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Clinical efficacy of gouty tea on chronic gouty arthritis and its effects on serum vascular endothelial function and inflammatory cytokines

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Abstract: To observe the efficacy of Gouty Tea on chronic gouty arthritis and its effect on vascular endothelial function and inflammatory factor levels. Totally 120 patients with chronic gouty arthritis were divided into control group (allopurinol orally, 100 mg/time, tid, for 12 weeks) and observation group (Gouty Tea, 1 bag/time, tid, for 12 weeks) randomly (n=60 per group). Compared with those before treatment, the TCM symptom scores, visual analogue score (VAS) and the levels of UA and XOD of the two groups were reduced, while the levels of NO, ET-1, VEGF, vWF, CRP, IL-1β, TNF-α and NALP3 of the two groups improved, 6 and 12 weeks after treatment ($P<0.05$). Nevertheless, after 6 weeks of treatment, there were no significantly difference of the level of VAS between the two groups. After 12 weeks of treatment, in the observation group, VAS was significantly lower compared to the control group. The TCM symptom scores and the levels of UA and XOD were significantly lower, while the levels of NO, ET-1, VEGF, vWF, CRP, IL-1β, TNF-α and NALP3 were significantly better in the observation group than those of the control group 12 weeks after treatment ($P<0.05$). The total effective rate was significantly higher and the incidence of adverse reactions was significantly lower in the observation group compared to the control group ($P<0.05$). Gouty Tea can effectively reduce the UA, XOD levels and VAS, effectively improve the vascular endothelial function and inhibit the inflammation of patients.

Keywords: Chronic gouty arthritis, Gouty Tea, uric acid, vascular endothelial function, inflammatory factors.

INTRODUCTION

Gouty arthritis (GA) is a common metabolic disease caused by abnormal purine metabolism and (or) the decrease of uric acid excretion, which leads to the increase of blood uric acid concentration and the injury of tissues and (or) organs. Chronic gouty arthritis (CGA) is a syndrome caused by repeated attacks of gout and aggravation of joint pain. Its main clinical feature is the formation of gouty tophus. If not controlled in time, GA can lead to joint deformities and dysfunction, even renal dysfunction (Akram *et al.,* 2014). Traditional Chinese medicine believes that CGA belongs to the category of "bi-syndrome" and "severe and migratory arthralgia" and its basic pathogenesis is spleen *qi* deficiency and dampness in the resistance of collaterals. Therefore, it is necessary to promote the excretion of uric acid (UA), inhibit the activity of xanthine oxidase (XOD) and reduce the damage of joint with Chinese medicine for invigorating spleen, drying dampness and mitigating arthralgia (Yang 2019).

GA is a common disease in the departments of orthopedics and endocrinology. It is a kind of aseptic inflammation caused by urate crystal in the joint and its surrounding tissues due to long-term purine metabolism disorder and (or) reduction of uric acid excretion and continuous increase of blood uric acid. Severe joint pain and activity limitation are found during GA attack. Repeated attacks can lead to joint deformity and movement disorder. In the late stage, the kidney may be endangered, resulting in renal insufficiency and death (Lu *et al.,* 2017). In recent years, with the development of economy and the change of people's eating habits, the incidence of hyperuricemia and gout is increasing, and the age of onset tends to be younger. At present, the research of western medicine in the treatment of CGA has reached the gene level, but the prevention and treatment of CGA are limited because the pathogenesis of gout has not been fully elucidated. At present, western medicine treats CGA mainly by promoting the excretion of uric acid, inhibiting the formation of uric acid and alkaline neutralizing drugs, but there are many problems such as adverse reactions, relapse or rebound after withdrawal and long-term use (Ailiyasi *et al.,* 2019). Although great progress has been made in the treatment of CGA in western medicine, there is no effective radical treatment at present. Therefore, it is of great significance to explore the treatment of CGA with traditional Chinese medicine.

This study observed clinical efficacy of Gouty Tea on CGA, and its effect on vascular endothelial function and inflammatory factor levels.

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MATERIALS AND METHODS

General information

Totally 120 CGA patients were selected from Outpatient Department of Haian Hospital of Traditional Chinese Medicine, China from January 2018 to February 2021. All cases were randomly divided into control group and observation group (n=60 per group). In the control group, there were 42 males and 18 females, at the age of 22-57 years, mean (45.21±8.83) years; with the body mass index of 21.61 kg/m^2–27.53 kg/m^2, mean (23.62±2.19) kg/m^2; the duration of gout ranged from 9 months to 11 years with a mean of (4.94±1.41) years. The gout occurred in the metatarsophalangeal joint of 32 cases, the ankle of 10 cases, the finger of 8 cases, and the knee of 10 cases. In the observation group, there were 39 males and 21 females, at the age of 23-56 years, mean (45.36±8.72) years; with the body mass index of 21.63 kg/m^2–27.24 kg/m^2, mean (23.81±2.27) kg/m^2; the duration of gout ranged from 7 months to 10 years with a mean of (4.98± 1.46) years. The gout occurred in the metatarsophalangeal joint of 34 cases, the ankle of 9 cases, the finger of 9 cases and the knee of 8 cases. There was no significant difference in sex, age, body mass index, duration of disease and location of disease between the two groups with comparability. The study was approved and supervised by the ethics committee of our hospital and all the selected patients signed informed consent.

