Research Progress of Taibaiqiyao in Treatment of Bone and Joint Diseases

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Keywords: Traditional Chinese medicine, Taibaiqiyao, bone and joint disease, osteoporosis

Abstract: Taibai seven medicines are precious medicines unique to Taibai Mountain, most of which have the effects of promoting blood circulation and removing blood stasis, dredging meridians and relieving pain, removing dampness and swelling, dispelling wind and removing arthralgia, etc., specializing in the treatment of wind-cold-dampness arthralgia, traumatic injury, strain and strain, such as: Jinniuqi, Tieniuqi, Changchunqi, Fenxiangqi, etc. Through literature mining, the potential correlation of Taibai Qiyao in bone and joint diseases was summarized and analyzed, in order to provide new ideas for the pathogenesis of Taibai Qiyao in the treatment of bone and joint diseases, put forward new ideas for its targeted treatment drugs, and provide strong evidence for the clinical application of Taibai Qiyao in orthopedics.

1. Introduction

Bone and joint diseases refer to the diseases related to tissue, structure and function of bone and joint under the influence of various pathological factors. The main clinical manifestations are pain, dysfunction and deformity. The nature of the disease is mainly multiple, degenerative and proliferative^[1]. Studies have shown that about 14 % of adults in the United States are affected by bone and joint diseases, and 23 % of the middle-aged and elderly people are affected by bone and joint diseases resulting in severe pain and limited mobility^[2,3]. Osteoarthropathy has become the second leading cause of incapacity in men over 50 years of age in the United States after cardiovascular disease^[4]. Osteoarthritis is the most common bone and joint disease. The health and quality of life of middle-aged and elderly people are seriously affected. The high-risk population tends to be younger^[5].

With the over-exploitation of natural resources and the need for natural resources protection, the replacement of traditional rare medicinal materials has gradually entered people 's vision. Taibai seven drugs refers to the growth in Taibai area ' seven drugs ' general term. 'Seven drugs' was first recorded in 1590' Compendium of Materia Medica ' Volume 12 of the 'Sanqi', now China's 'Pharmacopoeia' income Taibai 'seven drugs' ^[6]. Taibai ' seven drugs ' widely used, unique function, has aroused widespread concern. At present, Taibaiqiyao clinical treatment of bone and joint

diseases unique effect, its basic research has been reported.

2. Taibai Seven Drugs

Taibai seven drugs, the most prominent manifestation is the 'four beams and eight columns' like Chinese medicine prescriptions in the principle of Junchen Zuoshi the same. Four Liang (Jun Liang) refers to: Taoerqi, Changchunqi, Jinniuqi, Tieniuqi, eight columns in the column refers to: corpse seven, Zhushaqi, Hongmaoqi, Panlongqi, Taibaisanqi, Zhugenqi, Fengweiqi, Zuozhu refers to: button seven, entertainment clam seven, frog seven, chase wind seven, buckwheat seven, Aerqi, Touguxiao, Shenjincao, see blood fly, Zhuquancao, Taibaiyangshen, so that the column refers to: screw seven, Huangsanqi, Huluqi, Jinmaoqi, flying ant clam seven, linen seven, Jiuniuqi, Huoxuedan, Biandanqi, Jusanqi, Daoziqi, Zushima, Pibayu, Xiaoliuyuehan, etc. ^[6].

Although many varieties of Taibai seven drugs, but its pharmacological effects are more concentrated, 'Taibai seven drugs' mostly have blood stasis, through the pain, dampness swelling, wind and other effects, specializing in wind and cold dampness Bi, bruises, strain, strain of disease, such as: Jinniuqi, Tieniuqi, Changchunqi, Fenxiangqi and so on. ^[7] Modern pharmacological studies have proved that the special efficacy of Taibai Qiyao in analgesia, anti-inflammatory, anti-rheumatism, anti-bacterial, anti-tumor, anti-viral and other aspects has attracted widespread attention. ^[6, 8, 9, 10]

