

Research Progress in the Treatment of Diabetes Osteoporosis with Traditional Chinese Medicine

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Abstract: Diabetes osteoporosis is a common secondary bone Metabolic disorder, which seriously affects the quality of life of patients. Traditional Chinese medicine categorizes it as "diabetes" combined with "bone dysfunction". Through consulting the related literature of diabetes induced osteoporosis, this paper summarized the TCM understanding of the disease, etiology and pathogenesis, syndrome differentiation and treatment, and clinical treatment, with a view to providing some evidence and reference for clinical practice.

1. Introduction

With the improvement of social living standards, the incidence rate of diabetes is on the rise year by year, even up to 11.2% from 2015 to 2017^[1]. Diabetes osteoporosis (DOP) is one of the chronic complications of diabetes Skeletal system. It is a metabolic disease characterized by bone loss, destruction of bone tissue structure and easy fracture. It is becoming an increasingly serious public health problem worldwide. Albright has clearly proposed the concept of diabetes osteoporosis ^[2]. The awareness rate of the disease is low, and the symptoms are not obvious in the early stage of the disease development, but the disability rate and Case fatality rate rate are high in the late stage. The life activities of patients are severely restricted, which brings a great burden to the family and society. DOP patients generally feel pain in their back and hips, and may even experience spinal deformities and fractures^[3]. According to the diagnostic criteria for diabetes proposed by the World Health Organization (1999): typical diabetes symptoms plus random plasma glucose ≥ 11.1 mmol/L; Or add Fasting blood sugar ≥ 7.0 mmol/L; Or add OGTT 2 hours blood glucose ≥ 11.1 mmol/L; Or HbA1c level $\geq 6.5\%$. Diabetes patients who do not show typical symptoms should be re examined and confirmed at other times. In modern medicine, dual energy X-ray absorption method is commonly used to measure the bone mineral density of bones in patients with osteoporosis. Bone mineral density can be used to measure osteoporosis caused by various causes, and it plays an important role in the early detection and treatment of osteoporosis. The measurement value of dual energy X-ray absorption (DXA) is currently recognized as the gold standard for diagnosing osteoporosis worldwide. In clinical, L1-L4, as well as the hip and femoral neck, are generally measured. The diagnosis is based on a T-value, with a normal bone mass of T-value ≥ -1 ; Low bone mass is $-2.5 < \text{T-value} < -1$; Osteoporosis has a T-value ≤ -2.5 ^[4]. Osteoporosis patients with a history of diabetes can meet the diagnosis of diabetes osteoporosis. Osteoporosis patients with a history of

diabetes can meet the diagnosis of diabetes osteoporosis^[5]. The current Western medicine treatment is generally a combination of hypoglycemic drugs and osteoporosis inhibitors^[6]. However, long-term use has significant side effects, significant adverse reactions, and poor dependence. Traditional Chinese medicine treatment has its own advantages and has achieved good results. Therefore, exploring the treatment of DOP with traditional Chinese medicine is particularly important.

