (26/34)	T:62.83 ± 5.65 C:62.95 ± 5.71	POP	Jintiange capsules + C	Calcitriol soft capsules	6 months	Y	a, b, c
Wang RR 2018 [52]	68	T:34 C:34	T:63.01 ± 10.82 C:64.12 ± 10.86	PMOP	Jintiange capsules + C	Zoledronic acid injection	6 months	N	a, b, c

Table 1 (continued)

References	Sample size	T/C (M/F)	Age(years)	Diagnosis standard	Intervention	Control	Treatment duration	Adverse effects reporting	Outcome measures
Wei LY et al. 2018 [53]	76	T:38 C:38	/	POP	Jintiange capsules	Caltrate D3 + Vitamin D	6 months	N	b, d
Xu RM et al. 2017 [54]	100	T:50 C:50	T:61.47 ± 17.38 C:61.98 ± 6.92	PMOP	Jintiange capsules + C	Estradiol valerate tablets	12 months	N	a
Xu YF et al. 2018 [55]	60	T:30 C:30	T:65.32 ± 3.31 C:65.99 ± 3.02	PMOP	Jintiange capsules + C	Caltrate D3	1 months	N	b
Xue L et al. 2023 [56]	98	T:49 (24/25) C:49 (21/28)	T:62.17 ± 7.72 C:61.86 ± 7.65	POP	Jintiange capsules + C	Calcitriol soft capsules + Caltrate D3	6 months	Y	b
Yuan YF et al. 2019 [57]	160	T:80 C:80	T:67 ± 7 C:69 ± 7	PMOP	Jintiange capsules	Caltrate D3	3 months	N	c, e
Zhang XC et al. 2019 [58]	46	T:23 C:23	/	SOP	Jintiange capsules + C	Salmon calcitonin injection	3 months	N	b, c
Zhang Y et al. 2019 [59]	94	T:47 C:47	T:59.60 ± 7.40 C:59.40 ± 7.10	PMOP	Jintiange capsules + C	Risedronate sodium capsules	6 months	Y	a, c

Abbreviations C control, *F* female, *M* male, *N* no, *T* treatment, *Y* yes

Outcome measures: a: Femoral neck BMD; b: VAS; c: Lumbar BMD; d: ODI; e: TUG; f: Fracture incidence

characteristics included author name, year of publication, sample size, number of participants in the experimental and control groups, mean age of participants, diagnosis, interventions and controls, duration of treatment, reports of adverse events, and outcome measures. Blinding was not used in the process of extracting data and conducting analysis.

Statistical analysis

The meta-analysis was performed using Stata SE-64 software. For the results, weighted mean difference (WMD) and 95% confidence intervals (95% CI) were used to measure continuous variables and dichotomous variables. Continuous variables included VAS, femoral neck BMD, lumbar BMD, ODI, and TUG. Dichotomous variables included fracture incidence and adverse events. Relative risk (*RR*) was used for continuous results, and odds ratio (*OR*) was used for dichotomous results. The studies'heterogeneity was tested using I^2. A fixed-effect model was applied if there was no substantial heterogeneity ($I^2 \leq 50\%$). If there was significant heterogeneity among the included studies ($I^2 > 50\%$), the random-effect model was used to analyze the sources of heterogeneity. A Funnel plot was used to detect publication bias, and Egger's test was used to analyze whether publication bias existed. Subgroup analysis was used to analyze the reasons for the high heterogeneity. Sensitivity analysis was carried out to verify that the main result was stable. $p < 0.05$ was used to determine whether the difference was significant.

Results

Search results

Based on the search methodology, 293 references were found, including 4 in PubMed, 6 in Web of Science, 11 in Cochrane Library, 6 in Embase, 26 in CNKI, 151 in Wanfang Database, and 89 in SinoMed. Following the removal of 125 replicated studies and 10 inaccessible articles, the titles and abstracts were read, and a total of 90 articles of irrelevant, review, and basic research were excluded. Among the remaining 68 full papers, 47 articles were ruled out further according to the following criteria:: no data extraction ($n = 28$), nonstandard comparison ($n = 17$), and no RCT ($n = 2$). Finally, 21 studies were included [31, 40–59]. The flow diagram is shown in Fig. 1.

Study characteristics

The 21 studies involved a total of 2916 participants, with sample sizes ranging from 46 to 471. Among them, there

Table 2 Physiotherapy Evidence Database (PEDro) scores of the 21 included studies

References	Eligibility criteria	Random allocation	Concealed allocation	Baseline comparability	Blind subjects	Blind therapists	Blind assessor	Adequate follow-up dropout <15%	Intention-to-treat analysis	Between- group comparisons	Point estimates and variability	Score
Cao Q et al. 2019 [40]	1	1	1	1	0	0	0	1	1	1	1	7
Chen JR et al. 2019 [41]	1	0	1	1	0	0	0	1	1	1	1	6
Cheng JL et al. 2021 [42]	1	1	1	1	1	1	1	1	1	1	1	10
Deng XJ 2022 [43]	1	1	1	1	0	0	0	1	1	1	1	7
Huang HL et al.2014 [44]	1	1	1	1	0	0	0	1	1	1	1	7
Ji QX et al. 2021 [45]	1	1	1	1	0	0	0	1	1	1	1	7
Kong HY et al. 2022 [46]	1	1	1	1	0	0	0	1	1	1	1	7
Liang HT et al. 2022 [31]	1	1	1	1	1	1	1	1	1	1	1	10
Liu MY 2016 [47]	1	1	1	1	0	0	0	1	1	1	1	7
Liu ZY 2018 [48]	1	1	1	1	0	0	0	1	1	1	1	7
Luo Q et al. 2016 [49]	1	1	1	1	0	0	0	1	1	1	1	7
Qi YJ et al. 2017 [50]	1	1	1	1	0	0	0	1	1	1	1	7
Tian F et al. 2019 [51]	1	1	1	1	0	0	0	1	1	1	1	7
Wang RR 2018 [52]	1	1	1	1	0	0	0	1	1	1	1	7
Wei LY et al. 2018 [53]	1	1	1	1	0	0	0	1	1	1	1	7
Xu RM et al. 2017 [54]	1	1	1	1	0	0	0	1	1	1	1	7
Xu YF et al. 2018 [55]	1	1	1	1	0	0	0	1	1	1	1	7
Xue L et al. 2023 [56]	1	1	1	1	0	0	0	1	1	1	1	7
Yuan YF et al. 2019 [57]	1	1	1	1	0	0	0	1	1	1	1	7
Zhang XC et al. 2019 [58]	1	1	1	1	0	0	0	1	1	1	1	7
Zhang Y et al. 2019 [59]	1	1	1	1	0	0	0	1	1	1	1	7
Mean												7.2

