Treatment of 60 Cases of Gouty Arthritis with Modified Simiao Tang

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Objective: To observe the clinical effect of a modified Simiao Tang (加味四妙汤 Modified Decoction of Four Wonderful Drugs) for gouty arthritis and its influence on uric acid in blood. Methods: 120 cases of gouty arthritis were randomly divided into the treatment group and control group with 60 cases in each group. Modified Simiao Tang (MST) was orally administered to the patients in the treatment group and allopurinol tablet was orally administered to the patients in the control group. The clinical effects of two groups were evaluated after one-week treatment and uric acid (UA) and C-reactive protein (CRP) levels in blood were determined after 1-month treatment. Results: The total effective rate in the treatment group was significantly higher than in the control group, 86.7% vs. 68.3% ($P < 0.01$). And the treatment group was also significantly better than the control group in decreasing UA and CRP ($P < 0.05$ or $P < 0.01$). Conclusions: MST can significantly improve the symptoms and signs of gouty arthritis and decrease the levels of UA and CRP. It is good for gouty arthritis.

Key words: Gouty arthritis; Uric acid; Modified Simiao Tang (Modified Decoction of Four Wonderful Drugs)

Gouty arthritis is a disease characterized by redness, swelling and pain of joints, limited articular motion and dysfunction, and repeated attacks. It is caused by uratic deposition in the articular cavity or soft tissues due to hyperuricemia resulting from purine metabolic disturbance. In recent years it was found that this disease was accompanied with obesity, hyperlipemia, diabetes and high blood pressure, formed the syndrome of metabolism, which was caught much attention in clinic. The effect of western medications is definite during the acute onset, yet the side effects of serious gastrointestinal stimulation, injuries of the liver and kidney and arrest of marrow limit its clinical application. The 60 cases of gouty arthritis were treated with a modified Simiao Tang from 2003 to observe its clinical effect and adjusting function on uric acid (UA). A comparison was made with the 60 cases in the control group treated by allopurinol tablets. The report is as follows.

CLINICAL DATA
The 120 patients in this series were the outpatients of Rheumatic Department in Shenzhen Longgang Central Hospital from February 2003 to February 2007 and randomly divided into two groups. There were 60 cases in the treatment group, including 56 males and 4 females, aged 30–64 years (mean, 46.90±3.37), with duration of illness 1–10 years (mean, 3.70±1.68). Of them, 10 cases were an initial onset, 24 cases the second onset and 26 cases the multiple onsets. There were 60 cases in the control group, including 57 males and 3 females, aged 31–63 years (mean, 46.80±3.24), with the duration of illness 1–9 years (mean, 3.60±1.59). Of them, 8 cases were an initial onset, 25 cases the second onset and 27 cases the multiple onsets. There was no significant difference of the general data in the two groups after statistic analysis ($P > 0.05$), therefore, being comparable.

Diagnostic criteria
Inclusive criteria: Classified Criteria for Gouty Arthritis by American Society of Rheumatism in 1997 and the Diagnostic Criteria for Gout in Guiding Principles for Clinical Research on New drugs of Chinese Medicine issued by the Pharmaceutical
Bureau of Health Ministry of China in 1993 were followed.\(^1,2\)

Exclusive criteria: 1) Those with functional insufficiency of the heart, lung, liver, and kidney. 2) Those with an age over 70 year. 3) Those with severe deformation and stiffness of joints in late stage and those with loss of labor ability.

