

Clinical Efficacy of Kangguzeng Capsule Combined with Basic Anti Osteoporosis Drugs in the Treatment of Postmenopausal Osteoporosis

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Abstract: Objective: To investigate the clinical efficacy of kangguzeng capsule combined with basic anti osteoporosis drugs in the treatment of postmenopausal osteoporosis. Methods: 96 patients who met the inclusion criteria in the First Affiliated Hospital of Shaanxi University of Traditional Chinese Medicine from June 2020 to June 2021 were included in the study. According to the random number table, the patients were divided into treatment group (48 cases) and control group (48 cases). The control group was treated with basic anti osteoporosis drugs, including alendronate sodium and calcitriol capsules; the treatment group was given kangguzeng Capsule on the basis of the control group. The patients were followed up regularly, and the TCM clinical syndrome score, pain visual analogue score (VAS), serum type I procollagen amino terminal propeptide (PINP) and type I collagen carboxyl terminal peptide were observed and recorded (β - CTX) and other indicators. Results: the clinical syndrome scores of the treatment group and the control group were improved. Compared with those before treatment, the clinical syndrome scores of the treatment group and the control group decreased significantly after treatment, and the difference was statistically significant ($P < 0.05$). The score of the treatment group was significantly better than that of the control group after treatment, and the difference was statistically significant ($P < 0.05$); In terms of VAS score, compared with that before treatment, the VAS score of the treatment group and the control group decreased significantly after treatment, and the difference was statistically significant ($P < 0.05$). The score of the treatment group after treatment was significantly better than that of the control group after treatment, and the difference was statistically significant ($P < 0.05$); In terms of PINP, the PINP of the treatment group and the control group were significantly higher than that before treatment ($P < 0.05$). The PINP of the treatment group was significantly higher than that of the control group after treatment ($P < 0.05$); stay β - In terms of CTX, the treatment group and the control group were compared after treatment and before treatment, β - CTX decreased significantly, and the difference was statistically significant ($P < 0.05$) β - CTX and control group after treatment β - There was significant difference in CTX ($P < 0.05$). Conclusion: kangguzeng capsule combined with basic anti osteoporosis drugs is effective in the treatment of postmenopausal osteoporosis. It can improve the clinical symptoms, biochemical indexes of bone metabolism and bone mineral density, and improve the quality of life of patients.

Keywords: Kangguzeng capsule; Postmenopausal osteoporosis; Curative effect observation

1. Introduction

Osteoporosis (OP) is a systemic metabolic bone disease, which is characterized by decreased bone mass, decreased bone mass per unit volume and destruction of bone microstructure, resulting in increased bone fragility and prone to fracture. Literature [1] divides them into three categories, including primary, secondary and idiopathic osteoporosis. Among them, primary osteoporosis is the most common, which can be divided into two types: type I, postmenopausal osteoporosis (PMOP), type II, senile osteoporosis, and type I is more common in primary osteoporosis. There is no disease name of osteoporosis in traditional Chinese medicine, which belongs to the category of "bone wilt" and "bone arthralgia". Osteoporosis is a common and frequently occurring disease of the elderly. With the acceleration of China's aging and the arrival of the era of negative population growth, the new social

situation dominated by the aging population will have a far-reaching impact on China's economic and social development. Since 2018, China has carried out the epidemiological survey of osteoporosis among Chinese residents for the first time. The latest research shows that there are great differences in the prevalence of osteoporosis among people in different regions, gender and age stages. For the population over 50 years old, the prevalence of urban population is lower than that in rural areas, and the prevalence of women is higher than that of men. Among them, the prevalence of people over 65 years old can reach 32%, 25.6% in urban areas and 35.3% in rural areas, The prevalence rate of male is 10.7%, while the prevalence rate of osteoporosis in female population can be as high as 51.6%. It can be seen that the prevalence rate of patients with osteoporosis in China gradually increases with age, and the proportion of postmenopausal osteoporosis is the largest, and the prevalence rate of women is much higher than that of men [2]. Osteoporosis changes the biomechanical properties of bone due to the change of its internal structure, such as the decrease of maximum load, yield load and elastic modulus, resulting in the decrease of bone elasticity, energy absorption and compressive capacity. Fracture can occur under the action of slight external force [3], and osteoporotic vertebral compression fracture (OVCF) is the most common among osteoporotic fractures, and the proportion of thoracolumbar fracture is the highest. Studies have shown that the proportion of women with thoracolumbar compression fractures is higher than that of men, and is younger than that of men. It tends to occur at the age of 60 ~ 69, while the majority of men are at the age of 70 ~ 79 [4]. The research shows that the incidence of OVCF in China has increased step by step in recent years [5]. Based on a data model simulation study, the number of OVCF among people over 50 years old in China will reach 3 million in 2050, and the related medical expenses will reach 22 billion US dollars [6].