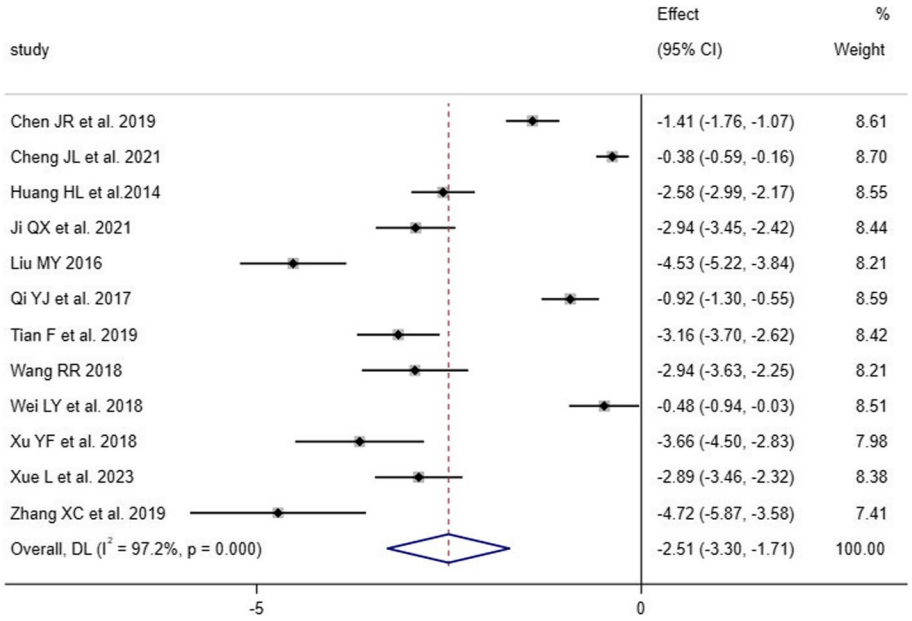

Fig. 2 Effect of JTG on the VAS

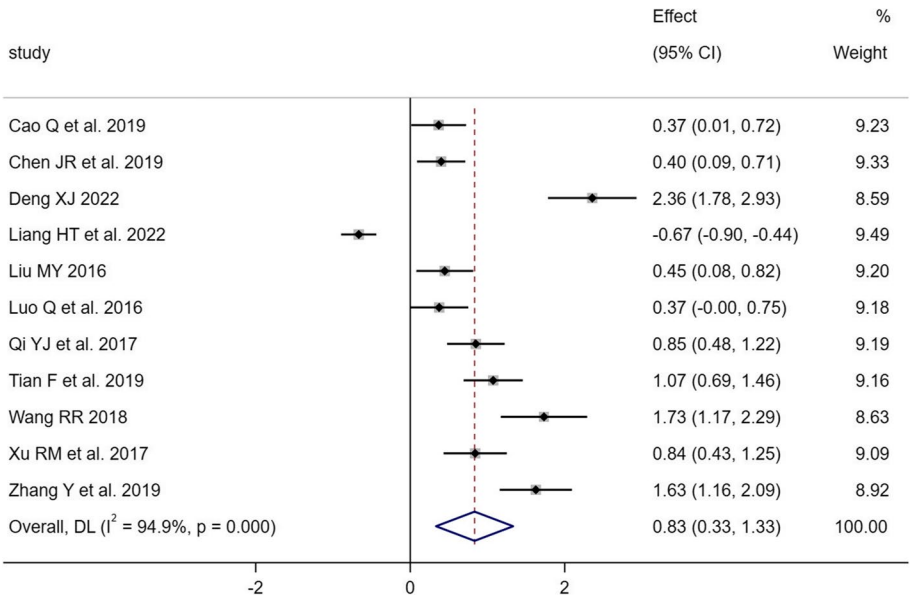

Fig. 3 Effect of JTG on the BMD(Femoral Neck)

were 7 POP studies [31, 42, 44, 45, 51, 53, 56], 10 PMOP studies [40, 41, 46, 48, 50, 52, 54, 55, 57, 59], and 4 SOP studies [43, 47, 49, 58]. Nineteen studies involved combination therapy [31, 40–52, 54–56, 58, 59], and two study involved monotherapy (JTG) [53, 57]. The treatment lasts at least three months and up to thirteen months. Adverse events were reported in 11 studies [40, 42, 44–46, 48–51, 56, 59]. The characteristics of the included studies are shown in Table 1.

Risk of bias assessment

Two authors independently assessed the quality of the included studies using the PEDro tool. The mean PEDro score of the included studies was 7.2. All 21 studies had a

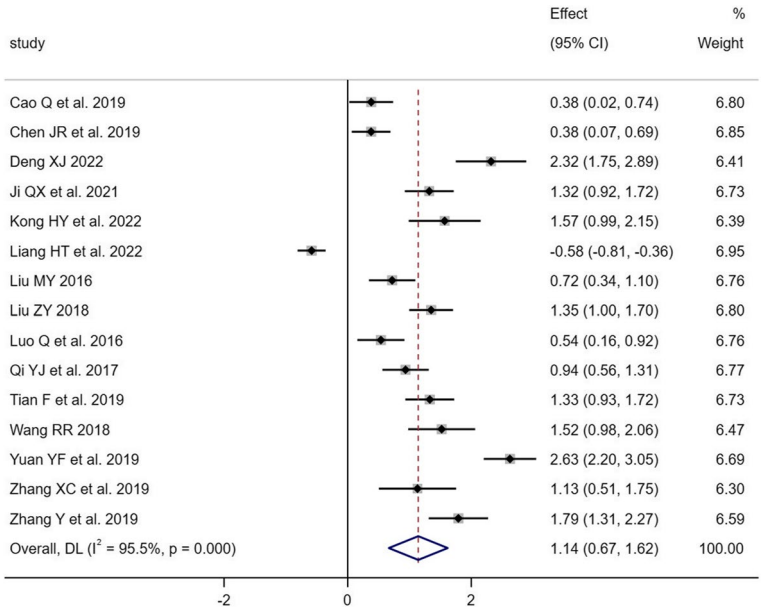

Fig. 4 Effect of JTG on the BMD(Lumbar)