METHODS

MST was administered to patients in the treatment group. The formula consisted of Huang Bai (\textit{黄柏} Cortex Phellodendri) 15g, Cang Zhu (\textit{苍术} Rhizoma Atractylodis) 15g, Yi Yi Ren (\textit{薏苡仁} Semen Coicis) 30g, Niu Xi (\textit{牛膝} Radix Achyranthis Bidentatae) 15g, Ren Dong Teng (\textit{忍冬藤} Caulis Lonicerae) 30g, Tu Fu Ling (\textit{土茯苓} Rhizoma Smilacis Glabrae) 30g, Zhi Mu (\textit{知母} Rhizoma Anemarrhenae) 15g, Chi Shao (\textit{赤芍} Radix Paeoniae Rubra) 10g, Wei Ling Xian (\textit{威灵仙} Radix Clematidis) 15g, Mian Bi Xie (\textit{棉萆薢} Rhizoma Dioscoreae Septemlobae) 15g, Ze Xie (\textit{泽泻} Rhizoma Alismatis) 10g and Wu Shao She (\textit{乌梢蛇} Zaocys) 15g. They were decocted in water and taken orally one dose each day, in the morning and evening respectively. Allopurinol tablet (produced by Shanghai Xinyi Wanxiang Pharmaceutical Company Ltd., Permission Number of the National Drugs H310200334, 0.1g per tablet) were given to patients in the control group in a dose of one tablet two times daily after meal. The therapeutic course for the two groups was 1 month. Other analgesics and the drugs interfering with the UA were contraindicated during the treatment.

Observation method

Clinical effect: The criteria for swelling and pain in the joints were in accordance with \textit{An Assemblage of Guiding Principles of Clinical and Pre-clinical Research on New Drugs (Western Drugs)}.\(^3\) Clinical cure: The index of swelling and pain in the joints within 1 week was decreased by \(\geq 75\%\); Markedly improved: The index of swelling and pain in the joints within 1 week was decreased by 50\%–74\%; Improved: The index of swelling and pain in the joints within 1 week was decreased by 30\%–49\%; Ineffective: The index of swelling and pain in the joints within 1 week was decreased by \(< 30\%\). The index of swelling and pain in the joints = (total scores of swelling and pain in the joints before treatment — total scores of swelling and pain in the joints after treatment) / total scores of swelling and pain in the joints before treatment\(\times100\%\). Total scores of swelling and pain in the joints during rest + score of tenderness + score of swelling and distension in the joints.

Comparison of the therapeutic effect between the two groups

Table 1 showed that among the 60 cases in the treatment group 19 cases (31.7\%) was cured, 22 cases (36.6\%) markedly improved, 11 cases (18.3\%) improved, and 8 cases (13.3\%) ineffective, total effective rate was 86.7\%. Among the 60 cases in the control group 9 cases (15.0\%) were cured, 13 cases (21.7\%) markedly improved, 19 cases (31.7\%) improved, and 19 cases (31.7\%) ineffective, total effective rate was 68.3\%. The effective rate in the treatment group was better than that in the control group (\(P<0.01\)).

Comparison of the changes of UA and CRP in the two groups

Table 2 showed that there were significant differences in UA and CRP levels before and after
treatment in the treatment group \((P<0.05\) or \(P<0.01\)). There was significant difference in UA level before and after treatment in the control group \((P<0.01)\). There was significant difference after treatment between the two groups \((P<0.05\) or \(P<0.01)\). The therapeutic effect in the treatment group was much better than that in the control group.

**Safety evaluation**

No significant side effect or reaction was found after taking MST.

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<th>Table 1. Comparison of clinical effect between the two groups</th>
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<th>Table 2. Comparison of changes in UA and CRP levels before and after treatment ((X \pm s))</th>
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Compared with the group before treatment * \(P<0.05\), ** \(P<0.01\), compared with the control group at the same time△ \(P<0.05\), △△ \(P<0.01\).

**DISCUSSION**

The primary gout belongs to a heterogeneous disease due to uric acid metabolic abnormality with its cause unknown. It may be the genetic disease of multiple genes, is often induced by intake of foods rich in purine such as meat and seafood and accompanied with obesity, diabetes, hyperlipemia and hypertension. The hyperuricemia of primary gout is mainly caused by excretory disturbance of uric acid. Chen Ying et al pointed out that a decrease in uric acid excretion occupied 90% of hyperuricemia, for instance a reduction in uric acid filtered off from the glomerulus and a reduction in uric acid excreted from the renal tubules and/or an increase in reabsorption of uric acid, all resulted in the decreased uric acid excretion, thus hyperuricemia occurred. \(^4\)

The main clinical manifestations of gouty arthritis are redness, swelling, heat and pain in the affected joints and the motion disturbance. It belongs to heat arthralgia or agonizing arthralgia of arthralgia in traditional Chinese medicine. The etiology and mechanism are thought to have a relation with phlegm, blood stasis, damp and toxic heat. It is due to excessive intake of greasy and sweet food or excessive drinking of wine, later damp and phlegm produced and turned to heat. The damp, heat and phlegm flowed downward and blocked the channels and collaterals in the joints, resulting in pain due to qi and blood obstruction, thus redness, swelling, heat and pain in the joints of feet and ankles. The joints will have varying degrees of destruction of bones and functional disorders if the gouty arthritis frequently flares up.