At present, drug treatment, exercise improvement and diet adjustment are the three main means to prevent and treat osteoporosis, but drug treatment is still the core [7], including calcitonin, estrogen, bisphosphonates, ipriflavone, fluoride, calcium and vitamin D [8]. There are many kinds of drugs, but the medication cycle is long, the effect of drugs is slow, some side effects are large and the price is relatively expensive, it has brought great economic pressure to the patients themselves and their families. Therefore, some patients have poor medication compliance, which greatly reduces the effect of anti osteoporosis treatment. Traditional Chinese medicine is a great treasure house in China. In recent years, fruitful achievements have been made in the research of single traditional Chinese medicine, prescription, compound and other anti osteoporosis drugs. A large number of traditional Chinese medicine preparations with clear clinical efficacy have been applied in clinic under the guidance of traditional Chinese medicine theory and achieved good response [9], but it is rare to use traditional Chinese medicine alone to treat osteoporosis in clinic, This study intends to explore the safety and effectiveness of the combination of traditional Chinese medicine and Western medicine in the treatment of postmenopausal osteoporosis through clinical trials.

2. Data and methods

2.1 Case selection

2.1.1 General data

96 patients with menopausal osteoporosis treated in the orthopaedic inpatient department and outpatient department of our hospital from June 2020 to June 2021 were selected as the research object. They were randomly divided into observation group and control group, with 48 cases in each group. The age of the observation group ranged from 52 to 66 years, with an average age of (55.93 ± 4.83) years; The course of disease was 1.86 ~ 11.33 years; The age of the control group was 51 ~ 67 years old, with an average age of (57.01 ± 4.89) ; The course of disease was 1.92 ~ 12.01 years; There was no significant difference in the general data of the subjects before they were enrolled ($P > 0.05$), which was comparable.

2.1.2 Diagnostic criteria

Refer to the guidelines for the diagnosis and treatment of primary osteoporosis (2017) [10] formulated by the osteoporosis and bone mineral salt branch of the Chinese Medical Association. For postmenopausal women, the bone mineral density t value measured by dual energy X-ray absorptiometry (DXA) ≤ -2.5 is the diagnostic criteria (normal: t value ≥ -1.0 ; low bone mass: $-2.5 < T$ value < -1.0 ; severe osteoporosis: t value ≤ -2.5 (combined with fracture). The TCM syndrome differentiation type refers to postmenopausal osteoporosis (bone wilt) Guidelines for diagnosis and treatment of traditional Chinese medicine (2019 Edition) [11], the syndrome type is kidney deficiency

and blood stasis type, which shows pain and discomfort in the waist, back and whole body, pain and refusal to press, definite location, muscle contracture, or fracture, accompanied by trauma, ecchymosis or ecchymosis on the tongue, purple and dark, astringent pulse or string.

2.1.3 Inclusion criteria

(1) meet the diagnostic criteria of postmenopausal osteoporosis, TCM syndrome differentiation meets the type of kidney deficiency and blood stasis, and has typical clinical manifestations of osteoporosis; (2) Natural menopause time ≥ 1 year; (3) No anti osteoporosis drug treatment and no drugs affecting bone metabolism have been used in recent 6 months; (4) No other diseases affecting the study, such as endocrine system, digestive system and spirit; (5) No obvious contraindications; (6) Good compliance, with treatment and follow-up; (7) Voluntarily sign relevant informed documents and agree to accept this study.

2.1.4 Exclusion criteria

(1) patients with secondary osteoporosis and idiopathic osteoporosis caused by endocrine system diseases and kidney diseases; (2) Unnatural menopause caused by gynecological diseases or other diseases; (3) Accompanied by liver and kidney insufficiency, digestive system diseases, mental diseases, etc; (4) Patients with allergic constitution or allergic to the drugs in this study; (5) Poor compliance, or unable to continue treatment or follow-up due to various reasons.