2. DOP disease name, etiology, and pathogenesis

In Traditional medicine, DOP is classified as diabetes and "bone dysfunction". Diabetes is caused by insufficient endowment, improper diet, emotional imbalance, and excessive labor and desire. Its basic pathogenesis is yin deficiency and dry heat, which can be divided into upper dissipation, middle dissipation, and lower dissipation. The disease is located in the lungs, spleen, and kidneys, with the kidney being the main cause. The name of "bone dysfunction" was first put forward in the Huangdi Neijing, and there is a saying that "the kidney governs the bone marrow of the body" in the Su Wen ·Wei Lun Pian. In the "Su Wen ·Yin Yang Ying Xiang Da Lun Pian", it is also recorded that "the kidney generates bone marrow" and "when the kidney is full, the marrow is solid". The kidney is the innate origin, storing essence, controlling bone to produce marrow, and the kidney is closely related to bone and marrow. Deficiency of kidney essence can easily lead to bone dysfunction. In the Huangdi Neijing Su Wen, "if the kidney qi is hot, the waist and spine will not lift, and the bone will wither and the marrow will be reduced, which will lead to bone dysfunction." It explains that the pathogenesis of bone dysfunction is mainly kidney deficiency. The book "Yi Zong Bi Du ·Wei" states that "Yang Ming deficiency leads to insufficient blood and qi...Therefore, dysfunction of foot can not be used"^[7], which also indicates that bone dysfunction is closely related to the spleen and stomach. The spleen and stomach are the source of qi and blood biochemistry. If the spleen and stomach are weak and the transformation of qi and blood is insufficient, the muscles and veins will lose nourishment, and bone dysfunction is prone to occur. Wang Sihai et al^[8]. proposed to treat from the spleen and kidney, tonifying the spleen and kidney, strengthening bones and tendons. In the theory of Traditional Chinese medicine, the liver and kidney are homologous, the liver stores blood, the kidney stores essence, and essence and blood breed and transform each other. The liver governs the tendons. If the liver is deficient, the tendons and veins cannot be replenished, and bone weakness may also occur. In ancient literature, many doctors have proposed that diabetes and "bone dysfunction" are mainly related to deficiency and blood stasis. According to the Clinical Guidelines Medical Record ·Wei, "Kidney stores essence, and essence and blood complement each other... Blood deficiency cannot nourish muscles and bones"^[9]. It is pointed out that long-term diabetes can lead to insufficient kidney essence, causing bone pain, and leading to "bone dysfunction. Li Huanyu et al^[10]. proposed that over time, Diabetes leads to kidney deficiency leading to spleen deficiency, which in turn leads to the lack of qi and blood for transformation. Qi deficiency leads to blood stasis, and blockage leads to pain. Blood stasis exists throughout the entire process of disease occurrence and development, and cannot be ignored. In summary, diabetes and "bone dysfunction" are mainly related to the lungs, spleen, and kidneys, and blood stasis is a pathological factor in their occurrence and development. Diabetes is mainly caused by the kidney, with a long course of disease. Yin deficiency and dryness lead to the loss of kidney essence, and due to "kidney governing bone", kidney deficiency leads to the loss of bone nourishment, resulting in "bone dysfunction"^[11].

3. Clinical differentiation and treatment of DOP in traditional Chinese medicine

At present, there is no clear traditional Chinese medicine syndrome type for diabetes and "bone dysfunction". Modern doctors have organized and summarized the DOP classification in order to

provide reference for later clinical practice. Shen Yuandong et al^[12]. divided it into liver and kidney deficiency syndrome, yin and yang deficiency syndrome, and qi stagnation and blood stasis syndrome. They respectively used Zhuanggu Wan to nourish the liver and kidney, Guilu Erxian Gao and Erxian Tang to supplement yin and yang, and Shentong Zhuyu Tang to regulate qi, promote blood circulation, and relieve pain. Fang Chaohui et al^[13]. divided it into liver and kidney deficiency syndrome, kidney essence deficiency syndrome, spleen and kidney yang deficiency with blood stasis syndrome, yin and yang deficiency syndrome, and qi stagnation and blood stasis syndrome. They were respectively used with modified Zhuanggu Wan, Yougui Wan, Gushuling Capsule, Guilu Erxian Gao and Erxian Tang, and Shentong Zhuyu Tang. Lin Xiaobo et al^[14]. divided diabetes osteoporosis patients into liver and kidney deficiency syndrome, yin and yang deficiency syndrome, qi stagnation and blood stasis syndrome, and gave them Zishen Jiangtang pills, Tanggukang capsules, and Guiwan Jiawei capsules respectively. Huang Xueqing^[15] divided it into liver and kidney deficiency, spleen and stomach qi deficiency syndrome, and treated it with the syndrome differentiation of tonifying spleen and kidney and regulating liver. Chen Le et al^[16]. divided the patients into an intervention group and a basic group. The basic group was treated with Gukang capsules, while the intervention group was treated with traditional Chinese medicine differentiation based on the basic group. The differentiation was divided into liver and kidney deficiency syndrome, yin yang deficiency syndrome, and qi stagnation and blood stasis syndrome. Wang Sihai et al^[17]. believed that the main of this disease is insufficient kidney essence, which is related to the liver and spleen. They divided it into liver kidney deficiency and spleen kidney deficiency, and skillfully used prepared rehmannia to achieve both symptoms and root causes in clinical practice.

4. Clinical Status of Traditional Chinese Medicine Treatment for DOP

4.1 Single drug treatment

Modern experimental results indicate that certain single drugs can significantly improve DOP. Rehmannia can regulate bone metabolism, increase bone density, and have good anti DOP effects^[18]. Cornus officinalis has functions such as lowering blood sugar, regulating bone metabolism, anti-aging, and immune function^[19]. Yam belongs to the three meridians of the lungs, spleen, and kidneys, and has the effects of lowering blood sugar, improving immunity, and resisting liver and kidney damage. It is a medicine with the same origin as food^[20]. Modern medicine believes that Achyranthes bidentata has anti-inflammatory, hypoglycemic, and anticoagulant effects^[21]. Pharmacological studies have shown that kidney tonifying drugs can effectively improve bone metabolism, increase bone density, regulate endocrine levels, and promote bone cell formation^{[22]-[23]}.