3. Taibai Qiyao in Treatment of Bone and Joint Diseases

3.1. Taibai Qiyao and Osteoarthritis

Osteoarthritis is an inflammatory disease involving articular cartilage, subchondral bone, ligament, joint capsule, synovial membrane and other joint structures, which is mainly caused by articular cartilage damage or loss ^[11]. Osteoarthritis is characterized by progressive cartilage degeneration, and its clinical manifestations are swelling and pain, stiffness, fricative sound, and limited mobility ^[12]. Studies have shown that ginsenosides have a clear positive effect on restoring SOD activity and maintaining the synthesis of type II collagen in chondrocytes. Some Taibai Qiyao contain a large amount of ginsenosides, such as Zhuzishen ^[13-15] and Yuerqi ^[16]. To achieve relief and therapeutic effect. Duan et al. ^[17] proved through animal experiments that Tieniuqi had an effect on the activity of SOD in synovial fluid. Single Tieniuqi tincture could eliminate free radicals in synovial fluid, increase the activity of SOD in synovial fluid, and promote the recovery of knee osteoarthritis.

3.2. Taibai Qiyao and Rheumatoid Arthritis

Rheumatoid arthritis is a multiple autoimmune and systemic inflammatory disease with diverse clinical manifestations, mainly chronic and migratory joint pain, and often accompanied by repeated attacks, especially in the morning hand and foot joint stiffness is the most serious. The pathogenesis of RA is closely related to the immune response regulation system and the release of inflammatory factors ^[18,19]. Previous studies have shown that resveratrol can affect the function of the immune system by regulating IL-17 to interfere with the progression of rheumatoid arthritis, and even play a direct therapeutic role. Modern pharmacological studies have shown that the effective components of Taibaiqiyao contain resveratrol, such as peach seven. ^[9,20,21]

3.3. Taibai Qiyao and Osteoporosis

Osteoporosis is a systemic bone disease caused by the loss of nutrients and calcium ions, such as bone structure degradation, bone loss, and increased bone fragility. Clinically, there are often signs such as spinal shortening or deformity, and pain in the affected area, which can easily lead to complications such as compression fractures. Because of its high incidence and low treatment rate, it often leads to various complications, disability or death, and the prognosis is very poor. Therefore, early intervention and treatment should be carried out ^[22].

Bone metabolism is divided into bone formation and bone resorption, and osteoporosis is a disease developed under the condition that the long-term bone resorption rate is higher than the bone formation rate. Weng J et al.^[23] have demonstrated that Wnt3a, a downstream protein of the Wnt signaling pathway, enhances bone formation by promoting the differentiation of bone marrow mesenchymal cells into osteoblasts. Qin X et al [24] confirmed that RUNX2 protein downstream of Wnt / β-catenin signaling pathway can enhance bone formation rate by promoting osteoblast synthesis of bone matrix. Yang Sen et al.^[25] through animal experiments confirmed that centipede flying seven can regulate the Wnt / β-catenin signaling pathway to improve the function of osteoblasts and enhance bone formation rate. Pan et al. ^[26] confirmed through animal experiments that Aralia taibaiensis can increase the expression of Wnt3a, β -catenin and RUNX2 proteins by regulating the Wnt / β -catenin signaling pathway, thereby enhancing bone formation rate. Wnt signaling pathway can weaken bone resorption rate through its downstream Wnt3 a protein and Wnt16 protein. Wnt3 a protein can inhibit osteoclast formation by regulating RANKL expression, and Wnt16 protein can enhance osteoclast differentiation ^[27]. At the same time, Li et al. ^[28] have shown through animal experiments that the extracts of Feitian Wugongqi and Zhuzishen in Taibai Qiyao can promote the proliferation, differentiation and mineralization of osteoblasts. Flying centipede seven and pearl ginseng have synergistic effect on osteoblasts. When the dose ratio of flying centipede seven and pearl ginseng is 1: 2, the synergistic effect is the best. Ni et al. ^[29] analyzed the fat-soluble components of Changchungi by GC-MS, and the main components contained osthole. Osthole can regulate the function of osteoblasts by reducing the mRNA expression of NO, IL-1, IL-6 and IL-6 produced by osteoblasts spontaneously or under the stimulation of inflammatory cytokines and LPS [30], and can also promote the proliferation of osteoblast-like cells UMR106 cells and stimulate alkaline phosphatase activity, which has a direct effect on promoting the proliferation and differentiation of osteoblasts ^[31]. Therefore, Taibai Qiyao can slow down the progress of osteoporosis by promoting osteoblast proliferation, differentiation and mineralization.