2.2 Treatment

The control group was given alendronate sodium tablets (Lepu Pharmaceutical (Beijing) Co., Ltd; Specification: 10 mg; Gyzz h2009334300) take it with warm water on an empty stomach in the morning. Do not lie down or eat within 30min after taking the medicine, 10mg / D; Calcitriol capsules (Shanghai Roche Pharmaceutical Co., Ltd.; specification: 0.25 μ g; gyzz j20150011) are taken orally, 0.25 μ g / time, 2 times / day. On the basis of the administration of the control group, the treatment group was added with anti bone hyperplasia capsule (Shenyang Noah Rongkang Biopharmaceutical Technology Co., Ltd.; specification: 0.35g; gyzz z19980144), 1.75g/time, 2 times / day. The two groups took medicine continuously for 3 months.

2.3 Observation indicators and methods

Record the TCM clinical syndrome score before and after treatment, and refer to the quantitative standard formulated in the guiding principles for clinical research of new traditional Chinese medicine (2002) [12]; Evaluate and record the visual analogue scale (VAS) of pain; According to the expert consensus on clinical application of biochemical indicators of bone metabolism (2019) [13], compare the amino terminal propeptide (PINP) and carboxyl terminal peptide of type I procollagen before and after treatment (β -CTX) level.

2.4 Statistical methods

Use spss26 0 software for data analysis. The measurement data is expressed in ($\bar{x} \pm s$), using t-test, and the counting data is tested by χ^2 . $P < 0.05$ showed that the difference was statistically significant.

3. Results

3.1 TCM clinical syndrome score

There was no significant difference in TCM clinical syndrome scores between the two groups before treatment ($P > 0.05$). The syndrome scores of the two groups after treatment were significantly lower than those before treatment ($P < 0.05$), and the syndrome scores of the treatment group after treatment were significantly lower than those of the control group after treatment ($P < 0.05$), as shown in Table 1.

Table 1: Comparison of TCM clinical syndrome scores between the two groups before and after treatment ($x \pm s$)

	Treatment group		Control group	
	Before treatment	After treatment	Before treatment	After treatment
Low back pain	4.22±0.69	1.99±0.67#△	4.13±0.72	2.96±0.65#
Weak waist and legs	4.29±0.59	1.57±0.76#△	4.19±0.72	2.74±0.75#
Back percussion pain	2.88±0.82	1.03±0.61#△	2.79±0.78	1.89±0.87#
Lower limb weakness	1.92±0.73	0.76±0.38#△	1.79±0.69	1.05±0.49#

Note: compared with that before treatment, # $P < 0.05$; Compared with the control group after treatment, △ $P < 0.05$.

3.2 VAS score

There was no significant difference in VAS score between the two groups before treatment ($P > 0.05$). The VAS score of the two groups after treatment was significantly lower than that before treatment ($P < 0.05$), and the VAS score of the treatment group was significantly lower than that of the control group ($P < 0.05$). See Table 2.

Table 2: Comparison of VAS scores between the two groups before and after treatment ($x \pm s$)

	Before treatment	After treatment
Treatment group	7.68±1.45	2.38±0.87#△
control group	7.59±1.56	3.98±1.12#

Note: compared with that before treatment, # $P < 0.05$; Compared with the control group after treatment, △ $P < 0.05$.

3.3 Biochemical indexes of bone metabolism

There was no significant difference in biochemical indexes of bone metabolism between the two groups before treatment ($P > 0.05$). After treatment, PINP in the two groups was significantly higher than that before treatment ($P < 0.05$), and the increase after treatment in the treatment group was more obvious than that in the control group ($P < 0.05$). Two groups of patients β -CTX was significantly lower than that before treatment ($P < 0.05$), and the decrease after treatment in the treatment group was more obvious than that in the control group ($P < 0.05$). See Table 3

Table 3: Biochemical indexes (PINP) of the two groups before and after treatment, β -CTX score comparison ($x \pm s$)

	Treatment group		control group	
	Before treatment	After treatment	Before treatment	After treatment
PINP	62.19±18.33	89.62±14.29#△	63.01±19.02	77.24±15.29#
β -CTX	0.69±0.04	0.32±0.03#△	0.65±0.05	0.45±0.03#

Note: compared with that before treatment, # $P < 0.05$; Compared with the control group after treatment, △ $P < 0.05$.