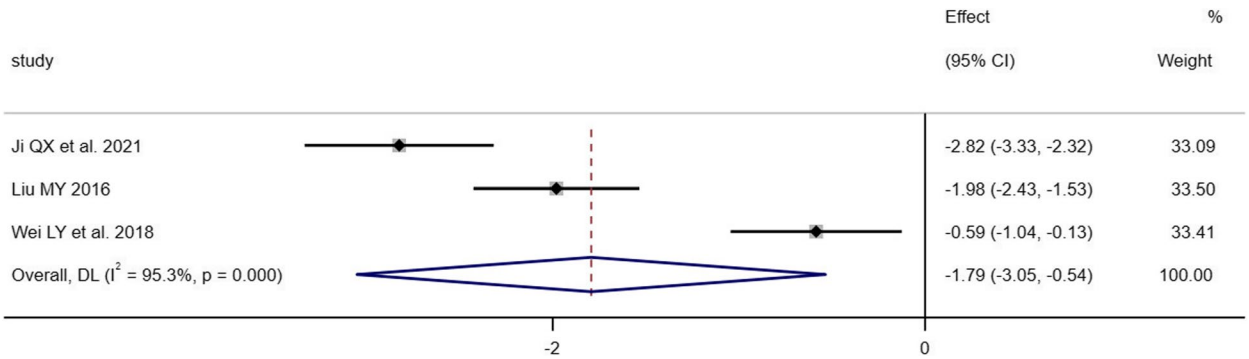

Fig. 5 Effect of JTG on the ODI

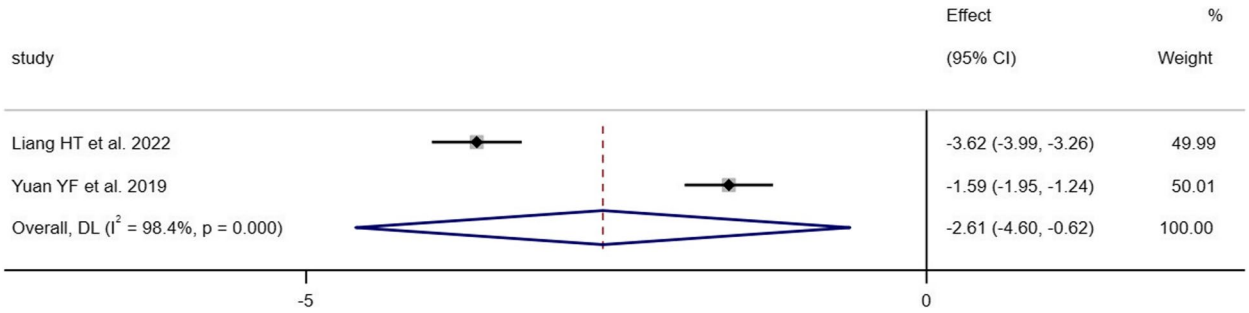

Fig. 6 Effect of JTG on the TUG

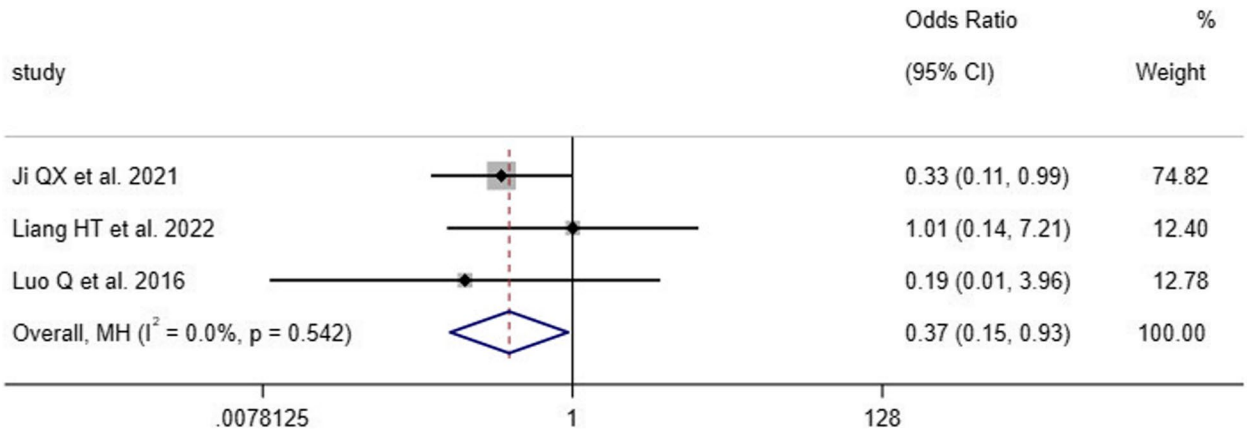

Fig. 7 Effect of JTG on the fracture incidence

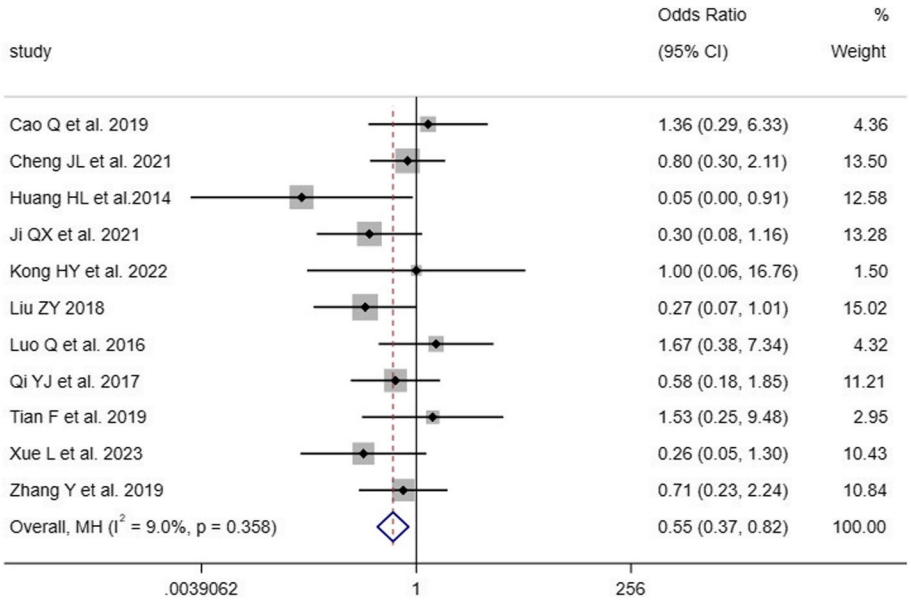

Fig. 8 Adverse event reporting

score greater than or equal to 6, indicating low risk bias (Table 2).

Primary outcomes

VAS

Twelve trials evaluated the VAS [41, 42, 44, 45, 47, 50–53, 55, 56, 58]. Meta-analysis showed a significant reduction in VAS in JTG (WMD: −2.51; 95% CI: −3.30, −1.71; $I^2 = 97.2\%$; $p < 0.05$). Compared to the control group, JTG was more effective in relieving pain. (Fig. 2).