3.4. Taibai Qiyao and Hyperosteogeny

Hyperosteogeny is a series of almost irreversible compensatory pathological changes caused by long-term effects of articular cartilage degradation, endocrine disorders and other factors. The clinical manifestations are often joint pain and numbness, limited activity, and often involving peripheral blood vessels and nerves, aggravating pain and local muscle atrophy. It is a common multiple degenerative metabolic disease in orthopedics. ^[12] Hyperosteogeny has been shown to be associated with the immune system (TNF- α , IL-1, etc.)

Humoral metabolism, cytokines (TGF, NGF, Wnt signaling pathway, etc.) and substance metabolism are directly related. Some effective pharmacological components contained in Taibaiqiyao^[8], such as quercetin, luteolin, triterpenoid saponins, etc. ^[32-34], can regulate immune system function, cytokine levels and substance metabolism by regulating blood lipids, anti-oxidation, anti-inflammatory (IL-1, TNF- α) and other pathways, ^[35] and ultimately achieve the purpose of affecting bone hyperplasia. ^[36]

4. Conclusion and prospect

In summary, the pathogenesis of bone and joint diseases is mainly caused by immune system, cytokines, energy metabolism and other factors, and Taibai Qiyao can promote osteoblast proliferation, restore SOD activity and maintain chondrocyte synthesis of type II collagen, regulate IL-17, by regulating blood lipids, anti-oxidation, anti-inflammatory (IL-1, TNF- α) and other ways to systematically intervene. The mechanism of bone and joint diseases is complex, which is related to the multi-component, multi-target and multi-channel treatment characteristics of traditional Chinese medicine, which is also the characteristics and advantages of traditional Chinese medicine in treating diseases. Taibai Qiyao has the advantages of abundant production and shorter culture cycle than commonly used precious Chinese medicine. Therefore, Taibai Qiyao can be used as a medicinal material for the treatment of bone and joint diseases. However, the specific pathogenesis of bone and joint diseases is not clear enough, and the specific compatibility and dosage of Taibaiqiyao in clinical application still need further study.

References

[1] He Xijing, Pei Fuxing, Tian Wei. Sports system injury and disease [M]. Beijing: People's Health Press, 2015: 345-353.

[2] Le TK, Montejano LB, Cao Z, et al. Health care costs in US patients with and without a diagnosis of osteoarthritis [J]. J Pain Res, 2012, 5(1): 23-30.

[3] Jinks C, Jordan K, Ong BN, et al. A brief screening tool for knee pain in primary care (KNEST).2.Resuilts from asurvery in the general population aged 50 and over [J]. Rheumatology (Oxford), 2004, 43(1): 55-61.

[4] Arden N, Nevitt Mc. Osteoarthritis: epidemiology [J]. Best Pract Res Clin Rheumatol, 2006, 20(1): 3-25.

[5] Qiu Guixing. Advances in epidemiology and etiology of osteoarthritis [J] Chinese Medical Information, 2004, 19 (12): 22.

[6] Song Xiaomei, Tang Zhishu, Wang Wei, Cai Baochang. Taibai ' seven drugs ' research progress [J]. Asia Pacific Traditional Medicine, 2009, 5 (02): 120-123.

[7] Nie Bochun, Li Wanbo. Investigation on Taibai 'Qiyao' [J]. Shaanxi Traditional Chinese Medicine, 1986 (06): 175-176.

[8] Zhang Lin, Yang Fanli, Zhang Gang, An Yanru, Liu Yuyong. Research progress of Taibai Qiyao in Qinling Mountains [J]. Central-Southern Pharmacy, 2017, 15 (12): 1750-1754.

