Journal of Experimental and Clinical Application of Chinese Medicine

ORIGINAL RESEARCH

Open Access

Observation on the Clinical Efficacy of Combination therapy of Jiangu Buyuan Zhuyu Decoction and Western Medicine in the Treatment of POP

Wujie Zhai[1#*] and Wenjie Zhai[2#]

[1]The Hospital of Sinochem Second Constructing Group co, LTD, 030000 Taiyuan, Shanxi, China

[2]Xi County Longquan Town Health Centre, 041300 Linfen, Shanxi, China

Keywords

Jiangu Buyuan Zhuyu decoction, Primary osteoporosis, Bone mineral density, Bone metabolism

***Correspondence**

Wujie Zhai, The Hospital of Sinochem Second Constructing Group co, LTD, 030000 Taiyuan, Shanxi, China. E-mail: zhaiwujie7322759@163.com

Received:9 July 2022; Revised:23 August 2022; Accepted:11 September 2022; Published:15 September 2022

***Journal of Experimental and Clinical Application of Chinese Medicine* 2022; 3(3): 83 – 89.**

Abstract

Background To explore the efficacy of combination therapy of Jiangu Buyuan Zhuyu decoction and Alendronate Sodium tablets and Caltrate D tablets in patients with primary osteoporosis (POP).**Methods:** 130 patients with POP were divided into control group and observation group, with 65 cases in each group. The patients in the control group were treated with Alendronate Sodium tablets and Caltrate D tablets. In addition to the therapy applied to the control group, those patients in the observation group were treated with Jiangu Buyuan Zhuyu decoction. The numerical rating scale (NRS), Oswestry disability index (ODI), bone mineral density (BMD), osteoprotegerin (OPG), tartrate-resistant acid phosphatase (TRACP), β-crosslaps (β-CTX), serum calcitonin (CT) levels and the occurrence of adverse effects were compared before and after treatment. **Results:** After treatment, the total effective rate in the observation group was obviously higher than that in the control group, and the observation indexes of both groups were lower, and those in the observation group were lower than the control group. The BMD in femoral neck, Wards triangle, lumbar vertebrae L_2-L_4 and CT of both groups were higher after treatment, and those in the observation group was higher than that in the control group. There was no significant difference concerning the incidence of adverse effects.**Conclusion:** Combination therapy of Jiangu Buyuan Zhuyu decoction, Alendronate Sodium tablets, and Caltrate D tablets has significant efficacy in the treatment of POP, with pain reduction, BMD improvement, and bone metabolism regulation.

1 Introduction

Osteoporosis, one of the most prevalent metabolic bone diseases, is characterized by the reduction on the bone mass and the degradation of the bone tissue, which causes the increase on bone fragility and the risk for fracture (1, 2). Osteoporosis includes both primary and secondary osteoporosis, of which primary osteoporosis (POP) is composed of postmenopausal osteoporosis and senile osteoporosis. The pathogenesis of POP remains unknown, and may be caused by several factors, such as low calcium intake, Vitamin D deficiency, smoking, alcohol consumption, and lack of exercise (3). At present, there remains a clinical controversy on the treatment of POP, and the Western medicine mainly centers on the applications of bone resorption inhibitors, bone mineralizers, and bone formation promoter. Nevertheless, it has been reported to have some side effects and to fail to achieve the anticipated clinical efficacy (4). The combination therapy of Traditional Chinese and Western medicine has a long history and has achieved better results in the treatment of a variety of diseases (5-7). Our current study mainly aims to investigate the clinical efficacy of the combination therapy of Jiangu Buyuan Zhuyu decoction and the tablets of Alendronate Sodium and Caltrate D in the treatment of patients with POP, and further evaluate its effects on the degree of pain, bone mineral density (BMD) and bone metabolic indexes in patients with POP.

2 Materials and methods

2.1 Ethics statement

Our hospital's Ethics Committee has reviewed and approved our study, and all patients or their legitimate guardians have also signed the written informed consent for our study.

2.2 Subjects

130 patients diagnosed with OP and admitted in our hospital from May 2018 to March 2020 were assigned to the control group and the observation group using the random number table method, with 65 cases in each group. All information on the patients was detailed in Table 1. There was no statistical significance between these two groups when it came to the basic data but the data were comparable. All patients enrolled complied to the criteria as listed.