Secondary outcomes

BMD(Femoral Neck)

Eleven trials evaluated the femoral neck BMD [31, 40, 41, 43, 47, 49–52, 54, 59] Meta-analysis indicated that the femoral neck of BMD was significantly improved in JTG (WMD: 0.83; 95% CI: 0.33, 1.33; $I^2 = 94.9\%$; $p < 0.05$). Compared with the control group, JTG improved BMD. (Fig. 3).

BMD(Lumbar)

Fifteen trials evaluated the lumbar BMD [31, 40, 41, 43, 45–52, 57–59]. The results of the meta-analysis demonstrated that JTG had significantly greater lumbar BMD

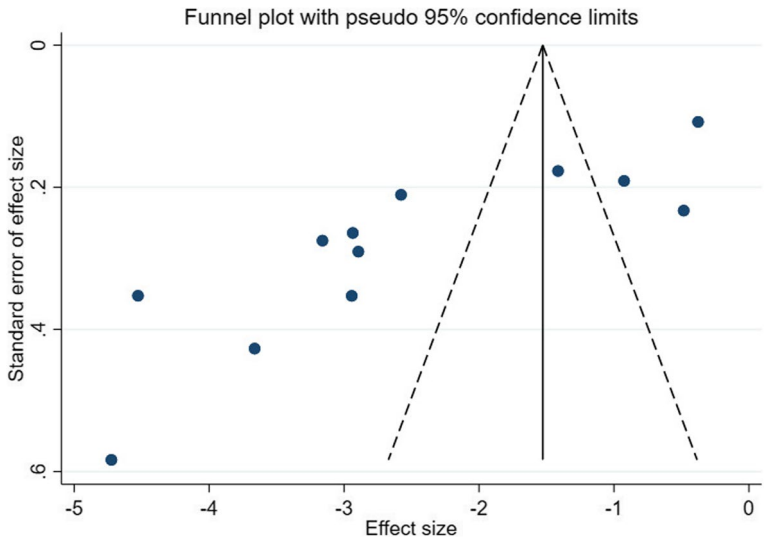

Fig. 9 Funnel plot of the VAS

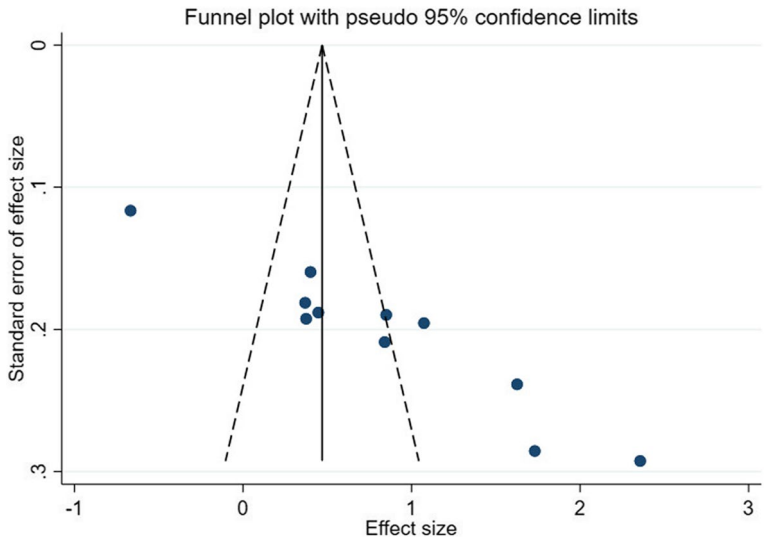

Fig. 10 Funnel plot of the BMD(Femoral Neck)

(WMD: 1.14; 95% CI: 0.67, 1.62; $I^2 = 95.5\%$; $p < 0.05$). In contrast to the control group, JTG produced greater increases in BMD. (Fig. 4).

ODI

Three trials evaluated the ODI [45, 47, 53]. Meta-analysis showed that ODI was significantly lower in JTG (WMD: −1.79; 95% CI: −3.05, −0.54; $I^2 = 95.3\%$; $p < 0.05$). Compared with the control group, JTG was more effective in improving activity function. (Fig. 5).

TUG

Two trials evaluated the TUG [31, 57]. The results of the meta-analysis indicated that TUG was significantly improved in JTG (WMD: −2.61; 95% CI: −4.60, −0.62; $I^2 = 98.4\%$; $p < 0.05$). Compared with the control group, JTG enhanced lower limb muscle strength and prevented falls better. (Fig. 6).

Fracture incidence

Three trials evaluated fracture incidence [31, 45, 49]. The incidence of fractures in JTG was much lower, according

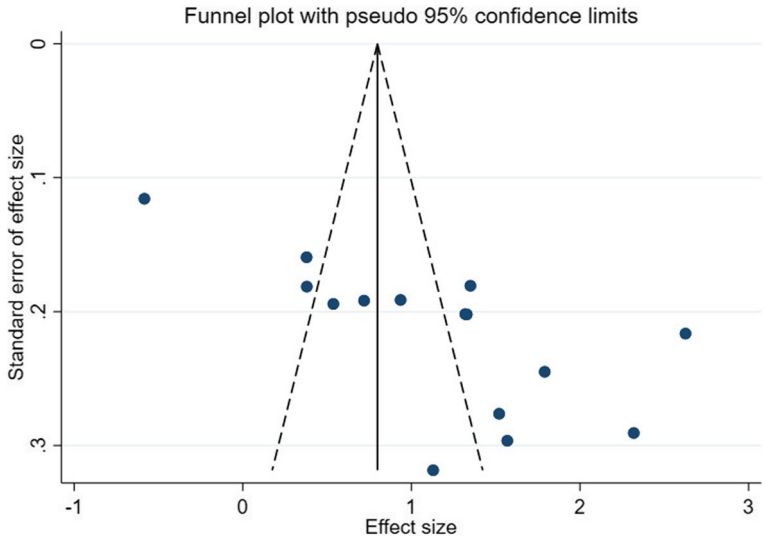

Fig. 11 Funnel plot of the BMD(Lumbar)

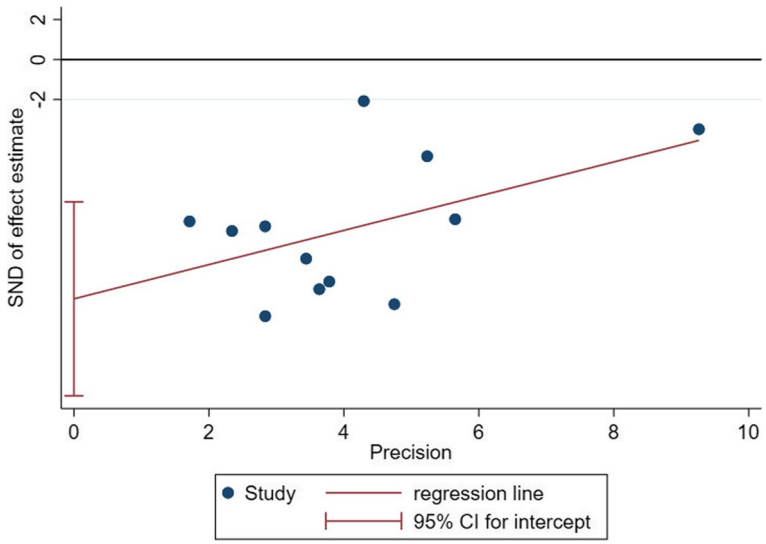

Fig. 12 Egger's test of the VAS

to the meta-analysis data (WMD: 0.37; 95% CI: 0.15, 0.93; $I^2 = 0.0\%$; $p < 0.05$). When it came to avoiding fractures, JTG performed better than the control group. (Fig. 7).