[9] Yan Shuting, Fan Hao, Li Ruolan, Guo Yanli, Liu Qiao, Gao Feng, Ou Li, Chen Lin, Li Min, Wei Peifeng, Zhang Lei. Research Progress on Chemical Constituents and Pharmacological Effects of Sinopodophyllum emodi [J]. Wild Plant Resources of China, 2020, 39 (07): 43-50.

[10] Shi Juan, Zhao Lintao, Fu Qiang, Song Jie, Kang Jun. Study on analgesic, sedative and anti-inflammatory effects of supercritical extract from Changchunqi [J]. Research and development of natural products, 2011, 23 (03): 428-431. DOI: 10.16333/j.1001-6880.2011.03.008.

[11] Abramoff B, Caldera FE. Osteoarthritis: pathology, diagnosis, and treatment options [J]. Med Clin North Am, 2020, 104(2): 293-311. DOI: 10.1016/j.mcna.2019.10.07.

[12] Zhang Qi, Wang Baojuan, Wang Lin, Li Tianyang, Zheng Shuguang. Research progress of traditional Chinese medicine fumigation therapy in the treatment of bone and joint diseases based on immune response regulation system [J]. Journal of Guizhou University of Traditional Chinese Medicine, 2021, 43 (04): 98-103.

[13] Wu Wenjun, Xu Xianxiang, Xia Lunzhu, Dai Yue. Research progress of plant active ingredients in the treatment of osteoarthritis [J]. Wild plant resources of China, 2008, (04): 6-10.

[14] Yang Renxuan, Wang Zhaopei, Xu Shuchai, Guo Yuhai, Deng Jinfeng. Effects of ginsenoside Rg_1 on chondrocyte proliferation and phenotype [J]. New Chinese medicine and clinical pharmacology, 2004 (01): 4-6. DOI: 10.19378/j.issn.1003-9783.2004.01.002.

[15] Wang Zhaopei, Yang Renxuan, Xu Shuchai, Chen Haiyun, Guo Yuhai, Deng Jinfeng. Effect of ginsenoside Rb1 on chondrocyte metabolism in vitro [J]. Traditional Chinese Medicine Orthopedics, 2004 (06): 8-9 + 63-64.

[16] Wang Xiaomei, Wang Yijie, Zhao Lifang, Duan Yuhang, Wang Jinsuo. Constituent Identification and Antioxidant Activity of Yuerqi [J]. Chemical Times, 2017, 31 (07): 18-20. DOI: 10.16597/j.cnki.issn.1002-154x.2017.07.005.

[17] Duan Jianhua, Cao Yi, Wei Lai, Ma Shiqiang, Jiao Jianbo. Effects of Tieniuqi and its compound tincture on SOD activity in synovial fluid of rabbits with knee osteoarthritis [J]. Journal of External Treatment of Traditional Chinese

Medicine, 2013, 22 (01): 5-6.

[18] Wang Zhen. Effect of Combination of Chinese and Western Medicine on Inflammatory Factors of Rheumatoid Arthritis [J]. Journal of Applied Traditional Chinese Medicine, 2019, 35 (1): 59-60.

[19] Javadi F, Ahmadzadeh A, Eghtesadi S, et al. The Effect of Quercetin on Inflammatory Factors and Clini-cal Symptoms in Women with Rheumatoid Arthritis: ADouble-Blind, Randomized Controlled Trial [J]. Jour-nal of the American College of Nutrition, 2017, 36(1): 9-15.

[20] Jiang Ji, Fang Haichuan, Jin Xiaochang, Miao Ping. The mechanism of resveratrol in improving rheumatoid arthritis by remodeling intestinal flora [J]. New Chinese Medicine, 2022, 54 (01): 8-14.

[21] Liu Yanjie, Wang Jian, Liu Lige. Research progress on chemical constituents and pharmacological effects of Sinopodophyllum hexandrum [J]. Northern Pharmacy, 2016,13 (04): 105-106.

