

Advances in the Application of State-target Dialectical Theory in the Treatment of Gouty Diseases

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Abstract: The theory of "state-target identification" was firstly proposed by academician Tong Xiaolin, and then Professor Xiong Hui organically combined the "macro-identification" of Chinese medicine with the "micro-targeting" of modern medicine. Combined with modern medical research, it is believed that in the acute stage of gouty arthritis, the entry point of treatment should be the adjustment of "damp-heat state" and "damp-heat state", and the treatment should be carried out by adding and subtracting "target formula" such as Si Miao San, and by using Target medicines such as Astragalus, Chicken Blood Vine, Poria cocos, etc. can be used to accurately "hit the target" for the "symptomatic target" and "target". The use of "target drugs" such as astragalus, chicken blood vine and tu fu ling to achieve precise "targeting" and "targeting" of "symptoms" and "targets" provides ideas for the use of traditional Chinese medicine in the treatment of gouty arthritis in the acute stage.

Keywords: Target identification; Gouty arthritis; Target formula; Progress of application

1. Introduction

Gouty arthritis is a metabolic joint disease due to the body's purine metabolism disorder, the formation of hyperuricaemia after the persistent elevation of blood uric acid, monosodium urate crystals and deposition of periarticular joints, inducing local inflammatory reaction and tissue destruction [1]. Its acute attack is often manifested as redness, swelling, heat and pain in the joints, which seriously affects the quality of life of patients [2]. In recent years, the incidence of gouty arthritis has been increasing year by year, and it gradually tends to be urbanised and aged, and there is no cure. The recurrence of the disease makes the patients' quality of life decline, and even affects the normal work and life. Gouty arthritis often occurs in the joints, especially in the joints of the lower limbs, and is more common in men over 40 years old. According to the clinical manifestations, it is divided into three phases: acute phase, intermittent phase and chronic phase [3]. The acute phase mainly manifests as red, swollen and hot pain in and around the joints, impaired joint movement, which can lead to the formation of gout stones by urate deposition in the long term, joint deformity, and renal function damage. Western medical treatment is based on drugs, including colchicine, non-steroidal anti-inflammatory drugs, glucocorticoids, etc. The short-term use of efficacy is remarkable, but long-term use of adverse reactions, and easy to relapse after stopping the drug [4]. Chinese medicine treatment is not only rich in means, easy to operate, and small adverse reactions, and the combination of Western medicine can play the role of increasing the effectiveness and reducing the toxicity. The new system of TCM diagnosis and treatment theory with the core of "state-target identification" was firstly put forward by academician Tong Xiaolin, i.e. the diagnosis and treatment model combining macroscopic state regulation and microscopic targeting, and this diagnosis and treatment model not only inherits the "state regulation theory" of TCM, but also absorbs the results of the research on the understanding of diseases and pharmacology of modern science. This diagnostic and treatment model not only inherits the "modulation theory" of Chinese medicine, but also incorporates the modern scientific understanding of diseases and pharmacological research results, which is an innovation of the theory of traditional Chinese medicine, "theory - method - formula - medicine - quantity" [5].

2. Etiology and pathogenesis of gouty arthritis

2.1. Modern medical understanding of gouty arthritis

Gouty arthritis is crowned as the first of the pain, which comes and goes like the wind, and is a self-limiting disease [6]. Clinically, it is often divided into asymptomatic hyperuricaemia phase, acute exacerbation phase, critical phase and chronic gouty arthritis and gouty stone phase. Uric acid is an exogenous and endogenous purine metabolic end product, which is closely related to hepatic and renal function and diet. The excretion of uric acid from the body is 2/3 metabolised by the kidneys and 1/3 through the gastrointestinal tract. In general, when the body's uric acid concentration reaches a certain threshold of 7.0 mg/dL (420 μ mol/L), it will promote the deposition of uric acid sodium salt crystals in the joints of the body, and the deposited crystals are recognised by the innate immune system through the membrane receptor as a foreign body, which induce the production of a variety of inflammatory chemokines and activating factors, and ultimately lead to redness, swelling and heat pain of the affected joints, and induce an acute attack of gouty arthritis [7]. In addition, clearance of pathogens is a defence mechanism against infection. When neutrophils accumulate, infiltrate and activate phagocytosis of intra-articular uric acid sodium salt crystals in the joint tissues, intra-articular uric acid sodium salt crystals will be released with the lysis of cell membranes, and the danger signals will persist, further exacerbating inflammatory reactions and eventually the typical symptoms of acute gouty arthritis [8]. Repeated attacks of gouty arthritis then form gout stones complicating chronic gouty arthritis, which are organised structures consisting of fibrovascular shells and deeper protein corona composed of cells of the innate and acquired immune system and nuclei of sodium urate crystals within the joint. As gout stones develop, the gradual deposition of urate triggers the continuous destruction of joints and tissues leading to severe loss of function and greatly reducing the quality of life of the patient.