Adverse event reporting

Adverse events were reported in eleven trials [40, 42, 44–47, 49–51, 56, 59]. According to the meta-analysis, there were fewer adverse events in JTG compared to the control group. (WMD: 0.55; 95% CI: 0.37, 0.82; $I^2 = 9.0\%$; $p < 0.05$). The patients present with dry mouth, constipation, and a loss of appetite. (Fig. 8).

Publication Bias

We conducted publication bias analysis of trials with more than 10 outcome indicators, and the results showed poor symmetry (Fig. 9, Fig. 10, Fig. 11). Therefore, we conducted Egger's test. The results showed that there was publication bias ($P < 0.05$, Fig. 12, Fig. 13, Fig. 14).

Subgroup analysis

Due to the high heterogeneity of the meta-analysis results, we performed subgroup analyses of the VAS and BMD (femoral neck) by disease type and duration of treatment. The results showed that the difference

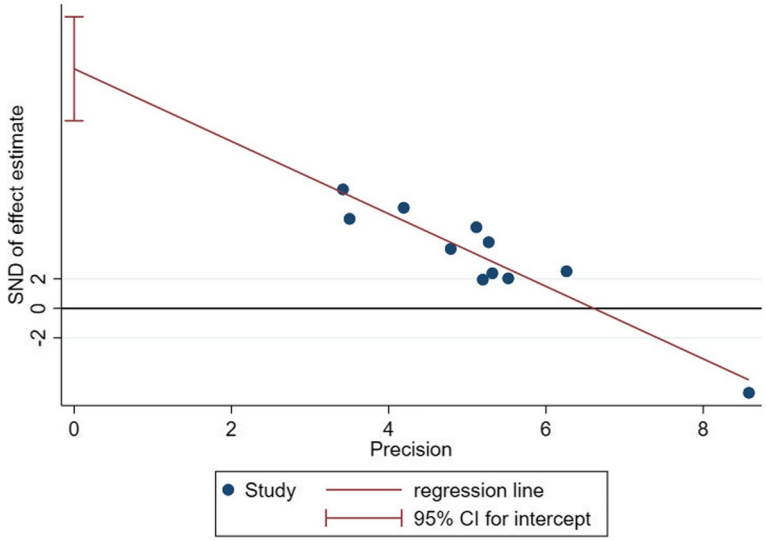

Fig. 13 Egger's test of the BMD(Femoral Neck)

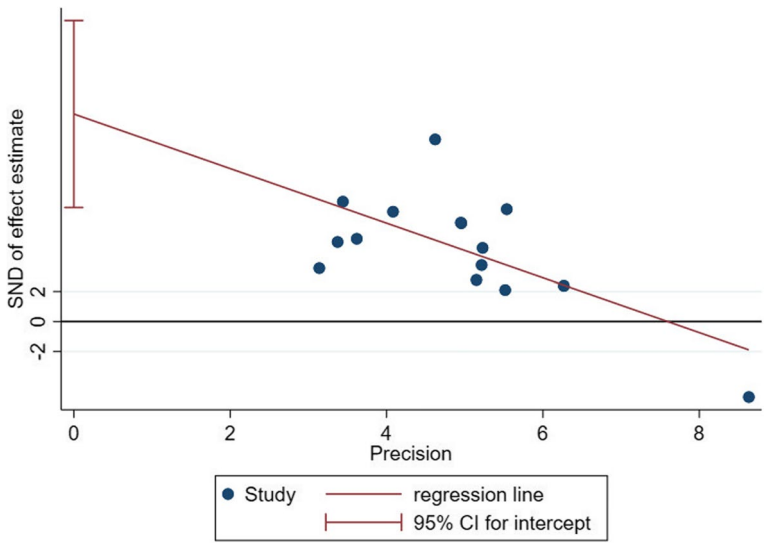

Fig. 14 Egger's test of the the BMD(Lumbar)

between the experimental group and the control group was statistically significant ($P < 0.05$, Fig. 15, Fig. 16, Fig. 17, Fig. 18).

Sensitivity analysis

Due to the high heterogeneity, we performed sensitivity analyses for the VAS and BMD(femoral neck). The results showed that it was still within the influence range, indicating that the results were stable (Fig. 19, Fig. 20).

Discussion

The most classic symptom in OP is generalized pain, and the risk of fracture increases with age as the muscles in the lower extremities diminish [60]. Therefore, relieving pain and preventing falls in OP patients are the primary goals. TCM has long been utilized as a supplemental and alternative treatment for OP. JTG is a capsule produced from artificial tiger bone powder. It contains bone-building characteristics and is used for the improvement of symptoms such as low back pain, lumbar and knee weakness, lower limb impotence, and difficulty walking [32].

