

Clinical Experience of Hulisán Used in Rheumatology

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Abstract Hulisán is a commonly used medicine in rheumatism clinical practice. The clinical experience of Chief Chinese Medicine Specialist Zhou Lamei using Hulisán to treat rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and gout is discussed, to provide a basis for the clinical promotion of Hulisán in the Department of Rheumatology.

Key words Hulisán, Clinical experience, Rheumatology

1 Introduction

Hulisán is composed of *Aconiti Kusnezoffii* Radix, *Notoginseng* Radix, *Radix Cynanchi Wallichii*, and *Radix Ginseng*. The taste is pungent and warm, with the effects of expelling wind and dampness, relaxing muscles and activating collaterals, promoting blood stasis, and reducing swelling and pain. It is mainly used for rheumatism and numbness, muscle and bone pain, injuries caused by falls, trauma and bleeding, and is taken orally with boiled water or warm wine. In 1995, Hulisán was contained in Volume 10 of the *Drug Standards of the Ministry of Health: Traditional Chinese Medicine Formulas* by the Ministry of Health. Hulisán is a commonly used medicine in the clinical practice of rheumatism. In this paper, the experience of Chief Chinese Medicine Specialist Zhou Lamei in the use of Hulisán in clinical rheumatism, such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and gout is discussed.

2 Application in clinical rheumatism

2.1 Rheumatoid arthritis In clinical practice, rheumatoid arthritis appears on the basis of swelling and pain in small and multiple joints, and acute attacks on rainy days, in seasonal changes, and after catching a cold in summer, with obvious shoulder joint pain and nighttime symptoms. The tongue is light purple, and the coating is thin and greasy. In response to this disease, Director Zhou Lamei combined short-term use of Hulisán, which has shown good therapeutic effects. In Hulisán, *Aconiti Kusnezoffii* Radix is spicy and hot, and could dispel wind and dampness, warm menstruation, and relieve pain, which is the principal drug. *Notoginseng* Radix could relieve swelling and pain, and nourish blood and qi, which is the ministerial drug. *Radix Cynanchi Wallichii* could tonify kidney, strengthen waist, muscle and bone, and detoxify. *Radix Ginseng* is also known as "indigenous ginseng", which is an adjuvant for strengthening the spleen and stomach, supplementing

lung qi, and promoting qi and blood circulation. It is consistent with the main causes and pathogenesis of rheumatoid arthritis, including cold and dampness feeling, prolonged illness leading to deficiency, and prolonged illness leading to blood stasis.

Zhao Yi *et al.*^[1] explored the action mechanism of Hulisán in treating RA using network pharmacology methods, and found that there are 8 main chemical components in *Aconiti Kusnezoffii* Radix, 22 main chemical components in *Radix Ginseng*, and 8 main chemical components in *Notoginseng* Radix. A total of 34 active ingredients and 530 drug target proteins were obtained. Using the GeneCards database, 1 071 RA related genes and 44 common targets for drugs and RA were obtained. Based on the STRING 11.0 database, protein interaction information was obtained, and the top 30 key therapeutic targets of Hulisán capsules for RA were mainly VEGFA, IL-6, EGFR, MAPK8, CASP3, *etc.* KEGG pathway enrichment analysis identified 100 related signaling pathways, including IL-17 signaling pathway, AGE-RAGE signaling pathway, Th17 cell differentiation signaling pathway, TNF signaling pathway, *etc.*

2.2 Osteoarthritis Osteoarthritis is the disease with the highest incidence rate in the department of rheumatism. About 300 million people nationwide are infected with the disease, which is related to joint overuse, aging and degeneration, genetics, occupation, and obesity. The most common affected areas are the knee joint, finger joint, and shoulder joint. When clinical knee osteoarthritis occurs, knee joint pains. When moving up and down stairs, climbing mountains, running, *etc.*, the local area becomes cool, and it worsens during cloudy and rainy days, climate changes, and seasonal changes. The tongue is light red or tender, and the coating is thin, white, or greasy, and the pulse string is thin. The effect of using non-steroidal anti-inflammatory and analgesic drugs or glucosamine is not ideal. The pain in the finger joints is obvious, with a sense of soreness. When encountering cold water, the symptoms worsen, and the grip, pinch, pull, and thrust of the fingers decrease. The use of non steroidal anti-inflammatory and analgesic drugs has no significant effect. The tongue is light purple, and the coating is thin and white, and the pulse strings are thin. The local cold sensation in the shoulder joint is obvious, and the nocturnal pain is obvious, which affects sleep at night. The lifting

Received: April 6, 2023 Accepted: July 5, 2023

Supported by the Optimization of Traditional Chinese Medicine Treatment by Database Based on Epidemiology of Rheumatoid Arthritis (ZYYZD21004).

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and stretching activities are affected, and the symptoms are relieved during the daytime. The use of non-steroidal anti-inflammatory and analgesic drugs has no significant effect. The tongue is pale, and the coating is thin and white, and the pulse is stringy. In response to this disease, Director Zhou Lamei added Hulusan, which significantly reduced the patient's pain level.