4.2 Compound therapy

With the continuous deepening of people's understanding of drugs, drugs are used in combination according to different situations, and added or subtracted according to the symptoms to adapt to changes in the condition. In order to improve the efficacy of drugs, many doctors provide compound therapy for patients with DOP. Liu Hongyi et al^[24]. divided patients with yin and yang deficiency type DOP into a control group and an observation group. The control group was given hypoglycemic, hypotensive, lipid-lowering, and calcium supplements. The observation group was supplemented with Zuogui Wan and Yougui Wan syndrome differentiation (yam, Angelica sinensis, cornus officinalis, radix rehmanniae, chuanfu Zi, antler glue, goji berry, semen cuscuta, achyranthes, etc.) based on the control group. After 3 months of treatment, clinical symptoms basically disappeared, while osteocalcin and bone density increased. Xu Tengfei et al^[25]. believe that the

Shenqi compound (Astragalus, prepared rhubarb, ginseng, cornus officinalis, yam, trichosanthin, etc.) can inhibit the formation of tumor cytokines, interleukin, and alkaline phosphatase, playing an important role in regulating bone metabolism levels. Yang Zhenyu et al^[26]. used Zishen Jiangtang Pills (Astragalus membranaceus, raw rehmannia, turtle shell, cooked rehmannia, turtle shell, dog spine, etc.) in combination with alendronate sodium to treat elderly DOP, which can effectively control blood sugar and increase bone density. For patients with DOP with both Qi and Yin deficiency, Min Lingtian et al^[27]. added Xiaoke Xuanbi decoction (cooked Rehmannia, Cornus officinalis, Huai Yam, Achyranthus rhizome, Rhizoma gleditsiae, Radix pseudostellariae, Radix ophiopogonis, epimedium, eucommia ulmoides, Guijian Yu, etc.) on the basis of conventional hypoglycemia treatment and achieved good results. Clinical symptoms and bone metabolism levels were significantly improved, and bone mineral density was increased. He Qingxiang et al^[28]. used compound osmanthus twig keel oyster soup (osmanthus twig, raw keel, raw oyster, paeonia paeoniae, cooked rehmannia rehmannii, Achyranthus rhizome, Rhizoma gleditsiae, etc.) to treat DOP with significant effect, and divided 64 patients into a conventional group and an experimental group. The conventional group was given conventional treatment. The experimental group took Compound Guizhi Longgu Oyster soup. The results showed that blood calcium, blood phosphorus, bone density were significantly improved, blood sugar was also well controlled, and the effective rate was higher than that of the conventional group. Li Zhongnan et al^[29]. treated DOP with Dan Zhi hypoglycemic capsules (peony bark, leeches, Rhizoma alismatidis, Semen cuscuta, raw rehmannia, etc.) to treat Qi and Yin deficiency syndrome DOP for 12 weeks, and found that clinical symptoms improved, parathyroid hormone decreased, and blood vitamin D increased. Lou Shujing et al^[30]. believe that the modified Liuwei Dihuang Tang (cooked Rehmannia glutinosa, Poria cocos, Alisma orientalis, Peony bark, Chinese yam, and Cornus officinalis, etc.) has a significant clinical effect and high safety in the treatment of liver and kidney deficiency type DOP.

4.3 Self prescribed treatment

In recent years, scholars have bravely explored and attempted to use self-designed formulas in the treatment of DOP, and have achieved good results. Zhu Jinqiu et al^[31]. divided 60 patients with DOP into the control group and the observation group. The control group was treated with vitamin D supplementation, Calcitonin injection and other conventional treatments. The observation group was treated with Bushen Zhuanggu Decoction on the basis of conventional treatment for three consecutive months. It was found that compared with the control group, Fasting blood sugar (FPG), two hour postprandial blood glucose (2hPG), Glycated hemoglobin (HbA1c) in the observation group significantly decreased, and bone density increased, The blood calcium and phosphorus levels remain normal, the treatment effect is more obvious, and the incidence of adverse reactions is low. The results indicate that Bushen Zhuanggu Tang can increase bone density, promote bone formation, and regulate the level of endocrine substances. Chen Shuo et al^[32]. used self-designed Bushen Zhuanggu Tang to treat type 2 DOP patients and found that FPG, 2hPG, and HbA1c were significantly reduced, while bone density in L2-4, femoral neck, and Wards triangle area was significantly increased. In addition, the patient's symptoms such as tinnitus, dry mouth, dry throat, and weak waist and knees were significantly improved. Fu Jiangtao^[33] and others believed that after treatment, the levels of Glucose test#Fasting blood sugar, blood glucose two hours after meal, and Glycated hemoglobin in the observation group added with Bushen Zhuanggu Decoction significantly decreased compared with the control group, the level of blood calcium increased, the level of blood phosphorus decreased, and the lumbar bone density increased significantly, and there was no adverse reaction in both groups. Liu Yongjin et al^[34]. conducted a meta-analysis on the efficacy of the kidney and bone strengthening method in the treatment of DOP. Under the premise