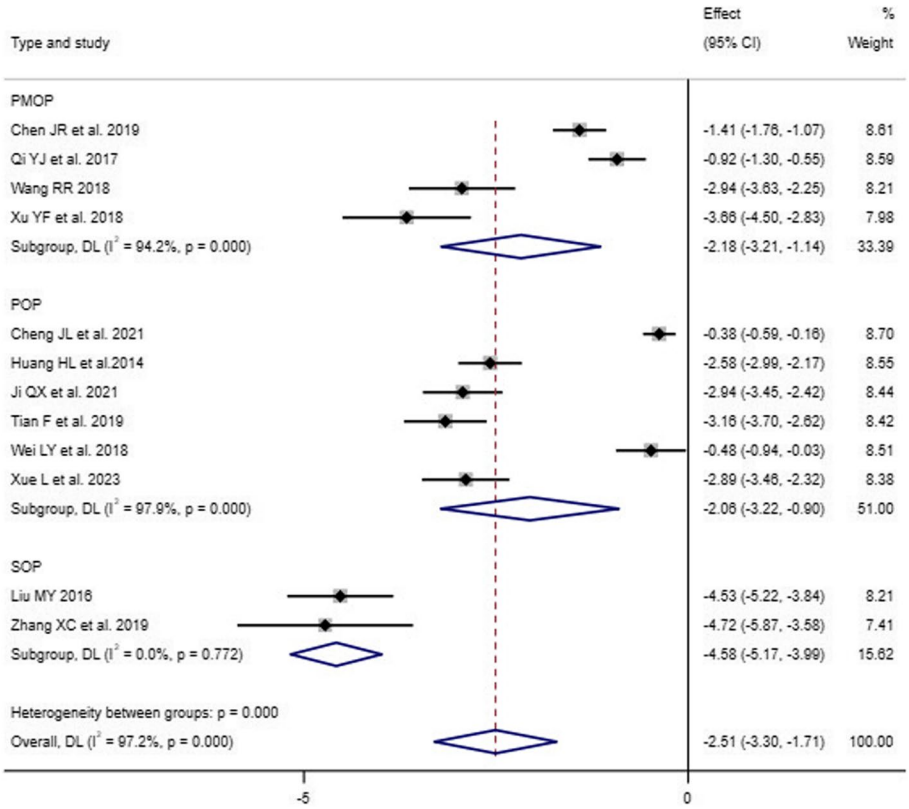

Fig. 15 Disease type subgroup analysis of the VAS

Tiger bone has significant anti-inflammatory, analgesic, and bone-building effects and is mainly used to treat OP and rheumatism. However, the production of medicines and other products containing tiger bone ingredients is currently prohibited. As a result, many proprietary Chinese medicines containing tiger bone ingredients can no longer be produced and used, resulting in the emergence of artificial tiger bone powder with similar ingredients. The main ingredient of JTG is artificial tiger bone powder, which contains 18 kinds of amino acids, more than 10 kinds of peptides, bone cell factors, and other bioactive substances, such as collagen and bone growth factor, which promote bone formation and regulate bone metabolism [61]. JTG can provide comprehensive bone-forming elements, which can improve bone quality, promote bone formation, and inhibit bone resorption via a bidirectional regulatory effect mechanism [62, 63]. Numerous studies have proven that JTG can be used to effectively treat OP, but the focus has not been on relieving pain or preventing fractures. Therefore, we synthesized a meta-analysis of the evidence related to the treatment of OP with JTG.

Chronic pain is a clinical manifestation of OP, and chronic pain in the musculoskeletal system can lead to disorders in the organ systems of the body, resulting in anxiety and depression [64]. Therefore, relieving painful symptoms was the primary goal in the treatment of OP. In this study, comparing JTG with conventional treatment, the results of twelve Rcts [41, 42, 44, 45, 47, 50–53, 55, 56, 58] showed a significant reduction in VAS. In a healthy skeletal micro-ecosystem, the activities of osteoblasts and osteoclasts maintained a delicate and fine dynamic balance, which was regulated by a variety of cytokines and hormones. The mechanism of OP was that bone formation lags behind bone destruction, and in the process of bone reconstruction, it was unable to completely repair the damaged bone, resulting in a continuous decrease in bone volume and bone quality. Therefore, the key to treating OP was to promote the osteogenic process of osteoblasts and relieve the osteoclastic process of osteoclasts. During the pathological evolution of POP, the activity of osteoclasts was abnormally enhanced, leading to an increase in the secretion of inflammatory factors, such as IL-1, IL-6, and TNF-α,