2.2. Chinese medicine's understanding of gouty arthritis

The description of gouty arthritis in Chinese medicine is first seen in Liang-Tao Hongjing's Famous Physician's Record: "The main treatment of all thieves wind, gout in 100 joints without a long time new." Tao Hongjing believed that gout was caused by the body feeling wind evil, which was different from what is now called gout and closer to what is now called paralysis. Paralysis was first recorded in the "Suwen - paralysis theory", that is, "wind, cold, dampness, three gas mixed to the combined and paralysis, the wind wins the paralysis for the line, cold wins the pain paralysis, dampness wins the paralysis for the paralysis," that the "paralysis" is due to the body to feel the wind, cold and dampness. Ming Dynasty Huangfu in the "Ming Medical Palm": "The gout, all over the body to go pain is also, the ancients called the White Tiger calendar section of the wind." Therefore, it has been called the "calendar section disease" "White Tiger calendar section", etc., belongs to the Chinese medicine "paralysis" category, the etiology of the disease is mainly dampness, heat, blood stasis and toxicity, paralysis blockage of the meridians. Dampness, heat, phlegm and stasis are the pathological factors in different stages of gout. The disease of gout is like a tiger's rodent, so it is called the disease of white tiger". The research results of domestic scholars on gouty arthritis patterns show that damp-heat syndrome is the main clinical pattern, and clearing heat and eliminating dampness is the main treatment [9]. Therefore, the etiology of this disease is often intemperance of taking food, leading to the dysfunction of the spleen in transport. The kidneys lose their ability to clear turbidity, and the dampness, heat, and turbidity toxins are endogenous. On the other hand, it may be due to insufficient natural endowment, and external pathogenic factors, such as wind, cold, and dampness, leading to prolonged depression and heat transformation, stagnation into phlegm, and blockage of meridians. Or it may be due to insufficient temper, endogenous dampness, heat, and toxins, flooding the blood vessels, flowing into the joints, and obstructing the meridians and blood vessels, which cannot be reached. If not, it will cause pain. The disease first occurs in the blood vessels, then in the meridians, joints, skin, and organs. The initial location of the disease is in the blood vessels, followed by the meridians, bones, skin, and organs. The syndrome belongs to spleen qi deficiency, damp heat stagnation, and meridian obstruction. The "Su Wen Qi Tong Tian Lun" points out that "If a person frequently eats a high-fat diet, the evil energy in the body is not easily released, resulting in internal heat and a tendency to develop ulcers". Bad dietary habits can cause spleen deficiency and indigestion. Over time, heat can fumigate the muscles of organs, leading to the accumulation of heat in the organs. Damp heat toxins flow into joints, muscles, and bones, causing poor circulation of qi and blood, leading to gouty arthritis.

2.3. Understanding of the pathogenesis of gouty arthritis based on the theory of "state-target identification"

"Conditioning" is the cornerstone of Academician Tong Xiaolin's state-target identification, and "conditioning" is based on the holistic view of Chinese medicine. "Targeting" refers to the precise treatment of clinical symptoms and physical and chemical indicators of the disease. Elevation of blood uric acid is caused by the poor operation of qi and blood, accumulation of turbidity, or further flow into the meridians and channels [10]. Abnormal blood uric acid is caused by eating too much fat and sweet, and dampness and heat are injected into the joints, if further injection into the joints, then gout will occur, so gouty arthritis clinically is mainly dampness and heat, and in the acute stage, the overall presentation of the "state of dampness and heat" and "dampness and turbidity state". The "target" of gouty arthritis in acute stage is mainly reflected in the redness, swelling, heat and pain of joints, joint dysfunction and other "symptomatic targets" as well as high blood uric acid, elevated white blood cell counts, increased blood sedimentation rate and other "targets". The "target" is the high blood uric acid, leukocyte count elevation, blood sedimentation speed. Therefore, clinical diagnosis and treatment of acute gouty arthritis should pay attention to its "damp-heat state" or "damp and turbid state", and pay attention to its "symptomatic target" and "target". The treatment of gouty arthritis in the acute stage should pay attention to the fact that it is in the "damp and hot state" or "damp and turbid state", and attach importance to the "target" of the disease.