Inclusion criteria

(1) It was in accordance with the diagnostic criteria in the *Guidelines for Diagnosis and Treatment of Primary Gout* formulated by Rheumatology Association of Chinese Medical Association in 2011; after diet control, blood uric acid was ≥ 420μmol/L; and in accordance with the diagnostic criteria of syndrome of phlegm-dampness blocking collaterals (refer to the standard of *Internal Medicine of Traditional Chinese Medicine* edited by Zhou Zhongying in 2007 Edition). (2) The patients strictly followed the doctor's orders, and the general information was complete. (3) The age was range from 18 to 60. (4) The patients were voluntarily tested and signed the informed consent.

Exclusion criteria

(1) Secondary gout; (2) combined with severe cardiovascular and cerebrovascular diseases, liver and kidney dysfunction, and hematological system diseases; (3) combined with mental diseases; (4) recently taken drugs that affect uric acid; (5) combined with other rheumatic diseases; (6) pregnant and lactating women; (7) those with severe gastrointestinal diseases that may affect drug absorption; (8) those with severe joint deformities and loss of labor.

Therapeutic method

The two groups of patients were given health education: Instruct patients to rest more, avoid tiredness and cold; drink more boiled water; change bad eating habits, avoid high purine diet; prohibit drinking and eating seafood, animal offal, and bean products. In the control group, the patients were administered allopurinol tablets (Shanghai Xinyi Wanxiang Pharmaceutical Co., Ltd, China; Batch number: 20180221, 100 mg/tablet), three times a day, one tablet every time, orally taken half an hour after a meal. In the observation group, the patients were administered Gouty Tea, three times a day, and one bag every time (Preparation Room of Haian Hospital of Traditional Chinese Medicine, China; approval number: SYZZ Z04001882, bagged steeping drugs, 10 g per bag). Gouty Tea prescription is composed of *Radix Angelicae Sinensis* 0.71g, *Rhizoma Atractylodis* 0.36g, *Rhizoma Smilacis Glabrae* 1.07g, *Rhizoma Alismatis* 1.07g, *Cortex Phellodendri* 0.71g, *Ramulus Cinnamomi* 0.71g, *Radix Codonopsis* 0.71g, *Rhizoma Atractylodis Macrocephalae* 0.36g, *Radix Gentianae Macrophyllae* 0.71g, *Radix Cyathulae* 1.07g, *Radix Puerariae* 0.71g, *Rhizoma Dioscoreae Septemlobae* 1.07g, *Rhizoma Cimicifugae* 0.36g and *Radix Glycyrrhizae* 0.36g. The course of treatment was 12 weeks in both groups.

Observation indicators

1) TCM symptom score: Before treatment, 6 and 12 weeks after treatment, the TCM symptom scores of the two groups were calculated according to the evaluation standard of Guiding Principles for Clinical Research of New Chinese Medicine in 2002 edition (Zheng *et al.*, 2002). The scores were evaluated from the aspects of local tenderness, joint swelling and pain, joint activity, skin temperature and skin color, and systemic symptoms. According to the severity, the patients were divided into four levels, and no symptom was counted as 0. According to mild, moderate and severe symptoms, the scores were 1, 2 and 3, respectively.

2) Visual Analogue Score: Before treatment, 6 and 12 weeks after treatment, joint pain of the two groups was calculated according to the evaluation standard of Visual Analogue Score (VAS). From painless to severe pain was 0-10 points. According to the degree of pain, the subjects scored by themselves.

3) Serum UA and XOD: Before treatment, 6 and 12 weeks after treatment, the serum UA level was measured by colorimetry and the serum XOD level was detected by enzyme-linked immunosorbent assay (ELISA).

4) Vascular endothelial function indexes: Before treatment, 6 and 12 weeks after treatment, the levels of plasma nitric oxide (NO) were measured by nitrate reductase method. The levels of plasma endothelin-1 (ET-1) were measured by radioimmunoassay. The levels of serum vascular endothelial growth factor (VEGF) and plasma von Wille brand factor (vWF) were measured using double-antibody sandwich enzyme linked immunosorbent assay.

5) Inflammatory factors: Before treatment, 6 and 12 weeks after treatment, the levels of serum C-reactive protein (CRP), interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α) and nucleotide-binding oligomerization domain-like receptor 3 (NALP3) were measured by ELISA in both groups.