Si Zijie *et al.*^[2] selected 71 patients with knee OA, 36 in the observation group (treated with Imrecoxib) and 35 in the control group (Imrecoxib combined with Hulusan capsules). After 4 and 8 weeks of treatment, the total effective rate of the observation group was higher than that of the control group, and the VAS scores of both groups were lower than that before treatment, and the observation group was better than the control group. Fu Minrui *et al.*^[3] systematically evaluated the effectiveness and safety of Hulusan in treating knee osteoarthritis. A total of 12 RCTs were included, with a sample size of 1 703 cases, including 1 075 cases in the experimental group and 628 cases in the control group. Meta analysis results showed that the use of Hulusan capsules/Hulusan capsules + conventional Western medicine treatment can improve the symptom relief rate, Lysholm score, knee joint function score, and VAS score of patients with knee osteoarthritis, and also alleviate symptoms such as knee joint pain, swelling, and movement limitations. The pathogenesis of osteoarthritis is deficiency in origin and excess in superficiality. The original deficiency is liver and kidney deficiency, while the excess in superficiality is blood stasis and wind cold dampness. In the *Internal Canon of Medicine*, it is stated that illness begins with overuse, and overuse leads to illness. For osteoarthritis, excessive use of joints can lead to deficiency of vital energy, while deficiency of vital energy is mainly due to excessive use and the accumulation of pathogenic factors, resulting in deficiency of vital energy. The main reason for the increased effect of adding Hulusan is that it can tonify deficiency and remove stasis, treat both manifestation and root cause of disease, and adapt to the pathogenesis of osteoarthritis based on deficiency and excess. According to modern medical research on the pharmacology of Hulusan, it has analgesic, anti-inflammatory, circulatory improvement, and humoral immune enhancement effects.

2.3 Spinal arthritis/ankylosing spondylitis It is more common in males aged 16–30 years old, mainly characterized by inflammatory lower back pain, which is evident at night and affects sleep. For patients who suffer from cold in winter and spring, air conditioning and electric fans in summer, cloudy and rainy days, and seasonal changes with regular medication, the symptoms of lower back pain worsen. Patients are afraid of cold, with a pale purple tongue, white and greasy fur, and stringy pulse. In response to this disease, Director Zhou Lamei combined the use of Hulusan, which has achieved good therapeutic effects. In the differentiation of advantageous diseases in traditional Chinese medicine, blood stasis obstructs the collaterals, which accounts for a considerable proportion. The main causes and pathogenesis are blood stasis obstruction, kidney deficiency and Du cold. The treatment mainly focuses on promoting blood circulation, resolving

blood stasis and pain, and tonifying the kidney, strengthening the Du and dispersing cold. In Hulusan, Notoginseng Radix could promote blood circulation and resolve stasis, reduce swelling and pain, supplement blood and qi; Radix Cynanchi Wallichii could tonify the kidney, strengthen the waist, tendons and bones, mainly treating kidney deficiency, low back pain, and weakness of the feet and knees; Radix Ginseng could replenish qi and activate blood. Therefore, the combination of non-steroidal anti-inflammatory and analgesic drugs can achieve good therapeutic effects in the treatment of spinal arthritis/ankylosing spondylitis.

2.4 Gouty arthritis Gout is based on hyperuricemia. The incidence of hyperuricemia in men is about 3%–18%, and gout occurs in 5%–6% of hyperuricemia. The key to a gout attack is the fluctuation of uric acid and the deposition of urate crystals. Director Zhou Lamei believes that a considerable proportion of acute gout attacks are caused by dampness, such as a decrease in temperature in the second half of the night, cooling after using air conditioning, and being caught in rain. The tongue is light red, and the fur is white and greasy, and the pulse is tight. Cold and blood stasis is also common, and these patients are the indications for Hulusan. Some gout patients have low inflammatory indicators during long-term recurrent episodes, and the use of non steroidal anti-inflammatory and analgesic drugs for pain relief is not ideal. On the basis of syndrome differentiation, the combination of Hulusan can achieve good therapeutic effects, and has a synergistic effect with non steroidal anti-inflammatory and analgesic drugs.

3 Conclusions

Currently, non steroidal anti-inflammatory and analgesic drugs are the most commonly used drugs for the treatment of rheumatoid arthritis, osteoarthritis, spinal arthritis, and gout, with some patients experiencing unsatisfactory therapeutic effects. Clinical studies have shown that^[4] Hulusan can reduce the inflammatory response of patients, thereby improving symptoms such as pain and joint stiffness. Mao Kunjun *et al.*^[5] determined 7 nucleosides (cytidine, uridine, adenosine, 2-deoxyuridine, guanosine, 2-deoxyguanosine, thymidine) and 3 bases (adenine, hypoxanthine, xanthine) in Hulusan. Adenosine has anti-inflammatory, analgesic, and anticoagulant effects. Hulusan mainly targets the pathogenesis of deficiency in origin and excess in superficiality. Origin deficiency is mainly liver and kidney deficiency, spleen and stomach weakness, while excess in superficiality is mainly cold dampness and blood stasis. Combined with non steroidal anti-inflammatory and analgesic drugs, Hulusan has good therapeutic effects. Hulusan has anti-inflammatory, analgesic, and microcirculation improving effects, and is worthy of clinical promotion and use in the rheumatology.

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conclusions.

4.2 Conclusions The iMRI revealed a remnant that required further resection, which was deemed safe and feasible based on our findings. Our systematic review and meta-analysis suggested that iMR images have a favorable discriminative capacity in diagnosing residual tumors in high-grade glioma. Surgeons should exercise caution when considering the implications of iMRI and choosing between 1.5 Tesla and 3.0 Tesla devices for medically fit patients.

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