3. The use of the theory and prescription of "state-target identification" in the treatment of gouty arthritis in the acute stage

From the perspective of traditional Chinese medicine, the theory of "state-target identification" clarifies the causes of diseases at different stages of the development process and the key mechanisms of diseases, and under the guidance of the overall concept of "state", combined with the specific targets of diseases, diseases and targets, the treatment is based on the "state" and the use of target drugs to hit the "target". On the basis of "state", target drugs are used to hit the "target", which improves the pertinence and directivity of treatment. Target prescription, target drug is not a simple list of drugs, but after obtaining a group of traditional Chinese medicine with the same targeting effect, according to the Chinese medicine classification, as well as pharmacological analysis of reclassification, used to "regulate the state" [11]. The "target" can be divided into disease target, disease target and target. Setting the "target" can help to understand the disease, and is also the main direction to consider when prescribing and administering medicines. The "target" refers to the point of action of traditional Chinese medicine at the macro and micro levels. At the macro level, for "disease target", it refers to the use of target formulae and target medicines with specific curative effects on diseases; for "disease target", it refers to the use of target formulae and target medicines with specific relieving effects on clinical symptoms; for "target", it refers to the use of target medicines with specific relieving effects on physical and chemical indexes. For the "target of disease", target prescription and target drug with specific relief effect on clinical symptoms are adopted; for the "target of target", target prescription and target drug with specific effect on physical and chemical indexes, imaging examination, etc. are adopted. For the "target", target drugs with special effects on physical and chemical indicators and imaging tests are used. On this basis, Professor Xiong Hui, according to years of clinical practice, believes that gouty arthritis belongs to the state of wet state, heat state, deficiency state and stasis state intermingled with each other. Gouty arthritis patients clinical manifestations to overweight and obesity is common, there are red face, dry mouth, bad breath, red tongue, yellow greasy moss, pulse flooding and powerful, daily over-eating alcohol, wine and thick flavour, paste sorghum and spicy things, presenting a piece of "wet" and "hot" state. In addition, the patient mostly has the symptoms of "spleen deficiency", such as unformed stools, loose stools, etc. In the local joints, there are red, swollen, congested and other "stasis". The cause and effect of the disease are examined, with spleen deficiency and dietary fat, sweet and thick flavour as the cause, damp-heat congestion and vein paralysis (joint swelling and pain) as the effect, and obesity, uric acid, blood sedimentation, and elevated C-reactive protein as the target and indicator. The treatment method refers to the general direction of treating and regulating by strengthening the spleen and nourishing the stomach, clearing internal heat, and promoting dampness, combined with substances such as bitterness, bitterness, and saltiness. It can achieve the goal of promoting dampness, promoting blood circulation, and removing blood stasis, with specific treatment targets. At the same time, we can also advise patients to adjust their emotions, adjust their diet, increase exercise, which can prevent the occurrence of diseases.

3.1. Target prescription

Patients tell mostly red, swollen and hot pain in the joints, with sharp and sudden onset of arthralgia. It may be accompanied by unfavourable joint movement, fever, heartburn and other symptoms. The tongue is red, the moss is yellow and greasy or yellow and thick, and the pulse is slippery or slippery. Acute gouty arthritis can be diagnosed by combining the primary and secondary symptoms with the tongue and pulse. The treatment is to remove heat and dampness, activate blood circulation. It can be treated with additions and subtractions such as Si Miao San, Angelica Sinensis Pain Relieving Soup, Bamboo Leaf Gypsum Soup, etc [12]. A study [13] showed that the treatment of gouty arthritis with the Chinese herbal formula of Si Miao San as the main formula was effective in the treatment of gouty arthritis. The total effective rate of treating gouty arthritis is high and the incidence of adverse reactions is low. Another study [14] showed that flavoured bamboo leaf gypsum soup for the treatment of acute gouty arthritis of the damp-heat accumulation type was similar to celecoxib capsule in terms of clinical efficacy and symptomatic efficacy.

However, celecoxib capsule was superior to celecoxib capsule in reducing blood uric acid levels. It also showed that [15], Angelica sinensis and pain relief soup in the treatment of acute gouty arthritis with damp-heat accumulation was effective in improving the symptoms and signs of joint pain, swelling, and unfavourable flexion and extension, as well as improving the blood uric acid level, tumour necrosis factor α , CRP and other indexes.