Inclusion criteria: a) patients were conformed to the diagnostic criteria of OP in accordance with the diagnostic criteria for osteoporosis in the *Guidelines for the Treatment of POP* (8); b) based on the results of DXA measurements, T-value ≥ -1.0 was considered normal, -2.5 < T-value < -1.0 was deemed as low bone mass, T-value ≤ -2.5 was suggested as osteoporosis and T-value ≤ -2.5 + indicated severe osteoporosis; c) patients who were conscious and were capable of normal communication.

Exclusion criteria: a) patients with a history of psychiatric illness or severe physical impairment; b) patients with combined cardiac, hepatic, or renal insufficiency; c) patients who were allergic to the investigational medication; d) patients with secondary osteoporosis.

Table 1.Patients' general information

Group	Case	Gender		Age (Year)	Course of diseases (Year)	BMI (kg/m^2)
		Male	Female			
Observation group	65	21	44	62.44±7.58	5.72±1.83	23.14±2.66
Control group	65	23	42	63.65±8.25	5.94±1.76	22.84±2.57
χ^2/t		0.137	-0.871	-0.699	0.654	
P		0.711	0.386	0.486	0.514	

2.3 Treatment regimens

For patients in the control group, they were orally

administrated with Alendronate Sodium tablets (Ouyi Pharmaceutic Co., Ltd., CSPC, Approval number for National Medical Products Administration: H20061303, specification: 70 mg) and Caltrate D tablets (Wyeth Pharmaceuticals, Inc., Approval number for National Medical Products Administration: H10950029, specification: 600 mg* 60 pieces). Each time, Alendronate Sodium tablets were administrated with 1 piece once for a week, while 2 pieces of Caltrate D tablets were applied once for a week. The entire course lasted for 12 weeks.

In addition to the therapy applied to the control group, the patients in the observation group were additionally treated with Jiangu Buyuan Zhuyu decoction which was composed of 30 g Huang Qi (*Radix Astragali Mongolici*), 15 g Yin Yang Huo (*Epimedii Herba*), 15 g Lu Jiao Jiao (*Cornus Cervi Colla*), 10 g Gui Jiao (*Colla Carapacis*), 10 g Bu Gu Zhi (*Psoraleae Fructus*), 15 g Shan Yao (*Psoraleae Fructus*), 10 g Shui Zhi (*Hirudo*), 10 g Shu Di (*Radix Rehmanniae Praeparata*), 10 g Fu Ling (*Poria*), 10 g Bai Shao (*Radix Paeoniae Alba*), and 10 g Chuan Niu Xi (*Radix Cyathulae*). All the formulas were decocted with 500 ml water to a final volume of 150 ml, which were taken in the morning and evening in divided doses for total 12 weeks of continuous treatment.

2.4 Observational index

(I) Clinical efficacy: the clinical efficacy of patients in these two groups was evaluated with reference to the assessment criteria of *the guiding principles for Clinical Research on New Chinese Medicines* (9). Excellent effective: the pain in the patients completely disappeared, and the bone density increased. Effective: the pain of the patients partially disappeared, and the bone density didn't change significantly. Ineffective: the pain of the patients didn't improve significantly, and the bone density did not change or even decreased. Total effective rate = cases of (cured + effective + effective) / total cases × 100%.

(II) Pain scoring and functional improvement grading: the numerical pain scoring method (NRS) was used for pain scoring of patients in both groups, with 0 being no pain, 1 to 3 being mild pain, 4 to 6 being moderate pain, 7 to 9 being severe pain, and 10 being severe pain (10). The Oswestry disability index (ODI) scale was used for functional improvement grading in patients of both groups, which included 10 aspects like intensity of pain, self-care, lifting, walking, sitting, standing, sleep disturbance, sexual life, social life, and travel, etc., with 10 questions for each aspect and a score of 0 to 5 for each question. The higher total scores indicated more severe dysfunction.

(III) BMD value: Dual-energy X-ray bone densitometer (Xuzhou Pingyuan Medical Technology Co., Ltd., model no. Dexa Pro-I) was used to measure the BMD of different parts of the patient, including femoral neck, Wards triangle, and lumbar vertebrae L_2-L_4.