[22] Wang Xiaoyan, Jin Hui, Han Jing, et al. Research progress on screening and prevention of osteoporosis in high risk population in community [J]. Chinese Journal of Osteoporosis, 2019, 25 (10): 1498-1501.

[23] Weng J, Wu J, Chen W, et al. KLF14 inhibits osteogenic differentiation of human bone marrow mesenchymal stem cells by downregulating WNT3A [J]. American Journal of Translational Research, 2020, 12(8): 4445-4455.

[24] Qin X, Jiang Q, KomoriH, et al. Runx 2 is required for bone matrix protein gene expression in committed osteoblasts in mice [J]. Journal of Bone and Mineral Research, 2021, 36(10): 2081-2095.

[25] Yang Sen, Pan Yalei, Li Yingang, et al. Protective effect of Feitian Wugongqi extract on rat osteoblasts and its regulatory effect on Wnt/β-catenin signaling pathway [J]. Zhongnan Pharmacy, 2020,18 (3): 435-439.

[26] Yang Y, Shuquan L I, Shen C, et al. TAA may induce bone and joint diseases[J]. Chinese Journal of Osteoporosis, 2016.

[27] Zhang Fan, Liang Qingyang, Han Chao, Liu Jia, Tang Yujin. The role of Wnt/β-catenin signaling pathway in regulating osteoblasts and osteoclasts in osteoporosis [J]. Chinese Journal of Osteoporosis, 2021, 27 (10): 1540-1544.

[28] Li Yingang, Liu Yanping, Pan Yalei. Basic research on the prevention and treatment of osteoporosis by 'Taibai Qiyao' -Regulation effect and mechanism of Feitian Wugongqi and Zhuzishen on osteoblasts [C] // 2019 Chutian Orthopaedic Summit Forum and the 26th China Integrated Traditional Chinese and Western Medicine Orthopedics Annual Conference Papers [Publisher unknown], 2019: 294. DOI: 10.26914/c.cnkihy.2019.018992.

[29] Ni Wenqi, Yan Hanwei, Li Ping, Zhang Ya, Li Weiyan, Cao Wei. GC-MS analysis of fat-soluble components of Changchunqi [J]. Shaanxi Traditional Chinese Medicine, 2016,37 (03): 361-363.

[30] Zhang Qiaoyan, Qin Luping, Tian Yeping, Zheng Hanchen, Huang Baokang, Wang Yin, Liu Zude. Regulatory effect of osthole on osteoblast function in neonatal rat calvaria [J]. China Pharmacology Bulletin, 2003 (04): 384-387.

[31] Li Lingzhi, Ni Ning, Zhang Yongliang, Gong Haiying, Cui Ying. Effects of osthole on proliferation and differentiation of osteoblast-like cells UMR106 [J]. China Clinical Rehabilitation, 2006 (09): 93-95 + 197.

[32] Yang Ying, Wang Yunyun, Jiang Qichen. Advances in pharmacological effects of quercetin [J]. Special economic animals and plants, 2020, 23 (05): 24-28.

[33] Ye Shulin. Luteolin inhibits allograft rejection in mice and its immunoregulatory mechanism [D]. Guangzhou University of Traditional Chinese Medicine, 2021. DOI: 10.27044/d.cnki.ggzzu.2021.000045.

[34] Yang Sumei, Mei Jiahui, Jiang Rui, Yang Xiliang. Research progress of tetracyclic triterpenoids in nervous system diseases [J]. Research and development of natural products, 2021, 33 (12): 2157-2167. DOI: 10.16333/j.1001-6880.2021.12.020.

[35] Simonaro C, Frohbergh M, Ge Y, et al. THU0361Bone and Joint Disease in Mucopolysaccharidosis Involves Tlr4-Related Inflammation and Improves upon Treatment with Pentosan Polysulphate[J]. Annals of the Rheumatic Diseases, 2014, 73(Suppl 2):307-307.

[36] Li Yunze, Zhao Xuli. Advances in pathogenesis of osteoarthritis [J]. Chinese Journal of Pain Medicine, 2016, 22 (10): 728-733.