Huang Bai (黄柏 Cortex Phellodendri), Cang Zhu (苍术 Rhizoma Atractylodis), Yi Yi Ren (薏苡仁 Semen Coicis) and Niu Xi (牛膝 Radix Achyranthis Bidentatae) are the ingredients of the original formula of *Simiao San* (四妙散 Powder of Four Wonderful Drug). Huang Bai (黄柏 Cortex Phellodendri) has the function of clearing heat, expelling damp and fire and removing toxicity. It acts on the lower Jiao. Cang Zhu (苍术 Rhizoma Atractylodis) having the therapeutic action on the spleen and stomach can internally expel the damp in the spleen and expel the external damp as well. These two herbs are the key herbs to treat arthralgia due to damp and heat. Yi Yi Ren (薏苡仁 Semen Coicis) can clear heat and remove damp, strengthen the spleen and relax muscles and tendons.
Niu Xi (牛膝 Radix Achyranthis Bidentatae) can tonify the liver and kidney, strengthen the bone and muscles, expel the wind-damp and guide the other drugs down to the affected part. A combination of the four herbs is a common formula to treat the redness, swelling, heat and pain in the joints of feet and ankles due to damp-heat in the lower limbs and the symptoms of flaccidity and numbness. On the basis of Simiao San (四妙散 Powder of Four Wonderful Drugs), Ren Dong Teng (忍冬藤 Caulis Lonicerae) added is to expel heat, remove toxicity, dredge collaterals and relieve pain in the muscles and bones. Wu Shao She (乌梢蛇 Black-tailed Snake, Zaocys) is good for expelling dampness, relaxing muscles and bones and clearing collaterals and is the key herb for arthralgia due to damp. Mian Bi Xie (棉萆薢 Rhizoma Dioscoreae Septemlobae) and Tu Fu Ling (土茯苓 Rhizoma Smilacis Glabrae) can expel wind and remove damp and are good at expelling wind-damp and treating severe arthralgia. Zhi Mu (知母 Rhizoma Anemarrhenae) and Wei Ling Xian (威灵仙 Radix Clematidis) can clear heat and dry damp and treat arthralgia. Ze Xie (泽泻 Rhizoma Alismatis) can remove damp turbidity. Chi Shao (赤芍 Radix Paeoniae Rubra) can tonify blood and soften tendons, in combination with Niu Xi (牛膝 Radix Achyranthis Bidentatae) promote the blood circulation to remove blood stasis and increase excretion of uric acid in the blood. The whole formula plays the role of clearing heat, dredging the collaterals, stopping pain and removing damp, thus the therapeutic effect is obtained. The modern pharmacology shows that Wei Ling Xian (威灵仙 Radix Clematidis) may increase excretion of uric acid and decrease uric acid content in the blood and has the significant function of stopping pain. Mian Bi Xie (棉萆薢 Rhizoma Dioscoreae Septemlobae), Tu Fu Ling (土茯苓 Rhizoma Smilacis Glabrae), Yi Yi Ren (薏苡仁 Semen Coicis) and Ze Xie (泽泻 Rhizoma Alismatis) may also increase excretion of uric acid and decrease uric acid content in the blood. Niu Xi (牛膝 Radix Achyranthis Bidentatae) has the function of protein assimilation, decreasing absorption of lipid, preventing the lipids from retaining in the serum or penetrating to the lining of the artery, changing the metabolism of lipid and purine, thus the aim of decreasing lipid and uric acid in the blood is obtained.

This research indicated that the modified Simiao Tang may effectively improve the symptoms and signs of gouty arthritis, significantly decrease UA and CRP and adjust the disordered metabolism of human body with no side effects, worth popularizing and further exploring.

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(Translated by Zhu Hanting 朱函亭)