(IV) Bone metabolic indexes: 5 mL of fasting venous blood was collected from patients before and after treatment, and the levels of osteoprotegerin (OPG) and serum calcitonin (CT) were measured by radioimmunoassay, while the levels of tartrate-resistant acid phosphatase (TRACP) and β-collagen degradation product (β-CTX) were measured by enzyme-linked immunosorbent assay.

(V) Adverse effects: the gastrointestinal reactions, fever and belching in patients of the both groups were evaluated.

2.5 Statistical analysis

Data were expressed as mean ± standard deviation (SD), which were analyzed using SPSS software (version 20.0, IBM Corporation, Endicott, NY, USA). Statistical significance was determined with both chi-square test and *t* test and comfirmedwhen *P*-value was below 0.05.

3 Results

3.1 Comparison on clinical efficacy

A statistical significance concerning clinical efficacy in the patients of these two groups was exhibited, and the clinical efficacy in patients of the observation group was evidently higher than of the control group (p<0.05; Table 2).

Table 2. The comparison on the clinical efficacy [case (%)]

Group	Case	Excellent effective	Effective	Ineffective	Total effective rate
Observation group	65	26 (40.00)	33 (50.77)	6 (9.23)	59 (90.77)
Control group	65	15 (23.08)	35 (53.85)	15 (23.08)	50 (76.92)
χ^2					4.600
P					0.032

3.2 Comparison on NRS and ODI scores

No significant difference was seen concerning NRS and ODI scores in patients before treatment (p>0.05; Table 3). After treatment, however, NRS and ODI scores for patients in these two groups were decreased, and patients in the observation group exhibited lower NRS and ODI scores when compared with those in the control group (p<0.05; Table 3).

3.3 Comparison on the BMD value

Before the treatment, no statistical significance concerning BMD value of different parts of the patients was reported (p>0.05; Table 4). However, as compared to those before treatment, the BMD values in femoral neck, Wards triangle, and lumbar vertebrae L_2-L_4 of all patients were increased evidently, among which patients in observation group presented with higher BMD value than those of control group (p<0.05; Table 4).

3.4 Comparison on the Bone metabolic indexes

Before treatment, there was no statistically significance in the levels of OPG, TRACP, β-CTX and CT between the two groups (P>0.05; Table 5) yet the levels of CT were significantly higher than before treatment (P<0.05; Table 5). After treatment, the levels of OPG, TRACP and β-CTX in the two groups were significantly lower than before treatment, and patients in the observation group presented lower levels of OPG, TRACP and β-CTX yet higher CT level in the control group (P<0.05; Table 5).

Table 3. The comparison on the NRS and ODI scores (Point)

Group	Case	NRS		ODI	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	65	5.85±1.64	1.02±0.34*	30.42±4.67	14.43±3.47*
Control group	65	5.62±1.52	1.75±0.48*	31.50±5.26	18.26±4.20*
t		0.829	-10.006	-1.238	-5.668
P		0.408	0.000	0.218	0.000

*p<0.05, vs. Before treatment

Table 4. The comparison on the BMD value of different parts (g/cm^2)

Group	Case	femoral neck		Wards triangle		lumbar vertebrae L_2-L_4	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	65	0.64±0.15	0.77±0.20*	0.48±0.14	0.60±0.16*	0.66±0.18	0.78±0.21*
Control group	65	0.66±0.18	0.70±0.16*	0.45±0.12	0.52±0.15*	0.62±0.20	0.70±0.19*

t	-0.688	2.203	1.312	2.941	1.199	2.387
P	0.493	0.029	0.192	0.004	0.233	0.018

*p<0.05, vs. Before treatment

Table 5. The comparison on Bone metabolic indexes

Group	Case	OPG (ng/L)		TRACP (U/L)		β-CTX (ng/mL)		CT (μg/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	65	463.50±62.43	223.44±35.72*	4.85±1.26	2.16±0.68*	0.62±0.18	0.31±0.10*	41.46±8.63	55.43±7.80*
Control group	65	452.64±58.44	284.62±48.66*	5.02±1.35	2.75±0.80*	0.65±0.20	0.42±0.12*	42.70±9.52	50.46±8.33*
t		1.024	-8.171	-0.742	-4.530	-0.899	-5.677	-0.778	3.596
P		0.308	0.000	0.459	0.000	0.370	0.000	0.438	0.001

*p<0.05, vs. Before treatment

3.5 Comparison on the adverse effects

The incidence of adverse effects in the observation group was 10.77% (7/65), including 4 cases of gastrointestinal reactions, 2 cases of fever and 1 case of belching. The incidence of adverse reactions in the control group was 15.38% (10/65), including 6 cases of gastrointestinal reactions, 1 case of fever and 3 cases of belching. There was no statistically significance on the incidence of adverse reactions in the two groups (χ^2=0.609, P=0.435).