3.2. Target drugs

For the treatment of gouty arthritis in the acute stage, there are a great variety of traditional Chinese medicines. With the progress of modern science and technology and the development of modern pharmacology, the mechanism of action of traditional Chinese medicine has also been studied in depth. In the treatment of acute stage of gouty arthritis, Chinese medicines mainly play the roles of lowering uric acid level, protecting renal function and inhibiting inflammatory reaction and relieving pain. Under the theoretical guidance of modern pharmacological research, the use of the theory of "state target identification" to identify and treat the "target" has achieved better efficacy in the clinic. Fenghuang, Cangzhu and Baijiao are drugs that inhibit inflammatory reactions and relieve pain [16,17].

4. Gouty arthritis state target diagnosis and treatment system construction

4.1. Acute stage of gouty arthritis: "damp-heat state"

In the acute stage of gouty arthritis, patients have sudden redness, swelling and heat pain in the small joints of the lower limbs, with pain that refuses to be pressed, burning when touched, and relieved when cooled, accompanied by fever and thirst, disturbed and uneasy, with yellow urine, a red tongue, yellow and greasy moss, and a slippery pulse. Most of them are caused by dampness-heat condensation, and are treated by adjusting the "dampness-heat state".

4.2. Acute gouty arthritis "wet and cloudy state"

Acute gouty arthritis patients appear joint redness, swelling and stinging pain, local swelling and deformation, flexion and extension of adverse, purple skin, numbness, hard to touch, around the lesion can be touched "small hard knot", dry skin, sallowness, purple tongue or petechiae, thin yellow moss, pulse is thin and astringent or sinking string. Most of them are caused by dampness and turbidity blocking joints and meridians, so they should be treated by adjusting the "dampness and turbidity state".

4.3. Staging the toxicity and targeting

4.3.1. Acute phase inhibition of inflammatory body activation as a target

Gouty arthritis in the acute phase of the patient's most obvious symptom is joint pain like a tiger eating, modern medicine due to the joints, synovial infiltration of a large number of inflammatory factors, so that the nociceptive afferent nerve hypersensitivity [18]. Clinical evaluation of the inflammatory response is most intuitively based on clinical manifestations and blood inflammation indicators, and a large number of current studies have demonstrated that nucleotide-binding

oligomerisation structural domain-like receptor protein 3, activated by sodium urate crystals, is an important pro-inflammatory mechanism in acute attacks of gout [19]. Through downstream apoptosis-associated speck-like proteins, it cleaves cysteine-1 precursor into active cysteine-1, which contributes to the maturation of LI-1 β and then upregulates the expression of pro-inflammatory mediators [20]. Therefore, the acute phase of gouty arthritis produces a strong amplification of the inflammatory cascade, which is supported by clinical manifestations and blood inflammatory indices. The activation of inflammatory bodies and the infiltration of up-regulated factors in the joints have a common point with the extreme heat and toxicity, and the toxicity damages the bones and collaterals. Therefore, in the acute stage, detoxification is the rule of treatment, and clearing heat and detoxification and fixing the wind are the treatments, and inhibiting the activation of inflammatory bodies is the target of the treatment in the acute stage.

4.3.2. Regulating intestinal dysbiosis as a target in remission period

Intestinal bacteria intestinal flora as another intestinal "organ", in the excretion of uric acid also plays an important role, about 24% of uric acid excretion to the intestinal tract and further metabolism by intestinal bacteria. Chinese medicine point of view on the role of intestinal flora and the small intestine secret other clear and turbid work together, such as the "medical original" description: "people Na Shuigu, the spleen of the essence of the gas to rise, the small intestine into the dregs of the large intestine and down." If an imbalance occurs in the intestinal bacteria, they are unable to transfer dross, such as uric acid, downward, leading to the accumulation of uric acid. After the acute inflammatory response of gouty arthritis is suppressed, the primary goal of treatment is to control the patient's blood uric acid index, and modern uric acid-lowering mechanisms include xanthine oxidase inhibitors that inhibit uric acid production: allopurinol and febuxostat, and urate reabsorption transporter-1 inhibitors that promote uric acid excretion: phenylbromarone. While both of these commonly used drugs have significant hepatic and renal side effects, gut flora, as one of the new targets for uric acid reduction, is a new approach for the treatment of gouty arthritis in remission and/or hyperuricaemia by regulating its own intestinal microecology and thereby reducing uric acid accumulation.