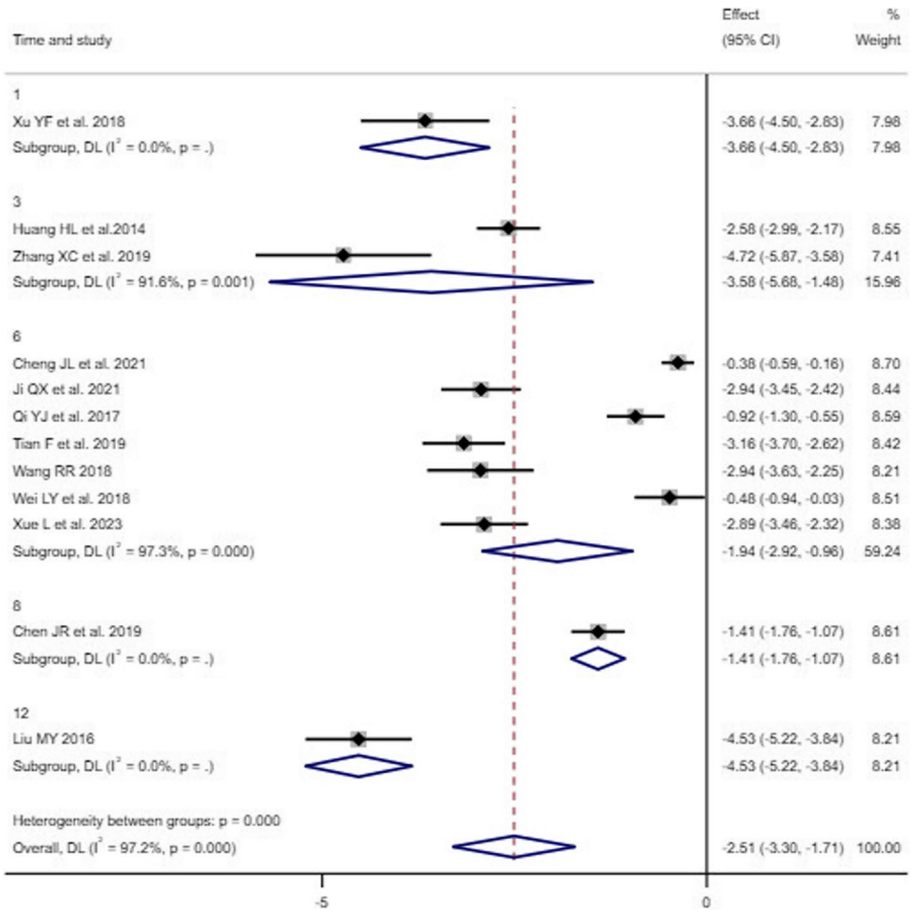

Fig. 16 Time subgroup analysis of the VAS

which in turn had a direct effect on cell differentiation and apoptosis [65]. Excess pro-inflammatory cytokines exacerbate pain and the deterioration of bone and cartilage [66]. It has been found that JTG can reduce serum IL-6 and IL-1β levels, inhibit inflammatory cytokine levels, and improve inflammatory responses, thereby relieving pain [67]. In addition, BMD was the criterion for the diagnosis of OP and patients with low BMD exhibited higher levels of pain [68]. In terms of BMD, eleven Rcts [31, 40, 41, 43, 47, 49–52, 54, 59] showed that the BMD of the femoral neck was higher in the JTG group than in the control group, and fifteen Rcts [31, 40, 41, 43, 45–52, 57–59] showed that the BMD of the lumbar spine was higher in the JTG group than in the control group, which suggested that JTG improved the BMD of the femoral neck and the lumbar spine, thereby relieving pain. JTG contained minerals, peptides, and proteins that exerted a regulatory effect on osteoblast and osteoclast activity, which increased BMD [29]. Thus, JTG can relieve pain by increasing BMD. Subgroup analyses were performed for disease classification and duration of treatment due to significant heterogeneity in results. Subgroup analyses showed a significant decrease in VAS and a significant increase in femoral neck BMD in the JTG group, suggesting that JTG was effective in relieving pain and improving BMD. Muscle and bone were closely related functionally, and higher muscle mass was strongly associated with increased BMD and reduced fracture risk in patients with POP. When the mechanical load exerted by muscle on bone exceeds a specific threshold, the increase in muscle mass led to tensile forces on the periosteum and collagen fibers, and the equilibrium of skeletal transformation changed significantly, from being dominated by bone resorptive activity to being dominated by bone formation, which triggered the release of skeletal growth potential and the acceleration of developmental processes [69, 70]. Therefore, three Rcts [45, 47, 53] showed that the ODI of JTG group was lower than that of the control group, two Rcts [31, 57] showed that the TUG of JTG group was lower than that of the control group,

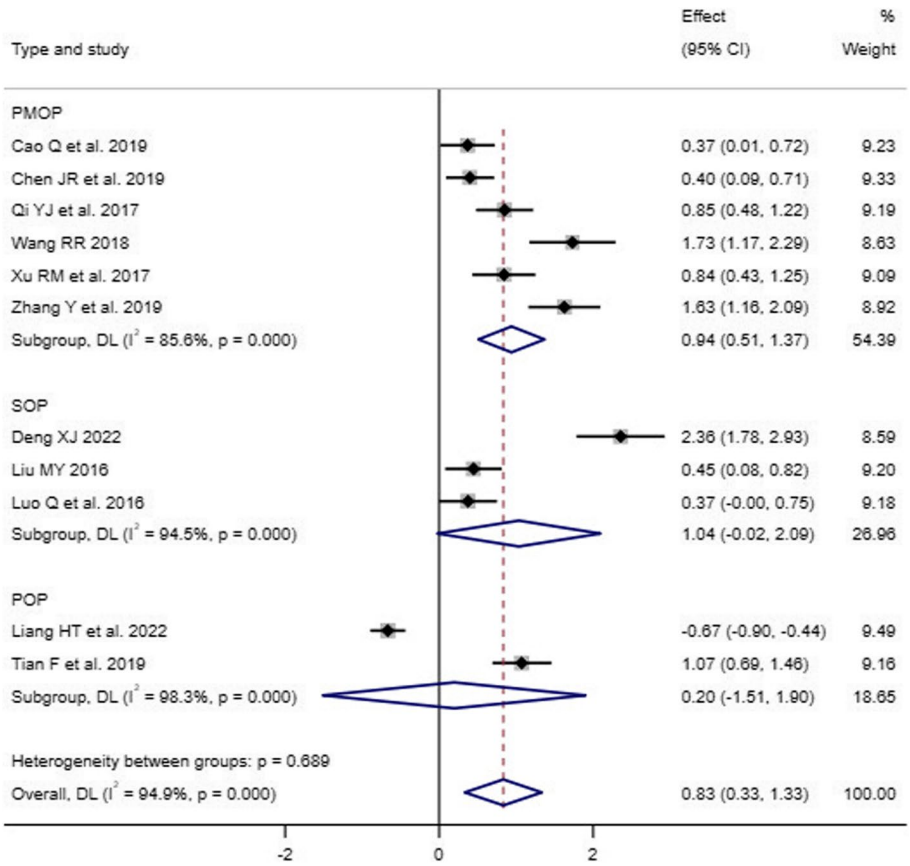

Fig. 17 Disease type subgroup analysis of the BMD(Femoral Neck)

and three Rcts [31, 45, 49] showed that the incidence of fracture of JTG group was lower than that of the control group, which suggested that JTG can effectively improve the function of activity, enhance the muscle strength of the lower limb, and reduce the incidence of fracture. The funnel plot showed the existence of publication bias, and we performed Egger's test, which showed the existence of publication bias, which may be related to the high heterogeneity. Therefore, we performed subgroup and sensitivity analyses, and the results were stable. JTG-related adverse events were mainly gastrointestinal problems such as dry mouth and constipation, and there was no serious hepatic or renal impairment or death. The adverse reactions reported in these studies were mild and of low incidence, with symptoms mostly resolving on their own after discontinuation of the drug or after symptomatic treatment, and no serious adverse reactions were seen, suggesting that JTG was safe for the treatment of POP.

There have been two articles [33, 71] on meta-analyses of JTG, both of which were meta-analyses of JTG for osteoporotic vertebral compression fracture pain, but no meta-analyses of JTG for OP. Both of these two articles and this study had VAS, BMD, and ODI, and both results showed better efficacy in the JTG group compared with the control group. However, in contrast to these two papers, the present study focused on the risk of falls and fractures in patients with OP, which was known to be a high risk of falls and fractures in patients with OP due to the brittleness of the bone and therefore must be emphasized.

This study had advantages and limitations that were worth mentioning. This study mentioned about the balance ability and fracture risk of the patients, which was an important aspect that needed to be focused on in order to prevent fracture in OP patients.

However there are several limitations. Firstly, The meta-analysis results were highly heterogeneous, and we only performed subgroup and sensitivity analyses, and further analysis of the reasons for the high heterogeneity was needed. Secondly, this study did not focus on serum indicators, especially BM. BM has a large impact on OP, which can reflect the status of BR and BF, and has