4. Discussion

PMOP is a systemic metabolic bone disease caused by the decline and imbalance of ovarian endocrine function and the decrease of estrogen level in postmenopausal women, resulting in the bone formation of osteoblasts less than the bone absorption of osteoclasts. It is characterized by the change of bone microstructure and the progressive decrease of systemic bone mineral density [14].

There is no disease name of postmenopausal osteoporosis in traditional Chinese medicine, which is mostly classified as "bone wilt", "bone arthralgia" and so on. Traditional Chinese medicine believes that its pathogenesis lies in deficiency of kidney essence, weakness of spleen and stomach, deficiency of liver blood and obstruction of collaterals by blood stasis [15]. The kidney stores essence, generates marrow and governs bone, which is the foundation of congenital. The weakness of bone is closely related to whether the kidney essence is full or not. Su Wen said that "when a woman is seven years old, her kidney qi is full, her teeth are more fat, and her intestines are more common... Qi Qi has a weak pulse, too Chong pulse is weak, the sky is exhausted, and the tunnel is blocked, so she is bad in shape and has no children". The physiological and pathological changes caused by the decrease of estrogen

level in postmenopausal women are consistent with the changes in the human body where "tianguijie" is located. The rise and fall of tianguijie is closely related to the kidney essence. The deficiency of kidney essence, the weakness of Chong and Ren, the lack of biochemical source of bone marrow, the inability to moisten and nourish bones, resulting in bone wilting and withering, which is the key to the pathogenesis of postmenopausal osteoporosis. The spleen and stomach are the foundation of the day after tomorrow and the biochemical source of Qi and blood. "Lingshu" says: "the valley is full of Qi, zhuoze is injected into the bone, and the bone belongs to flexion and extension...", According to the required reading of medical school: "deficiency of Yang and brightness leads to less blood gas and can not nourish the Zong tendon, so it is galloping. When the Zong tendon is galloping, the pulse can not be retracted, so the foot is paralyzed and not used". It describes the close relationship between the spleen and stomach and the bones. The kidney stores essence and governs bones, the liver stores blood and governs tendons, and the liver and kidney are of the same origin. The survival of the two depends on each other. Ye Tianshi's clinical syndrome guide medical case said: "covering the liver governs tendons, liver injury will not be used by people, and muscles and bones are contracture", indicating that the occurrence of wilt syndrome is related to the liver. In conclusion, the basic pathogenesis of postmenopausal osteoporosis is deficiency of kidney essence, lack of biochemical source of bone marrow and loss of bone nourishment, which is related to the dysfunction of liver, spleen and stomach, and blood stasis promotes the further occurrence of the disease [16].

Kangguzeng capsule combined is a traditional Chinese medicine compound reagent based on the method of Tonifying the kidney and activating blood circulation. A large number of clinical studies have confirmed that the drugs based on tonifying the kidney and activating blood circulation can achieve a certain effect on the treatment of osteoporosis. MRTA analysis [17] shows that unfamiliar traditional Chinese medicine compound preparation can improve bone mineral density and blood calcium in the treatment of postmenopausal osteoporosis, with definite evidence of total effective rate and good safety. Liu Wei [18] and others used the method of Tonifying the kidney and activating blood circulation to treat 100 elderly patients with osteoporosis. The randomized controlled study showed that the method of Tonifying the kidney and activating blood circulation can improve the clinical symptoms, improve the quality of life, improve bone mineral density and biochemical indexes of bone metabolism. A large number of animal experimental studies also show that the traditional Chinese medicine compound of Tonifying the kidney and activating blood circulation can affect the signal transduction pathway, inhibit bone absorption and promote bone formation [19].

Alendronate sodium is the third generation bisphosphate bone resorption inhibitor. As a first-line anti osteoporosis drug, it has been widely used in clinic, and many studies have also confirmed the accuracy of its efficacy. Considering that the subjects of this study are mostly elderly people, and the absorption capacity of gastrointestinal tract to calcium is reduced, calcitriol can improve the absorption and utilization of calcium and consolidate the curative effect.

It is found that kangguzeng capsule combined with basic anti osteoporosis drugs has satisfactory curative effect in the treatment of postmenopausal osteoporosis. It can improve clinical symptoms, improve bone mineral density and related bone biochemical markers. It has good safety and is worthy of further clinical application.

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