4.4. Gouty arthritis state-targeted system staged treatment of toxic applications

4.4.1. In the acute stage, detoxification is the mainstay: clearing away heat and detoxifying the wind is the method, targeting the inflammatory body

Gouty arthritis acute phase due to dampness and heat fight, heat extreme into poison, Yang move wind, heat and poison with the wind through the channels, poisonous damage to the bones and veins, the most common clinical heat and poisonous state, so at this time to detoxification as the principle, to clear the heat and detoxification of the wind for the method, correcting the heat and poisonous state of the bias. Among them, detoxification includes treating heat with cold, clearing the hot seedling; all tangible and intangible evils from the body of the Xuanfu, orifices, the two jiao by the evil and out of the pain, through the pain, detoxification is not only to clear, but also to pass. Modern gout pathogenesis has been clearly related to NLRP3 inflammation, from the perspective of Chinese medicine, when the body of dampness and heat accumulation of toxic dense condensation, equivalent to the above mentioned inflammatory body activation and assembly process, so gouty arthritis staged treatment of toxicity in the acute stage of the core of the main detoxification to block the activation of NLRP3, assembly. Modern pharmacology has confirmed that the active ingredients of heat-clearing and detoxifying traditional Chinese medicines can effectively increase selective activated macrophages to block the activation of inflammasome NLRP3, thus playing an anti-inflammatory role [21]. Chinese medicine can choose Huangbai, Poria cocos, rhubarb, forsythia, dandelion and other heat and toxin removing drugs, heat and toxin, inflammatory reaction of the heavy can be added to the white flower snake Tongguoqiao, bitter ginseng, Zihaodi Ding to strengthen the target of the generation of inflammatory body inhibition, and ultimately the macro-reaction of the blood inflammation indicators have been effectively improved, heat and toxin to be resolved, pain relief, healing of the bone and the complex can be. However, it should be noted that the heat and toxin removing drugs should be in the disease, not overuse, in order to prevent over-service injury to Yang Qi. Clinical gout develops in the big toe, but not only the big toe, the whole body size joints can occur, for the wind through the meridians to promote the flow of heat and toxins, into the wandering pain, so the acute attack of gouty arthritis also need to "set the wind" to hit the second target, can be applied to live, qiangwu, wind and so on to set the wind to stop the pain. Modern research has found that traditional Chinese medicine for wind medicine, can reduce vascular permeability [22], gouty arthritis acute hyperthermia, vascular wall permeability increases, inflammatory body NLRP3 exacerbated inflammatory factors through the whole body capillary flow injection of the whole body, fixed wind treatment can cut off the systemic

adsorption effect of inflammatory factors.

4.4.2. In the remission period, the main purpose is to resolve toxins: removing dampness, resolving toxins and clearing the channels is the method, targeting the intestinal flora

Gouty arthritis remission period due to heat toxin to dissolve, but the dampness of the evil lingering to stay, diffuse difficult to melt, entrenched in the bones and channels, internal ambush bone meridians, induced re-emergence, clinically the most common for the state of dampness and toxin. At this time, the dampness and poison in the bone veins is the external performance, the internal reason for the dampness and poison without dissolution, including the spleen transport failure, wet intestinal tract, not to drive away the evil. The Treatise on Typhoid Fever says: "Yangming is in the centre, the main earth is also the place where everything goes, and nothing is transmitted again." Spleen and earth healthy transport can be poison, poison, decomposition of poison, not only can transport and transformation of water and dampness to remove the dependence of poison, but also reduce the intensity of poison, promote the decomposition of poison metabolism, to prevent it from spreading and damage to its organs. The small intestine is the master of fluid, the large intestine is the master of liquid, when the spleen transporting and transforming fluid obstacles, the lower jiao water and dampness can not be opened, and further dampness gathered into poison. This stage is based on the principle of transforming toxins, and the main method is to remove dampness, transform toxins and pass through the channels. By strengthening the spleen and resolving dampness, the flow of fluid can be relaxed, the dampness in the intestinal tract can be resolved, and the imbalance of intestinal bacteria can be regulated. After restoring the homeostasis of intestinal bacteria, the up-regulation of the abundance of intestinal probiotics *Lactobacillus* and *Pseudomonas* can promote the synthesis of uric acid metabolism enzymes, such as uric acid enzyme, allantoin enzyme and allantoinase, which can degrade uric acid into 5-hydroxyisovaleric acid, allantoin, allantoic acid, and ultimately degraded to urea, and reduce the accumulation of purines [23]. Clinically available Chen Pi, Citrus aurantium, Chinese yam, Radix et Rhizoma Ginseng and other spleen-healthy and dampness-resolving herbs, if the dampness and toxicity is heavy, accompanied by poor nativity, diarrhoea, high uric acid, can be added Cangzhu, Houpao, half-summer, Poria, Huo Xiang to remove the dampness of the product, to strengthen the dampness and resolve toxins targeted at the regulation of the intestinal flora. During the period of remission, the joints can be due to the dampness and poison for a long time, the local qi and blood run poorly, resulting in unfavourable joint flexion and extension, which is manifested as the deposition of urate in the joints causing aseptic adhesion and stiffness of the joints in the modern medicine. Therefore, at the same time, supplemented with the collateral drugs, such as Sangzhi, Weilingxian, Sangsheng and other traditional Chinese medicines, the joint collateral method targets the unfavourable sub-targets of the joints.

