

Research progress in Chinese medicine treatment of hormonal femoral head necrosis

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Abstract: Steroid-induced avascular necrosis of the femoral head is a common refractory chronic disease in orthopedics. In recent years, with the improvement of people's living standards, the harmfulness and prevention of this disease has gradually been paid attention to. Research on the treatment of steroid-induced necrosis of the femoral head in China is increasing and good efficacy has been achieved. Based on the literature research in recent years, this paper focuses on the etiology and pathogenesis of traditional Chinese medicine, the progress and mechanism of traditional Chinese medicine treatment, etc. This paper summarized and briefly analyzed the research status of steroid-related necrosis of femoral head in recent years, and prospected a more reasonable application of traditional Chinese medicine in the treatment of steroid-related necrosis of femoral head in the future, in order to provide reference for the further prevention and treatment of steroid-related necrosis of femoral head by traditional Chinese medicine.

Keywords: steroid-induced avascular necrosis of the femoral head, traditional Chinese medicine, etiology and pathogenesis, research progress

Steroid-induced Avascular Necrosis of the Femoral Head (SANFH) is a complex pathological process caused by intra-medullary microangiopathy, such as thrombosis, resulting in inadequate blood and oxygen supply to the femoral head and subsequent bone cell death due to a combination of factors such as excessive use of hormones^[1]. The most common clinical manifestations of SANFH are hip pain and impaired mobility^[2]. SANFH can be classified as "hip paralysis" and "bone erosion" in Chinese medicine, and is more common in young and middle-aged people and has a very high disability rate^[3]. The pathogenesis of SANFH is complex, but the more commonly accepted mechanisms include vascular endothelial damage and apoptosis^[4]. Western medical treatment for SANFH is mainly surgical and non-surgical, but due to its complex pathological process and lingering disease, western medical treatment has problems such as high surgical costs, many surgical sequelae and uncertain drug side effects^[5]. Chinese medicine has often achieved good results by adopting a variety of treatment methods and measures through the dialectic of this disease. A review of recent research on the treatment of SANFH in Chinese medicine is presented.

1. Chinese medical etiology and pathogenesis

The discussion of the etiology and pathogenesis of SANFH in classical Chinese medicine dates back to the Qin and Han dynasties. For example, in *The Spiritual Pivot-Stabbing the True Evil*, it is stated that "the evil of emptiness is also in the midst of the evil, sprinkling and moving the form, starting the hair and moving the couples, its entry is deep, and the internal fight with the bone is bone erosion"^[6]. Subsequent studies were more refined, for instance, the treatise on the spleen and stomach-spleen and stomach victory and decline said: "Spleen disease is downstream multiplied by kidney, earth over water, then the bones are weak and powerless, this is bone erosion, so that the bone marrow is empty, the foot can not walk on the ground"^[7]. In recent years, many scholars inspired by the classical theory of Chinese medicine, the etiology and pathogenesis of SANFH are doing various discussions. The main causes of SANFH are phlegm stasis and paralysis, withered marrow and bones, liver and kidney deficiency, and loss of glory of tendons and bones.

1.1. Stasis and phlegm paralysis, withered marrow and bones

The evils of phlegm and stagnation are Yin evils, which hinder the promotion of Yang Qi and the

flow of Qi and blood, and stagnation in the tendons, bones and blood vessels will inevitably lead to localized lack of glory and nourishment, followed by withering of marrow and bone. Some scholars[8] have based on the article "When the vital energy is deficient, it will not reach the blood vessels, and when the blood vessels have no energy, it will stay and stasis", combined with the regulation mechanism related to bone metabolism in modern medicine, focusing on "stasis", hold the view that if the blood in the veins does not run properly, the tendons and bones will lose nourishment, resulting in marrow and bone impotence, damage to the thighs and bones, and the development of this disease. Cao[9] based on the theory of phlegm and stasis, which states that "phlegm and stasis have the same origin and cause the same disease", combined with the fact that the evil of phlegm and dampness is a Yin evil, and that dampness is heavy and turbid in nature, causing the disease with the characteristic of being lingering and difficult to heal. The key to this disease is the accumulation of phlegm and dampness and the stagnation of blood vessels and veins. Wang[10] based on the classical theory of "deficiency, phlegm and stasis", combined with the TCM theory of "paralysis caused by phlegm", and by studying the regulation of SANFH-related signalling pathways, confirmed that the treatment of phlegm can achieve the goal of preventing and treating SANFH, and concluded that the pathogenesis of SANFH is related to "deficiency, phlegm and stasis".

