Tropical Journal of Pharmaceutical Research October 2024; 23 (10): 1631-1637
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v23i10.6

Original Research Article

Effect of Henggu gushang mixture on low back pain, bone transformation, serum IGF-1 and Apelin-13 in elderly patients with osteoporosis

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Sent for review: 25 January 2024 *Revised accepted: 18 September 2024*

Abstract

Purpose: *To investigate the effect of Henggu gushang mixture on low back pain, bone transformation, serum insulin-like growth factor (IGF-1) and apelin-13 (Apelin-13) in elderly patients with osteoporosis.*
Methods: *A total of 80 elderly patients with osteoporosis in Ningbo Rehabilitation Hospital, Ningbo, China were divided randomly and equally into study and control groups. Study group received Henggu Gushang mixture in addition to calcium carbonate D3+ alfacalcidol for three months. Control group received calcium carbonate D3+ alfacalcidol. The effectiveness of therapy, visual analogue scale (VAS), levels of bone transformation markers (procollagen type I N-terminal propeptide (PINP) and type 1 collagen cross-linked C-telopeptide (CTX-1)), serum insulin-like growth factor (IGF-1), and Apelin-13 were compared. Adverse drug reactions were also recorded.*
Results: *Total response rate in the study group was significantly higher compared to control group ($p < 0.05$). It also showed significantly lower VAS scores after 7 days, 1 and 3 months of treatment compared to control group ($p < 0.05$). After treatment, the levels of PINP and CTX-1 were significantly lower while serum osteocalcin (OC), IGF-1 and Apelin-13 were significantly higher in the study group compared to control group ($p < 0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($p > 0.05$).*
Conclusion: *Henggu gushang mixture significantly relieves low back pain in elderly patients with osteoporosis, which is beneficial to improving bone transformation and metabolism. Future studies should focus on long-term outcomes using larger sample sizes from multi-center to better assess the therapeutic potential of this combined regimen.*

Keywords: *Elderly osteoporosis, Henggu gushang mixture, Low back pain, Bone transformation, Insulin-like growth factor, Apelin13*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, Web of Science, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Inadequate calcium intake presents a significant global nutritional challenge, particularly in developing nations and among populations primarily consuming plant-based diets, such as those in China. In developing countries, changes in dietary habits due to inconsistent food availability and uneven economic growth have affected calcium intake. In China, the adoption of vegetarian diets has exacerbated this issue. Addressing this challenge requires urgent

solutions and educational campaigns to raise public awareness about calcium intake and promote healthy eating habits.

Osteoporosis is characterized by decreased bone mass, microarchitectural deterioration, and susceptibility to fractures [1]. It is prevalent across various ethnicities and affects many older women and men. Attaining normal peak bone mass is crucial in preventing osteoporosis [2]. Adequate nutrition, including sufficient calcium and vitamin D intake, regular menstrual cycles, and a balanced exercise regimen, are key factors in achieving peak bone mass. During menopause, women experience accelerated bone loss. Major risk factors for fragility fractures include low body weight, prior fracture history, family history of osteoporosis, and smoking. To maintain bone health, individuals should ensure adequate calcium and vitamin D intake, engage in regular exercise, and take preventive measures against falls. These actions contribute to stronger bones, reducing the risk of fractures and osteoporosis [3].

Current treatment often involves bisphosphonates and calcium metabolism-regulating drugs to modulate bone metabolism [4]. However, long-term use of Western medicine is often hindered by various limitations and significant side effects, which affect adherence levels [5]. Traditional Chinese medicine attributes osteoporosis to bone atrophy and obstruction resulting from constitutional weakness, visceral deficiency, and weakened vital energy [6]. Deficiencies in the liver and kidneys, weakness in the spleen and stomach, insufficient vital energy, and difficulty in blood production and nourishment lead to blockages that hinder bone channel nourishment [7]. Treatment strategies should focus on kidney and spleen nourishment, vital energy invigoration, blood circulation promotion, and stasis dispelling. The Henggu Gushang mixture comprises traditional.