5. Treatment of gouty arthritis with Chinese medicine formula based on the theory of "state-target diagnosis"

5.1. Composition of Remission of Gouty Arthritis by Clearing the Joints of Paralysis Formula

According to the characteristics of gouty arthritis, the treatment of gouty arthritis should be based on the basic principles of taking into account both deficiency and reality, and treating the symptoms and root cause at the same time. The formula of Remission of Gouty Arthritis is a collection of famous prescriptions of famous doctors, which is derived from the addition, subtraction and modification of San Miao Pill in Yu Tuan's "The True Biography of Medicine" of the Ming Dynasty and Dang Gui Xiang Pain Soup in Zhang Elemental's "The Origin of Medicine" of the Jin Dynasty, and embodies the therapeutic feature of "clearing dampness and heat and dredging the joints". The Chinese character "Juan" has the meaning of removing, expelling and dredging, and "Juan Bi" means to expel gouty arthritis from all aspects of the cause and symptoms of the disease, so as to achieve the purpose of treating both the symptoms and the root cause. This formula is composed of Rhizoma Atractylodis Macrocephalae, Rhizoma Cyperus rotundus, Rhizoma Scutellariae, Poria cocos, Rhizoma Pinelliae, Radix Angelicae Sinensis, Rhizoma Alba, Rhizoma Atractylodis Macrocephalae, Radix Angelicae Sinensis, Radix Glycyrrhizae. The formula is composed of Atractylodes macrocephala and Cyperus rotundus, which are aromatic and dry, and Cyperus rotundus clearing dampness and heat in the lower Jiao. The two herbs are used together as a classic combination formula for clearing heat and inducing dampness, with the effects of strengthening the spleen, clearing heat and inducing dampness. Scutellaria baicalensis, Poria cocos and Cao Wu are the main medicines, which have the effects of drying dampness and resolving turbidity, strengthening the tendons and bones, and benefiting the joints. Angelica sinensis activates blood circulation and disperses blood stasis, restores qi and blood to their

original state, dispels blood stasis and generates new blood, dredges blood vessels and prevents paralysis and pain. The auxiliary medicines are Fenghuang and Zedoaria for promoting water retention and seepage of dampness, Atractylodes Macrocephala for strengthening the spleen and drying dampness, and Liquorice for harmonising the herbs.

5.2. Remission of Paralysis and Clearing of Joints Formula to regulate the "pathological state" of gouty arthritis "deficiency of spleen qi and stagnation of dampness, heat and stagnation"

Typical gouty arthritis attack is characterised by acute onset, sometimes even fulminant, usually the first attack occurs at night, severe pain and swelling in the affected joints, mostly in the first metatarsophalangeal joints, followed by the ankles, hands, wrists, knees, elbows, and other joints of the feet, with lightness of the day and heaviness of the night, redness and swelling of the involved joints and their surrounding soft tissues, heat, pressure pain and limitation of activities, pain aggravated by local contact, and limitation of the activities of lower limbs in the severe cases. MSU may be accompanied by body heat, thirst, yellowish red urine, dry stools, etc., with red tongue, yellowish greasy tongue coating, and moist or slippery pulse. With the increase of episodes, MSU deposits inside and outside the joints and other soft tissues, local swelling, joint stiffness, and in severe cases, joint deformity. Experts and scholars believe that "dampness, heat and stagnation" is the main mechanism of gouty arthritis, modern people's dietary structure has changed significantly, over-eating fat, sweet and thick flavour or excessive alcoholism, resulting in the accumulation of cream and sorghum, the liver, lungs, spleen, kidneys, triple jiao, bladder and other viscera dysfunction and cause the disease. Dampness is an evil of yin and obscurity, and tends to flow downward, flowing in the foot Taiyin spleen meridian, invading the big toe and the first metatarsophalangeal joints, dampness poison for a long time, in-depth blood, dampness and blood congestion, phlegm and stasis wrestling knot, gathering for gout nodules. If the dampness is immersed and stagnates in the bones, the poison burns the essence and marrow, and the bones are not nourished, so the tendons and bones can be seen to be eroded or deformed. Dampness is heavy and sticky, and when it is stored for a long time, it turns into heat, and when it turns into poison and flows into the joints and meridians, it evolves into heat poison. As the "General Records of the Holy Spirit - Volume 30 - typhoid" said: "heat and poisonous gas, guest in the internal organs, the evil knot in the interior, through the meridians and out, injected in the limbs, so people have hands and feet hot red swelling pain." In addition, phlegm condensation, dampness and other pathological products accumulate, interact with each other, mutual cause and effect, not scattered for a long time, and contain and turn poisonous, long toxicity does not go, accumulation into stasis, and ultimately stasis toxicity formation, prolonged disease. The reason for this is that the essence of gouty arthritis is the diminished function of the spleen. On the one hand, people have a high-fat diet and eat too much food, resulting in the accumulation of food in the intestines and stomach and damage to the spleen and stomach. On the other hand, "spleen controls the four limbs and muscle", irregular balance of work and rest, lack of sleep at night, and insufficient exercise during the day can lead to spleen damage and exacerbate spleen deficiency. Therefore, the aggravation of gouty arthritis is due to spleen qi deficiency and damp heat in the body.