4 Discussion

POP is a systemic bone disease which occurs in the middle-aged and elderly population, and patients diagnosed with POP may present clinically with some symptoms such as weakness, generalized bone pain, shortened body length, hunchback, and even fractures (11). Alendronate sodium and Caltrate D tablets are commonly used in the practice of Western medicine for the treatment of POP, of which alendronate is a bisphosphonate drug that reduces bone resorption and inhibits osteoclast activity (12). In addition, Caltrate D tablets are a combination of calcium carbonate and Vitamin D3, the latter of which acts on the small intestine to promote its reabsorption of calcium ions (10). In the belief of Chinese medicine, osteoporosis belongs to the categories of “bone impotence” and “bone pole”, which is mainly related to the deficiency of kidney essence, the weakness of spleen and stomach, the deficiency of liver and blood, and the obstruction of blood stasis. Therefore, the treatment of osteoporosis should be based on tonifying the kidney and benefiting the marrow, strengthening the spleen and stomach, de-stressing the liver, and activating blood circulation and removing blood stasis (13).

Patients with POP often exhibit the damage to the bone microstructure of the body and disorders of calcium and phosphorus metabolism and suffer from decreased bone density and bone loss, which cause pain and the degeneration of body functions. The NRS and ODI scores are two important indicators for the determination on the pain and function in patients with POP. BMD is an important indicator for the diagnosis of osteoporosis, the change of which can reflect the severity of osteoporosis in the organism. The results of our present study showed that after treatment, the total effective rate of the patients in observation group was significantly higher than that of the control group, and the BMD, NRS and ODI score, femoral neck, Wards triangle and lumbar L2-L4 in both groups were improved significantly as compared with those before treatment. More importantly, the degree of improvement of the observation group was significantly better than that of

the control group, indicating that the pain level and BMD of different parts of POP patients were improved after treatment. This is due to the fact that Alendronate Sodium tablets can bind to hydroxyapatite on the surface of the bones and inhibit the formation of hydroxyapatite crystals, thus repressing bone resorption, improving bone mineralization, effectively increasing the thickness of the bone cortex and bone density, and finally enhancing the bone strength of the body in the end (14, 15). The Vitamin D component in Caltrate D tablets can participate in the body's metabolism of calcium, promote calcium absorption and facilitate the bone formation. In the present study, we applied the formula of Jiangu Buyuan Zhuyu Decoction to treat patients with POP, which contains Huang Qi (*Radix Astragali Mongolici*), Yin Yang Huo (*Epimedii Herba*), Lu Jiao Jiao (*Cornus Cervi Colla*), Gui Jiao (*Colla Carapacis*), Bu Gu Zhi (*Psoraleae Fructus*), Shan Yao (*Psoraleae Fructus*), Shui Zhi (*Hirudo*), Shu Di (*Radix Rehmanniae Praeparata*), Fu Ling (*Poria*), Bai Shao (*Radix Paeoniae Alba*), and Chuan Niu Xi (*Radix Cyathulae*), among which Huang Qi (*Radix Astragali Mongolici*), Shan Yao (*Psoraleae Fructus*), and Fu Ling (*Poria*) have the effect of tonifying Qi, strengthening the spleen, eliminating swelling and detoxifying. Yin Yang Huo (*Epimedii Herba*) and Bu Gu Zhi (*Psoraleae Fructus*) can tonify liver and kidney and strengthen tendons and bones. Lu Jiao Jiao (*Cornus Cervi Colla*), Gui Jiao (*Colla Carapacis*), Shu Di (*Radix Rehmanniae Praeparata*), and Bai Shao (*Radix Paeoniae Alba*) nourishes blood and Yin, opens the channels and relieves pain. Shui Zhi (*Hirudo*) and Chuan Niu Xi (*Radix Cyathulae*) are contributory to activating blood circulation, removing blood stasis, clearing menstruation and reducing inflammation. The combination of these drugs can detoxify toxins, invigorate blood circulation, tonify the kidney and benefit the stomach. The combination therapy of Jiangu Buyuan Zhuyu Decoction with Alendronate Sodium tablets and Caltrate D tablets has a synergistic effect in treating patients with POP, which effectively relieves patients' pain and improves body dysfunction and bone density.