Chinese medicinal herbs such as astragalus, ginseng, and safflower. It invigorates vital energy, nourishes the liver and kidneys, and alleviates pain and swelling. Previous studies have utilized Henggu gushang mixture in treatments for fractures and knee osteoarthritis, demonstrating its efficacy in accelerating fracture healing, promoting local bone formation, and facilitating joint function recovery [4]. However, studies on the use of Henggu gushang mixture in elderly patients with osteoporosis, particularly regarding pain relief, bone turnover, and serum biomarkers, are limited. Investigating the therapeutic effects of this agent on osteoporosis is fundamental for patient benefit. Hence, this study was aimed at investigating the effect of Henggu Gushang mixture on back pain, bone turnover, and serum markers in elderly patients with osteoporosis.

METHODS

Patients

This study was a retrospective analysis of 80 elderly patients with osteoporosis treated at Ningbo Rehabilitation Hospital, Ningbo, China from July 2022 to July 2023. The participants were randomly and equally divided into study and control groups This study was approved by the Institutional Review Board of Ningbo Rehabilitation Hospital (approval no. NBR-043) and performed in accordance with the Declaration of Declaration of Helsinki guidelines [8]. All participants provided informed written consent prior to commencement of the study.

Inclusion criteria

Participants who met the Western medical diagnostic criteria [9], met the diagnosis and treatment guidelines for osteoporosis, with a T-score determined by x-ray absorptiometry below -1.0, met the Traditional Chinese Medicine diagnostic criteria [10] presenting with kidney deficiency pattern (main symptoms include generalized bone pain, lumbago with pain, aggravated pain upon prolonged standing or sitting, or exacerbation in the evening, dizziness, tinnitus, nocturia, pale tongue with white coating, and thin pulse), and above 65 years of age.

Exclusion criteria

Presence of severe liver or kidney dysfunction, secondary osteoporosis, history of osteoporosis-related fractures, participants experiencing severe adverse reactions or unexpected effects during treatment period that make it difficult to continue therapy, and voluntary withdrawal from the study. Study group comprised of 16 males and 24 females, body mass index (BMI) of 20 to 27 kg/m^2 (mean: 23.65 ± 1.62 kg/m^2). A total of 14 cases had concomitant hypertension, and 7 had diabetes. Control group comprised 13 males and 27 females, BMI of 20 to 28 kg/m^2 (mean: 24.01 ± 1.91 kg/m^2). A total of 17 cases had concomitant hypertension, and 6 had diabetes. There was no significant difference in baseline characteristics between the two groups (p > 0.05).

Treatment

Control group received 1 tablet of calcium

carbonate D3 (National Medicine Standard H10950029; 600 mg × 30 tablets; Wyeth Pharmaceuticals Co. Ltd) in addition to 1 capsule of alfacalcidol (National Medicine Standard J20171090, 0.25 µg × 20 capsules; Kunming Beikangdun Pharmaceutical Co. Ltd, Kunming, China) once daily for 3 months. Study group received 2 bottles of Henggu Gushang mixture (National Medicine Standard Z20025103; 25 mL × 6 bottles; Shenzhen Salubris Pharmaceuticals Co. Ltd, Shenzhen, China) once daily for 3 months in addition to the treatment given to the control group.

Evaluation of parameters/indices

Efficacy

Efficacy was classified as; *cure* (C): main and secondary symptoms disappeared, and an overall reduction in the score of traditional Chinese medicine syndromes exceeded 90 %); *marked improvement* (MI): main and secondary symptoms after treatment showed significant improvement compared to before treatment, and overall reduction in the score of traditional Chinese medicine syndromes was > 70 ≤ 90 %; *effective* (E): main and secondary symptoms improved to a certain extent compared to before treatment, and the overall reduction in the score of traditional Chinese medicine syndromes was > 40 % ≤ 70 %, and *ineffective* (I): no improvement or the condition worsened) [11]. Total effectiveness (TR) was calculated using Eq 1.

$$TR = ((C+MI+E)/n)100 \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

Level of lumbar back pain

Lumbar back pain was evaluated at 1, 4, and 12 weeks after treatment using the visual analogue scale (VAS) [12]. Scores on this scale range from 1 to 10, with higher scores indicating more severe pain.

Bone turnover index

Fasting venous blood (3 mL) was collected before and after treatment, and centrifuged. Levels of N-terminal propeptide of type 1 procollagen (PINP), and C-terminal telopeptide of type I collagen (CTX-1) were evaluated using enzyme-linked assays. Also, radioimmunoassay was used to measure the level of osteocalcin (OC). All reagent kits were purchased from Shanghai Yanshen Biotechnology Co., Ltd. (Shanghai, China).