5.3. Remission of paralysis and clearing of joints formula to hit the "target" of gouty arthritis "turbid toxins within the ambush"

The "target" of gouty arthritis is mainly reflected in the "symptomatic target" of red, swollen and hot pain in the joints, difficulty in flexion and extension, body heat, thirst, yellow and red urine, diarrhoea, dry stools, etc., as well as the "target" of high blood uric acid, accelerated erythrocyte sedimentation rate (referred to as haemosiderosis), and elevated inflammatory factors. "Targets". Therefore, gouty arthritis has elevated hyperuricemia as the main "target", and is usually accompanied by high blood lipids, high blood sugar, hypertension and other triggering factors, these patients usually over-eat fat, sweet and thick flavours, resulting in the accumulation of lipids, sugars, proteins, trace elements, uric acid, etc., in the body, thus creating a pathological state, and the products of these pathological states can be attributed to the Chinese medical science. These pathological products can be attributed to the Chinese medicine "turbid evil", "turbid evil" in the body for a long time into "turbid toxicity", the formation of an obscene, sticky, adhesive properties of the poisonous evil. Clinical diagnosis of gouty arthritis should be clear that it is in the state of "deficiency of spleen qi, dampness, heat and stagnation", pay attention to its "symptomatic target", but also to eliminate the "turbid venom within the ambush" produced by the "target". The "target" is to eliminate the "turbid toxin". The formula of Remission of paralysis and calendar clear formula is refined, many drugs can not only "adjust the state", but also "hit the target", belonging to the formula of "state and target adjustment".

Clinical studies have shown that the formula can reduce the pain score and joint swelling and heat pain of gouty arthritis, improve body heat, thirst, yellow and red urine, and improve joint mobility and other "targets" [24], and its mechanism of action is related to the lowering of uric acid, blood sedimentation, C-reactive protein, and inflammatory factors such as tumour necrosis factor-alpha (TNF- α), and interleukin-1beta (Ileukin-6) , interleukin-6 [25].