Patients with POP often show abnormal bone metabolism, and bone metabolic indexes such as OPG, TRACP, β-CTX and CT can reflect the bone transformation of the body: OPG and TRACP are metabolic indexes to evaluate bone formation and bone resorption in the body (16). β-CTX is a typical product of the de-gradated type I collagen, whose level reflects the degree of bone resorption in the body. CT can inhibit the activity and proliferation of osteoclasts, which represses the bone resorption function of osteoclasts and promotes the bone growth of the body (17). The results of this study showed that after treatment, the levels of OPG, TRACP and β-CTX in patients of both groups were significantly lower yet the levels of CT were evidently higher than before treatment. Additionally, the levels of OPG, TRACP and β-CTX in the observation group were significantly lower yet the levels of CT in the observation group were significantly higher than those in the control group, indicating that the combination therapy of Jiangu Buyuan Zhuyu Decoction with Alendronate Sodium tablets and Caltrate D tablets can improve the bone metabolism of patients with POP. The level of bone metabolism indexes in POP patients is improved, which is because Alendronate Sodium tablets can reduce the number of osteoclasts and inhibit their activity, thus reducing bone resorption and the indexes of OPG, TRACP and β-CTX, increasing bone formation and bone conversion rate as well as the index of CT level, and restoring the balance of bone metabolism, all of which can improve the bone conversion in the body. In addition, the active ingredients of Bu Gu Zhi (*Psoraleae Fructus*) and Lu Jiao Jiao (*Cornus Cervi Colla*) in Jiangu Buyuan Zhuyu Decoction have the effect of promoting the DNA synthesis of bone marrow cells and the proliferation and differentiation of osteoblasts, which can promote bone formation, inhibit bone resorption, and further improve bone trabecular structure and bone density. Yin Yang Huo (*Epimedii Herba*) has been found to promote the proliferation and differentiation of osteoblasts through the induction of bone marrow mesenchymal stem cells (BMSCs), thus facilitating bone formation, inhibiting

bone resorption, and ultimately reestablishing the balance of bone metabolism. The extract from Huang Qi (*Radix Astragali Mongolici*) has been documented to down-regulate the expression of toll-like receptor 4 (TLR-4) in osteoblasts, which thus affects the expression of its associated proteins, promotes osteoblast proliferation and differentiation, and improves bone transformation in the organism (18, 19). In this study, no statistically significant difference in the incidence of adverse effects between the two groups after treatment was reported, indicating that the combination therapy of Jiangu Buyuan Zhuyu Decoction with Alendronate Sodium tablets and Caltrate D tablets has better safety.

In conclusion, the combination therapy of Jiangu Buyuan Zhuyu Decoction with Alendronate Sodium tablets and Caltrate D tablets has significant efficacy, which can relieve the pain, improve patients' body function, bone density and bone metabolic index level, and maintain bone transformation balance in patients with POP.

Acknowledgements

Not applicable.

Conflict of Interest

The authors declare no conflicts of interest.

Author contributions

Conceptualization, Wu.J.Z and Wen.J.Z; Data curation,Wu.J.Z; Formal analysis, Wen.J.Z Methodology, Wu.J.Z; Writing-Original draft, Wen.J.Z and Wu.J.Z; Writing-review and editing, Wen.J.Z and Wu.J.Z; All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

The study was approved by the Medical Ethics Committee, and the patients were informed and consented.

Funding

This research received no external funding.

Availability of Data and Materials

The data presented in this study are available on request from the corresponding author.

Supplementary Material

Not applicable

References

[1] Kelch S, Balmayor ER, Seeliger C, Vester H, Kirschke JS, van Griensven M. miRNAs in bone tissue correlate to bone mineral density and circulating miRNAs are gender independent in osteoporotic patients. Sci Rep. 2017;7(1):15861.

[2] Liu R, Chao A, Wang K, Wu J. Incidence and risk factors of medical complications and direct medical costs after osteoporotic fracture among patients in China. Arch Osteoporos. 2018;13(1):12.