Serum indices

Fasting venous blood (3 mL) was collected before and after treatment, centrifuged at 3000 rpm for 10 min, and serum was collected and radioimmunoassay was used to measure the level of insulin-like growth factor (IGF-1). Also, enzyme-linked assay was used to measure the level of endogenous ligand 13 (Apelin-13).

Adverse reactions

Adverse reactions during treatment were recorded and compared between the two groups.

Statistical analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) v22.0 software (IBM, Armonk, NY, USA). Normally distributed measurement data were presented as mean ± standard deviation (SD) and compared using the independent samples t-test. Paired t-test was used to compare differences within groups before and after treatment. Count data were presented as frequency and percentages and compared using chi-square test. $P < 0.05$ was considered statistically significant.

RESULTS

Efficacy

The study group showed significantly higher total effectiveness/efficacy after treatment compared to control group ($p < 0.05$; Table 1).

Level of pain

The study group showed significantly lower VAS scores at 1, 4, and 12 weeks after treatment compared to control group ($p < 0.05$; Table 2).

Table 1: Clinical efficacy (n = 40)

Group	Cure	Marked improvement	Improvement	Ineffectiveness	Total effective rate
Study	14(35.00)	17(42.50)	6(15.00)	3(7.50)	37(92.50)
Control	9(22.50)	12(30.00)	9(22.50)	10(25.00)	30(75.00)
χ^2					4.501
P-value					0.034

Table 2: Level of pain (n = 40; mean ± SD)

Group	Before Treatment	After treatment		
		1 week	*4 weeks*	*12 weeks*
Study	5.62±0.65	4.15±0.49*	3.22±0.48*#	1.04±0.32*#&
Control	5.41±0.78	4.74±0.48*	3.65±0.43*#	1.58±0.40*#&
F-value	0.934	5.440	4.221	6.667
P-value	0.353	< 0.001	< 0.001	< 0.001

*P < 0.05 vs before treatment, #p < 0.05 vs 1 week after treatment, &p < 0.05 vs 4 weeks after treatment

Table 3: Bone turnover (N = 40 in each group, mean ± SD)

Group	PINP (μg/mL)		CTX-1 (ng/mL)		OC (ng/mL)	
	Before	*After*	*Before*	*After*	*Before*	*After*
Study	35.86±4.45	26.39±3.12*	0.34±0.09	0.20±0.06*	5.07±1.02	9.83±1.02*
Control	36.15±4.66	29.70±3.19*	0.36±0.07	0.24±0.05*	5.19±1.13	8.16±1.13*
T-value	0.284	4.691	1.109	7.287	0.747	6.939
P-value	0.776	< 0.001	0.271	< 0.001	0.456	< 0.001

Note: *P < 0.05 vs before treatment

Table 4: Serum IGF-1 and Apelin-13

Group	IGF-1 (ng/mL)		Apelin-13 (pg/mL)	
	Before	*After*	*Before*	*After*
Study	80.19±6.52	105.49±9.93*	804.78±50.78	885.51±52.17*
Control	81.06±6.77	98.54±9.08*	806.12±50.98	853.34±53.49*
T-value	0.585	3.267	0.118	2.723
P-value	0.560	0.002	0.906	0.008

Note: *P < 0.05 vs before treatment

Bone turnover

Study group showed significantly lower levels of PINP and CTX-1 after treatment compared to control group (p < 0.05). Furthermore, study group showed significantly higher level of OC after treatment compared to control group (p < 0.05; Table 3).

Serum IGF-1 and Apelin-13

Study group showed significantly higher serum levels of IGF-1 and Apelin-13 after treatment compared to control group (p < 0.05; Table 4).

Incidence of adverse reactions

During treatment period, there were 2 cases of gastrointestinal reactions and 1 case of constipation which resolved after discontinuing the medication and providing dietary guidance in the study group. However, there was 1 case each of gastrointestinal reactions, liver damage, and dizziness. Symptoms in the control group were relieved after a brief rest. There was no significant difference in the incidence of adverse reactions between the two groups (p > 0.05).