1.2. Deficiency of the liver and kidneys, loss of glory of the tendons and bones

If one organ is deficient, not only will the function of the organ be out of order, but also the function of the other organ will be affected, and the tendons and bones will inevitably lose their glory. According to Liu[11], in light of the Nei Jing, "Kidney qi is hot and the marrow is withered, resulting in bone impotence", and since the kidney is the innate essence of the human body, if the kidney is deficient, it cannot play its role of qi-transformation and propulsion, and the qi and blood cannot run and warm and moisten the tendons and bones, then the new bone It is believed that "bone is the root of the disease, the source is blood, and the root is connected to the kidney", emphasizing the key role of kidney deficiency in the development of this disease. Zhang[12] believed that the disease is caused by congenital deficiency of endowment and external evil, and that the key to the pathogenesis is deficiency of the liver and kidney and internal obstruction of blood stasis, with kidney deficiency as the root and evil as the symptom. As the patient has a deficiency in the kidney and has been taking hormonal drugs for a long time, the Yin and Blood are depleted and cannot moisten the limbs and bones.

2. Advances in Chinese medicine treatment

2.1. Internal treatment methods

Chinese medicine is increasingly accepted by patients in clinical practice for its advantages of painless and non-invasive treatment process, accurate dialectical evidence and low treatment cost. Studies have confirmed that single herbs such as *Salvia miltiorrhiza*, *Panax ginseng*, *Chuanxiong*, Red peony, *Safflower* and *Epimedium* have certain efficacy in preventing and treating SANFH, while the above herbs mainly exert their effects by invigorating blood circulation, promoting microvascular formation in necrotic bone tissue, improving local microcirculation in the femoral head and promoting new bone production[13,14].

2.1.1. Removing phlegm and blood stasis, promoting circulation and removing paralysis

Clinical studies[15] found that the formula of invigorating blood circulation and removing blood stasis and Tongluo had significant effects on the improvement of bone metabolism, reduction of pain symptoms, hip function and joint mobility in patients with early SANFH, which provided factual support for the further clinical promotion of the use of the formula of invigorating blood circulation and removing blood stasis and Tongluo in the treatment of early SANFH. Zhou[16] treated 54 rabbits with SANFH with Bone Paralysis Tongluo Bone Building Granules and found that the destruction of the femoral head in the treatment group was significantly lighter than that in the model and control groups as the treatment time increased, suggesting that the drug could reduce osteoclast necrosis, which provided a reference for clinical treatment.

2.1.2. Tonifying the kidney and nourishing the liver, strengthening the bone and producing marrow

Zheng[17] summarised professor Qiu Xiangzhong's experience in treating non-traumatic femoral head necrosis in young adults and concluded that the disease was caused by the internal invasion of phlegm, dampness, stasis and toxicity due to long-term hormone use and alcohol consumption,

insufficient blood in the liver, disorder of liver qi, obstruction of the meridians, and local loss of glory and obstruction. "In the treatment, it is important to nourish the liver and treat both the symptoms and the root cause. Wang[18] collected 142 cases of SANFH and used a randomized grouping method, with the control group given interventional treatment and the study group given Duzhong tonifying kidney and strengthening bone granules on top of the control group. The difference in efficacy between before and after 24 months of treatment was observed, and it was found that compared with the control group, the study group had significant advantages in terms of reduction of hip pain and improvement of joint function, indicating that Duzhong tonifying kidney and bone building granules are effective in SANFH.

2.2. External treatment methods

The external treatment method of Chinese medicine for SANFH is based on acupuncture and external application of Chinese herbs. Bai[19] selected 40 rabbits and randomly divided them into a blank control group (half of each sex, no treatment), an animal model group (no treatment after modeling), a Chinese medicine group (oral administration of Xian Ling Bone Depot after modeling), and an acupuncture treatment group (electro-acupuncture after modeling, acupuncture points: Huan Yu, Thigh Pass, Hanging Bell). The results showed that there were five significant differences in serum BGP and local tissue blood flow between the electroacupuncture group and the Chinese medicine group, but they were higher than the other two groups, while the morphological indexes of femoral head bone tissue observed under electron microscopy were better than the other three groups, suggesting that electroacupuncture has certain preventive and curative effects on SANFH. In his study, Liu[20] adopted bone pain cream to intervene in the model rabbits with SANFH. 30 rabbits with SANFH model were randomly divided into blank group, model group and experimental group, 10 rabbits in each group, and the rabbits in the blank group and model group were given general feeding, while the rabbits in the experimental group were given bone pain cream applied to both hips. The results showed that the expression of BMP-2 and VEGF in the bone tissue of the femoral head of the rabbits in the experimental group was higher than that of the other two groups, which further promoted the formation of local microvessels and bone tissue repair, confirming the preventive effect of bone pain cream on SANFH.

2.3. Integrated Chinese medicine treatment

In clinical practice, external treatments such as acupuncture and fumigation are often used in combination with other therapeutic techniques to achieve good results in SANFH.