of routine treatment, the kidney and bone strengthening group used decoction and pills of the kidney and bone strengthening method, while the control group used drugs such as calcic D or alendronate sodium tablets to treat osteoporosis for 12 weeks. It was found that the kidney and bone strengthening group had a significant therapeutic effect, with a significant increase in femoral neck bone density and male and female bone density. Zhao Jiajing et al^[35]. used a self-designed formula for tonifying the kidney and unblocking the collaterals combined with hypoglycemic drugs to treat DOP of kidney deficiency and blood stasis type. The results showed that it can improve the levels of calcium and phosphorus in the blood, increase bone content, and have a significant therapeutic effect. In summary, traditional Chinese medicine can control blood sugar, increase bone density, have high safety, and have good therapeutic effects on DOP, which is worthy of clinical promotion.

4.4 Traditional Chinese patent medicine treatment

Proprietary Chinese medicine is widely used because of its stable nature, definite efficacy, relatively small toxic and side effects, and portability. Liang Shuang et al^[36]. selected 100 patients with DOP and divided them into an observation group and a control group. After 12 months of treatment with Jintiange capsules (artificial tiger bone powder, etc.) on top of the control group, the observation group showed significantly better efficacy than the control group, with blood sugar levels adjusted to normal, bone density increased, clinical symptoms and bone metabolism levels improved. Li Yuejing^[37] and others used Zhuchun capsule to treat type 2 diabetes osteoporosis patients, and found that osteocalcin was significantly increased, the clinical symptoms of patients were also significantly improved, and bone density was increased. Elias Abra^[38] divided 138 patients with diabetes osteoporosis into a control group and a treatment group. The control group was given zoledronic acid injection, and the treatment group added Xianling Gubao capsule on this basis. The results showed that the effect of the treatment group was significantly better than the control group. Xianlinggubao capsule combined with zoledronic acid injection can effectively improve patients' pain and bone density, regulate bone metabolism levels, and have high safety.

4.5 Traditional Chinese Medicine Characteristic Therapy

Relevant literature shows that traditional Chinese medicine characteristic therapy, as a unique auxiliary method, has significant therapeutic effects in clinical treatment of this disease. Yang Guofang et al^[39]. divided DOP patients into a control group and an observation group. The control group was treated with Alfacalciferol soft capsules, while the observation group was treated with mild moxibustion and massage therapy on the basis of the control group, with a definite therapeutic effect. Selecting acupoints such as Shenshu, Pishu, Mingmen, and Yaoyangguan improved the clinical symptoms of patients and achieved good results. Research has shown that acupuncture at Jiaji point has a certain effect on controlling blood sugar and improving endocrine indicators. At the same time, ear points such as the kidney, endocrine, and spleen can also be taken for treatment. Traditional Chinese medicine acupoint application therapy uses the method of traditional Chinese medicine syndrome differentiation to select acupoints according to the patient's symptoms for application, achieving the effect of warming meridians, dispersing cold, promoting blood circulation, and relieving pain, with significant therapeutic effects. Traditional Chinese medicine sports such as Baduanjin and Taijiquan can help to improve immunity and have a certain auxiliary therapeutic effect on this disease. Under the mature theoretical framework of traditional Chinese medicine, traditional Chinese medicine treatment has the advantages of rich experience and fewer adverse reactions^[40].

5. Outlook

The development of osteoporosis is irreversible, but we can delay its course by timely prevention. Nowadays, the incidence rate of DOP is getting higher and higher, and the early symptoms are not easy to be taken seriously. We should make early detection, early diagnosis, and early treatment to prevent it from tending to various diseases or even worsening. Traditional Chinese medicine has a rich theoretical basis. It has achieved good results in the treatment of DOP by starting from the whole, treating according to syndrome differentiation, and classifying according to its clinical manifestations. However, there is currently no unified classification of the disease, so we need to further explore more effective methods in clinical practice to truly reverse the development of DOP.

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