DISCUSSION

The increasing trend of an aging population has led to a rise in cases of osteoporosis [13]. Underlying causes of osteoporosis are commonly linked to hormonal imbalances, nutritional deficiencies, and genetic factors. According to traditional Chinese medicine, primary causes of osteoporosis in the elderly are blood stasis, blockage of the collaterals, and deficiencies in the spleen and kidneys, which disrupt the balance of tendons and bones. Therefore, treatment aims to enhance blood circulation, nourish the liver and kidneys, and strengthen tendons and bones [14]. This study investigated the efficacy of Henggu gushang mixture (a traditional Chinese medicinal compound) in treating osteoporosis among the elderly. The compound includes a variety of traditional ingredients such as astragalus, safflower, notoginseng, and Eucommia ulmoides.

Eucommia bark is known for its properties to nourish the liver, tonify kidneys, strengthen tendons, and invigorate bones. Safflower and notoginseng enhance blood circulation, alleviate pain, and dissolve blood stasis. Similarly, *Eucommia ulmoides* is effective in activating blood circulation, dispelling wind, and alleviating pain. Honeysuckle also shares these benefits, promoting blood circulation and relieving pain. When these ingredients are combined, they synergistically nourish the liver and kidneys, promote blood circulation, and invigorate qi. Recent studies support these traditional uses, showing that astragalus inhibits bone resorption and boosts cellular metabolism [15], while

Eucommia ulmoides regulates the NF-κB pathway, reducing inflammation and promoting osteoblast proliferation [16]. Safflower and notoginseng possess anti-inflammatory effects, enhance blood circulation, reduce swelling, relieve pain, and improve tissue regeneration [17].

The findings of this study revealed that the study group showed significantly higher total efficacy compared to control group. Furthermore, study group showed significantly lower VAS scores 1, 4 and 12 weeks after treatment which is in tandem with recent findings [18]. This study also addresses the common symptom of lower back pain in osteoporosis patients, primarily caused by a reduction in lumbar vertebral mass. This loss compromises the supportive function of the spine leading to compensatory contraction of back muscles, fatigue, and persistent lower back pain even during rest [12]. The results of this study revealed that Henggu gushang mixture significantly lowered the symptoms of lower back pain in elderly patients with osteoporosis.

Furthermore, treatment with Henggu gushang mixture significantly reduced serum levels of PINP and CTX-1. Non-terminal propeptide of type 1 procollagen (PINP), derived from type I procollagen is a key component of the bone matrix which serves as a specific and sensitive marker of new bone formation occurring during osteoblast synthesis. C-terminal telopeptide of type 1 collagen (CTX-1) is the C-terminal peptide of type I collagen degradation product, and it is a sensitive marker for bone resorption. Elevated CTX-1 levels suggest increased bone resorption, indicating faster and more severe bone degradation [19]. Also, osteocalcin (OC) is a non-collagenous protein abundant in bone tissue, primarily produced by osteoblasts and certain chondrocytes which reflects bone activity and metabolic capacity [20].

The study group showed significantly higher levels of IGF-1 and Apelin-13 after treatment compared to control group. Insulin-like growth factor (IGF-1), a cytokine crucial for bone metabolism, aids in maintaining the integrity of trabecular bone and bone density and enhances osteoblast proliferation, differentiation, and recruitment. Reduction in IGF-1 has been associated with a higher fracture risk [21].

Apelin, a vasoactive peptide, participates in various bodily functions, including anti-inflammatory actions and fluid balance regulation. Apelin-13 plays a role in bone remodeling by activating intracellular signaling and promoting protein expression, with lower levels associated with more severe bone damage, suggesting its involvement in bone resorption and metabolism [22]. This study also revealed that Henggu gushang mixture in combination with Western medicine, provides synergistic benefits in calcium and phosphorus absorption and bone metabolism enhancement in osteoporosis patients. Also, there was no significant difference in the incidence of adverse reactions, suggesting that the integration of Henggu gushang mixture with conventional treatment remains safe and does not increase drug-related toxic side effects.

Limitations of the study

The small sample size, short-term follow-up, and single-center approach may limit the applicability of the study findings to a broader population.

CONCLUSION

Henggu gushang mixture improves efficacy, reduces pain, and lowers bone resorption, fracture risk and incidence of adverse reactions. Future studies should focus on long-term outcomes in larger sample sizes from various study centers to better assess the therapeutic potential of this combined regimen.

DECLARATIONS

Acknowledgements

None.

Funding

None provided.

Ethical approval

This study was approved by the Institutional Review Board of Ningbo Rehabilitation Hospital (approval no. NBR-043).

Availability of data and materials

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

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

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

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