2.3.1. Combination of acupuncture and medicine

Clinical studies have reported[21] that in the treatment of patients with SANFH, the combination of buried acupuncture with oral bone erosion capsules was significantly more effective in terms of pain reduction, improvement in hip function and mobility than oral Xian Ling Bone Depot capsules alone, indicating that the combination of buried acupuncture with oral bone erosion capsules is effective in SANFH. Wu[22] concluded that the key to the pathogenesis of SANFH according to the Shih's wound family is that "blood stasis does not work" causing paralysis and "lung heat causes impotence", and treatment should be based on "combining acupuncture and medicine, treating both inside and outside together" He also introduced a case of SANFH treated by Professor Du Jiong using a combination of acupuncture and medicine, with good results.

2.3.2. Manipulation combined with Chinese herbal medicine

Zhu[23] collected 187 patients with middle to late stage femoral head necrosis caused by hormones and alcohol and compared their clinical efficacy, imaging and hip function scores before and after 3 months of treatment with Tui Na combined with Chinese herbal medicine and found that the patients showed significant improvement in pain and hip mobility, confirming that internal Chinese herbal medicine to tonify the kidney and strengthen tendons and external Chinese herbal medicine to The combination of internal Chinese medicine to tonify the kidney and strengthen the tendons, and external Chinese medicine to warm the meridians and invigorate the blood, together with Tui-na manipulation to smooth the tendons and relieve pain, had a reliable clinical effect on reducing pain and delaying the course of the disease in patients with middle and advanced femoral head necrosis. Li[24] collected 72 patients with SANFH and divided them into a control group and a treatment group, each with 36 cases, the control group was only treated with warm gall bladder soup plus or minus internal medicine, while the treatment group was treated with warm gall bladder soup plus or minus internal medicine combined with Chinese medicine manipulation. The data suggested that compared with the control group, the treatment group had better effect in reducing the pain symptoms, improving the hip joint movement and

function, and lowering the blood lipids of the patients, which proved that the effect of Chinese medicine manipulation combined with the addition and subtraction of warm gall bladder soup on the treatment of SANFH was better than that of the addition and subtraction of warm gall bladder soup alone.

3. Research on the mechanism of Chinese medicine in the treatment of SANFH

Xue[25] found that rhodiogenin could alleviate dexamethasone-induced apoptosis in osteoblasts by activating the PI3K/Akt signaling pathway and downregulating cystein-3 expression in osteoblasts. induced apoptosis in osteoblasts. Yu[26] found that Icarin (ICA) was effective in improving the angiogenic capacity, migratory capacity and cell viability of hormonal BMECs, which in turn had a good protective effect on femoral head blood transport in rats. It has also been shown that ER α -Wnt/ β -catenin is a key pathway through which epimedium promotes the proliferation and osteogenic differentiation of BMSCs[27]. Rui[28] found that Bone Paralysis Tongxiao Formula could effectively delay or stop the collapse of the femoral head in mice and was closely related to the increase in OB and OC apoptosis, increase in osteogenesis and decrease in osteolysis, and this process was due to the formula's ability to promote OPG expression while inhibiting the expression of PLC γ 2, CTSK, TRAP and others.

4. Summary and outlook

The prevalence of SANFH has been increasing in recent years, with studies showing that approximately 8.1 million people in China suffer from non-traumatic femoral head necrosis, of which more than 50% are SANFH patients[29]. The most important cause of SANFH is the overuse of hormones, and bone-related adverse effects due to hormone use have been reported in clinical practice, such as ischaemic necrosis of the femoral head due to a single intra-articular steroid injection[30], therefore, a more rational use of hormones in the clinical setting would be self-evident in reducing SANFH. Nevertheless, when hormones have to be used clinically to treat the disease, we can make full use of modern medical technology, such as the use of MRI as the best radiological technique to diagnose femoral head necrosis[31] and take care to monitor the imaging presentation of patients to identify which joints may be at risk[32] and treat them accordingly.

In this paper, we conclude that for SANFH, Western medical treatment is short and effective, but has many side effects, sequelae and the risk of repeated surgery[33], whereas TCM treatment is non-invasive, has few side effects, low treatment costs and a better prognosis. For example, there is still no unified standard for the classification of hormonal femoral head necrosis in Chinese medicine, and the diagnosis and treatment methods and efficacy evaluation system are not yet perfect. In addition, there is a lack of evidence-based research on the treatment of hormonal femoral head necrosis, which hinders clinical application and promotion. Therefore, in the future, we need to further improve the theoretical system of TCM for the treatment of hormonal osteonecrosis of the femoral head and use it as a guide to strengthen experimental and clinical research on TCM for the treatment of hormonal osteonecrosis of the femoral head. We will also develop new drugs with good efficacy and low cost that are easily accepted by patients, so that Chinese medicine can become a new choice for the clinical treatment of hormonal osteonecrosis of the femoral head.

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