[3] Chen J, Hong Z, Zhao C, Bi Q, Qiu B. Associations between polymorphisms of the PDLIM4 gene and susceptibility to osteoporotic fracture in an elderly population of Han Chinese. Biosci Rep. 2019;39(1).

[4] Na J, Yang D. Traditional Chinese Medicine Research Progress of Targeted Therapy of Pimary Osteoporosis. Chinese Archives of Traditional Chinese Medicine. 2017;35(9):2429-32.

[5] Liu F, Qiu Y. Acupuncture and Other Chinese and Western Medicine Treatment of Children with Cerebral Palsy. Chinese Archives of Traditional Chinese Medicine. 2017;35(8):2161-4.

[6] Fu H, Wen X. Effect of Traditional Chinese Combined with Western Medicine in Treating Patients with COPD. Chinese Archives of Traditional Chinese Medicine. 2015;33(11):2650-2.

[7] Huang W, Li Z, Zheng X, Yang F. A systematic review of the efficacy of Chinese patent drugs on primary osteoporosis. Chinese Journal of Osteoporosis. 2019;25(12):1798-808.

[8] Xia W, Zhang Z, Lin H. Guidelines for the diagnosis and management of primary osteoporosis (2017). Chinese Journal of Osteoporosis. 2019;25(3):281-309.

[9] He X, Zhou Y. Clinical effect of Jianpi Zhuanggu decoction combined with Alendronate Sodium on

osteoporosis. Chinese Traditional Patent Medicine. 2019;41(5):1193-6.

[10] Lvu J, Luo J, Gu S, Zhu Q. Effect of Method of Tonifying Kidney and Spleen and Removing Blood Stasis on Patients with Primary Osteoporosis Postmenopausal and the Influence on Indicators of Bone Metabolism. Chinese Archives of Traditional Chinese Medicine. 2017;35(5):1278-81.

[11]Zhang Q, Cai J, Jin Y, Li Z, Hu N, Xu S. A study on the relationship of serum 25-hydroxyVitamin D levels, bone mineral density and body mass index in middle-aged and elderly women. Chinese Journal of Osteoporosis. 2020;26(3):328-32.

[12]Songpatanasilp T, Rojanasthien S, Sugkraroek P, Ongphiphadhanakul B, Robert L, Robert CS, et al. Open-label study of treatment with Alendronate Sodium plus Vitamin D in men and women with osteoporosis in Thailand. BMC Musculoskelet Disord. 2018;19(1):392.

[13]Zhao Z, Yan X. A study on the improvement of clinical symptoms of primary osteoporosis with tonifying kidney method by traditional Chinese medicine. Chinese Journal of Osteoporosis. 2018;24(3):371-5,410.

[14]Zhang Y, Chen X, Tang Y, Lu Y, Guo L, Zhong D. Bioequivalence of generic Alendronate Sodium tablets (70 mg) to Fosamax(®) tablets (70 mg) in fasting, healthy volunteers: a randomized, open-label, three-way, reference-replicated crossover study. Drug Des Devel Ther. 2017;11:2109-19.

[15]Que M, Shi C, Huang Y, Zhan Q, Huo C, Zhou C, et al. Network meta-analysis of different drugs for the treatment of primary osteoporosis. Chinese Journal of Tissue Engineering Research. 2020;24(35):5715-22.

[16]Xu X, Li S, Dai F, He Y, Zhang N, Yang Y, et al. Correlation among body weight, bone metabolic markers and osteoporosis of postmenopausal women. Chinese Journal of Osteoporosis and Bone Mineral Research. 2018;11(3):255-60.

[17]Zhang M, Zhang X, Deng W, Zhang Z, Xu H, Ge J, et al. Expert consensus on clinical application of biochemical indicators of bone metabolism (2019). Chinese Journal of Osteoporosis. 2019;25(10):1357-72.

[18]Li J, Liu X, Li D, Huang J, Zhou W, Pan X, et al. Research progress of traditional Chinese medicine epimedium for the treatment of osteoporosis. Chinese Journal of Osteoporosis. 2018;24(3):389-93.

[19]Gong Y, Zhang Y, Zhang H. The influence of traditional Chinese medicine astragalus on bone metabolism and related basic research progress. Chinese Journal of Osteoporosis. 2019;25(3):404-7.