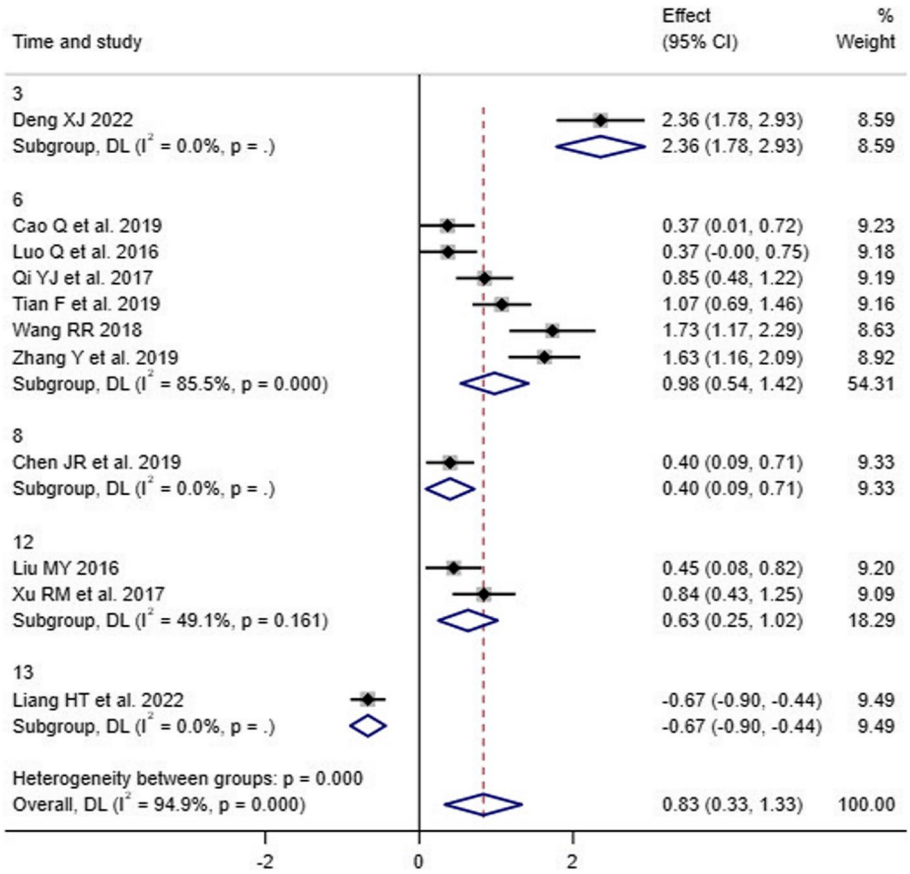

Fig. 18 Time subgroup analysis of the BMD(Femoral Neck)

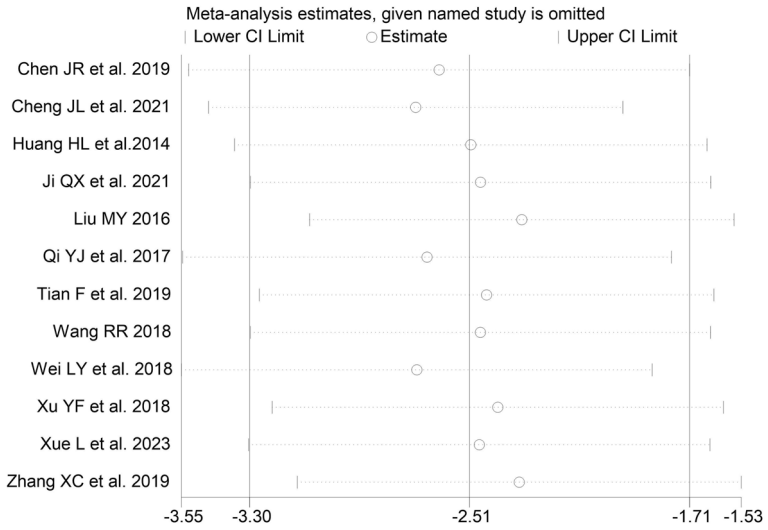

Fig. 19 Sensitivity analysis of the VAS

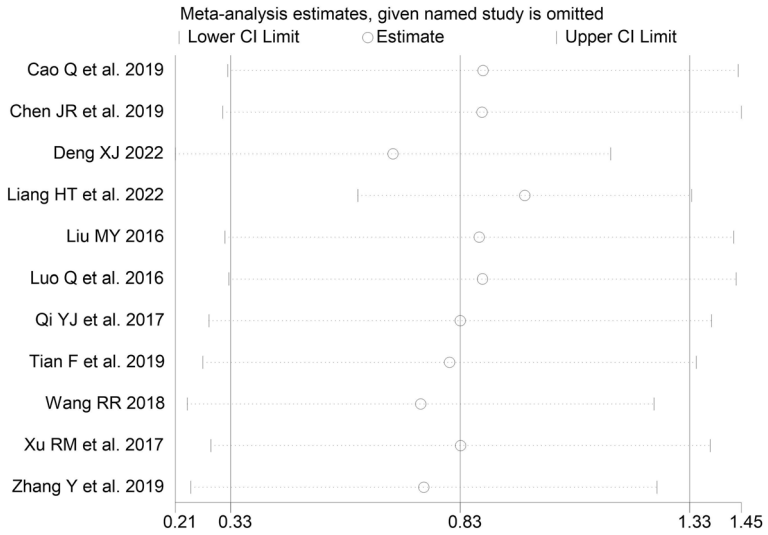

Fig. 20 Sensitivity analysis of the BMD(Femoral Neck)

a significant impact on the treatment of OP, so it needs to be emphasized. Thirdly, most of the literatures included in this study were in Chinese, with a lack of high-quality English literatures, which might limit the generalizability of the results. Given the limitations of this study, the efficacy of JTG in the treatment of OP needs to be verified in future clinical studies.

Conclusion

In conclusion, JTG can relieve pain, improve BMD and activity function, and reduce the risk of falls and fractures. It is an effective option for pain relief for patients with POP. Furthermore, the adverse events of JTG are mainly gastrointestinal problems, which require attention.

Abbreviations

ASIC-3	Acid-sensing ion channel-3
BF	Bone formation
BM	Bone metabolism
BMD	Bone mineral density
BMSCs	Bone marrow mesenchymal stem cells
BR	Bone resorption
CGRP	Calcitonine-Gene Related Peptide
CI	Confdence intervals
DXA	Dual-energy X-ray absorptiometry
JTG	Jintiange capsules
NMDA	N-methyl-D-aspartate
ODI	Oswestry disability index
OP	Osteoporosis
OR	Odds ratio
PEDro	Physiotherapy Evidence Database
PMOP	Postmenopausal osteoporosis
POP	Primary osteoporosis
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomized controlled trial
RR	Relative risk
SOP	Senile osteoporosis
TCM	Traditional Chinese medicine
TRPV1	Transient receptor potential vanilloid 1
TUG	Timed up and go test
VAS	Visual analogue score
WHO	World Health Organization
WMD	Weighted mean difference

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12891-025-08694-w.

Supplementary Material 1

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Not applicable.

Authors' contributions

The study was prepared by WL, MEL and XLS. Study selection and data extraction were performed by WL and BSY. Data analysis and interpretation were conducted by ZH, BSY and SLM. The manuscript was drafted by WL, BSY and SLM. Critical revision of the manuscript was performed by XJ, FQQ and YSL. All authors read and approved the final manuscript.

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Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests
The authors declare no competing interests.

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