In terms of "hitting the target", it was found through analysis that Phellodendron Bark and its active ingredients in the formula have anti-inflammatory, analgesic, uric acid-lowering, anti-gout and other effects [26]. And Phellodendron Bark raw and salt products can reduce hepatic xanthine oxidase activity and inhibit uric acid production, resulting in a decrease in serum uric acid levels in hyperuricemic rats [27]. Berberine is the main active ingredient of Phellodendron Bark, which has anti-inflammatory and analgesic effects, and it can also significantly reduce the serum uric acid level of mice in the model of high uric acid [28], and it promotes uric acid excretion by inhibiting glucose transporter protein 9 and MSU anion transporter protein 1 levels in renal tissues [29]. In addition, Cortex Phellodendron Bark and its active ingredients can be used to treat gouty arthritis through anti-inflammatory and anti-oxidative stress, modulation of intestinal flora [30], modulation of purine metabolism [31], and nephroprotection. Atractylodes macrocephala is a key medicine for strengthening the spleen and removing dampness in clinical practice. Modern research has shown that atractylodes macrocephala has the efficacy of protecting the intestinal tract, promoting intestinal motility, resisting diarrhoea and anti-inflammatory effects [32], and it can effectively target the symptoms of "diarrhoea", "gastrointestinal discomfort", "sticky stool" and "sticky bowel movements" in patients with gouty arthritis. "The total extract, volatile oil and aqueous decoction can significantly reduce the uric acid level in model mice [33]. The total extract of Scutellaria baicalensis can clear heat and dry dampness, and promote uric acid excretion. Scutellaria baicalensis can clear heat and dry dampness, and can be used to treat gouty arthritis through anti-inflammatory, analgesic, anticoagulant, antithrombotic, and immunomodulatory effects [34], such as red, swollen, and hot pain in the joints, heat in the body, and yellowish redness in the urine, etc. The active ingredient of Scutellaria baicalensis can inhibit the expression of the structural domain-associated protein 3 of the NOD-like receptor thermoprotein and reduce the expression of the inflammatory factor TNF-inducer (TNF-). Its active ingredients can inhibit the expression of NOD-like receptor thermoprotein structure domain-related protein 3, reduce the secretion of inflammatory factors TNF- α , IL-1 β and IL-18, and treat the inflammatory response of gouty arthritis. Poria cocos has the effects of removing dampness, detoxification, and facilitating the joints, Poria cocos and its active ingredients have the functions of lowering uric acid, increasing uric acid excretion, and improving the circulatory system of the human body, as well as raising the threshold of pain, inhibiting the function of T-lymphocytes, inhibiting the activation of the NLRP3 inflammatory body axis, and reducing the downstream inflammatory factors such as the expression of IL-1 β , IL-6, and TNF- α , as well as protecting the liver and kidneys, and so on, and it has the effects on the "gouty arthritis" of gout. The treatment of gouty arthritis "targets" and "targets" by reducing the expression of downstream inflammatory factors IL-1 β , IL-6, TNF- α , and protecting the liver and kidney [35]. Yin Chen has the effect of regulating blood glucose and blood lipids and lowering uric acid [36], which can be used to treat the accumulation of "turbid evil" in gouty arthritis. Fangji has anti-inflammatory, anti-cellular fibrosis, cardio-renal vascular protection, antioxidant, improve immunity and other pharmacological effects, can improve the gouty arthritis "turbid toxicity" of the "target" [37]. Zedoary has the effect of diuresis and osmosis, which can reduce the number and degree of gouty arthritis attacks through the multiple effects of lipid-lowering, antihypertensive, diuretic and anti-gouty stone formation, etc. [38], and Zedoary can also inhibit the activity of xanthine oxidase to reduce the production of uric acid, so as to achieve the same time on the "target" of gouty arthritis. "Target" treatment. Atractylodes macrocephala has immunomodulatory, neuroprotective, gastrointestinal mucosal protective, hepatoprotective, hypoglycemic, and antioxidant pharmacological effects, which can regulate the "spleen qi deficiency" pathology, and can have therapeutic effects on MSU-induced experimental gouty arthritis in rats, and the mechanism of action may be related to the reduction of inflammatory factor IL-1 β , TNF- α release and inhibiting the activation of Toll-like receptor-4/nuclear factor- κ B signalling pathway [39].

6. Summary

Macro "state", micro "target" is the future development trend of Chinese medicine. According to the research of Tong Xiaolin academician's "target identification", in the treatment of acute gouty arthritis, we can use Si Miao San plus Astragalus, Poria, Ze Xie and so on. On the basis of regulating the "damp-heat state" and "damp-heat state", we can also accurately target the "symptomatic target" such

as inhibiting inflammatory factors to reduce inflammatory reaction and pain, and the "target" such as lowering the blood uric acid level. The "target" of the treatment is to inhibit inflammatory factors to reduce inflammation and pain, and to reduce the blood uric acid level. The "state target identification" mode effectively realises the complementary advantages and integration of Chinese and Western medicines, and improves the targeting and accuracy of disease treatment in the clinical diagnosis and treatment process, which needs to take the disease as the first priority, and to understand the whole occurrence of the disease in a comprehensive way from the perspective of the "disease" of Western medicine under the prerequisite of clear diagnosis of the disease in Western medicine. Under the premise of clear diagnosis of the disease in Western medicine, we will understand the whole process of disease development from the perspective of "disease" in Western medicine. At the same time, we should focus on the syndrome and apply holistic thinking to the four diagnostic methods of traditional Chinese medicine. Secondly, we should clearly define evidence-based treatment and incorporate the developed target as a part of the core etiology and mechanism of disease development. As a result, we will use the target as a reference to screen target drugs to improve a certain clinical symptom and objective indicator.

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