6) Evaluation of efficacy: At 12 weeks after treatment, the clinical efficacy of the two groups was evaluated according to the *Guiding Principles for Clinical Research of New Chinese Medicine* in 2002 edition (Trial). Ineffective: No improvement or even aggravation of clinical symptoms, reduction rate of TCM symptom score <30%; effective: clinical symptoms improved, 30%≤ reduction rate of TCM symptom score <70%, inflammatory indicators significantly improved; significantly effective: clinical symptoms improved significantly, 70% ≤ reduction rate of TCM symptom score <95%, inflammatory indicators returned to normal; recovery: clinical symptoms basically disappeared, reduction rate of TCM symptom score ≥95%, and the inflammatory index returned to normal. Total effective rate was equal to (recovery + significantly effective + effective) cases / total cases × 100%.

7) Adverse reactions: Adverse reactions such as nausea and vomiting, allergy, abdominal pain, diarrhea and bone marrow suppression that may occur during the treatment were recorded.

STATISTICAL ANALYSIS

All data were analyzed and processed using SPSS24.0 statistical software. The data were expressed as the mean ± SD and compared with paired *t*-test. The count data were expressed as (%) and compared with $\chi 2$ test. The significance level (two-sided) was 0.05. A *P* value < 0.05 was considered to be statistically significant.

RESULTS

Comparison of TCM symptom scores between the two groups after treatment

There was no significant difference in scores of local tenderness, joint swelling and pain, joint activity, skin temperature and skin color, and systemic symptoms between the two groups before treatment. Compared with those before treatment, scores of local tenderness, joint swelling and pain, joint activity, skin temperature and skin color, and systemic symptoms were decreased after 6 and 12 weeks of treatment in both groups ($P<0.05$). Nevertheless, scores of local tenderness, joint swelling and pain, joint activity, skin temperature and skin color, and systemic symptoms were not significantly different between the two groups after 6 weeks of treatment. At 12 weeks after treatment, scores of local tenderness, joint swelling and pain, joint activity, skin temperature and skin color, and systemic symptoms were significantly lower in the observation group compared to the control group ($P<0.05$; table 1).

Comparison of Visual Analogue Score between the two groups after treatment

There was no significant difference in score of Visual Analogue Score between the two groups before treatment. Compared with those before treatment, VAS was decreased continuously after treatment in both groups ($P<0.05$). Nevertheless, VAS was not significantly different between the two groups 6 weeks after treatment ($P>0.05$). At 12 weeks after treatment, VAS was significantly lower in the observation group than in the control group ($P<0.05$; table 2).

Comparison of serum UA and XOD levels between the two groups after treatment

Before treatment, there was no significant difference in UA and XOD levels between the two groups. Compared with those before treatment, the levels of UA and XOD were decreased significantly 6 and 12 weeks after treatment ($P<0.05$). However, there was no statistically significant difference in the levels of UA and XOD between the two groups 6 weeks after treatment ($P>0.05$). The UA and XOD levels of the observation group were significantly lower compared to those of the control group 12 weeks after treatment ($P<0.05$; table 3).

Comparison of vascular endothelial function indexes between the two groups after treatment

There was no significant difference in the levels of NO, ET-1, VEGF and vWF between the two groups before treatment, with comparability. Compared with those before treatment, the levels of ET-1, VEGF and vWF were decreased ($P<0.05$), but NO levels were increased in the two groups 6 and 12 weeks after treatment ($P<0.05$). However, there was no statistically significant difference in the levels of NO, ET-1, VEGF, and vWF 6 weeks after treatment between the two groups ($P>0.05$). The levels of NO, ET-1, VEGF and vWF were significantly better in the observation group than those in the control group 12 weeks after treatment ($P<0.05$; table 4).

Comparison of serum inflammatory factor levels between the two groups after treatment

Before treatment, the levels of CRP, TNF-α, IL-1β and NALP3 had no significant difference between the two groups, with comparability. Compared with those before treatment, the levels of CRP, TNF-α, IL-1β and NALP3 in the two groups were decreased 6 and 12 weeks after treatment ($P<0.05$), but there was no significant difference in the levels of CRP, TNF-α, IL-1β and NALP3 between the two groups 6 weeks after treatment ($P> 0.05$). The levels of CRP, TNF-α, IL-1β and NALP3 were better in the observation group than those in the control group 12 weeks after treatment ($P<0.05$; table 5).

Table 1: Comparison of TCM syndrome scores of two groups before and after treatment (x±S, *n*=60)

Item	Group	*n*	0 weeks	6 weeks	12 weeks
Local tenderness	Observation	60	2.53±0.46•	1.71±0.37▲•	0.81±0.25▲■
	Control	60	2.55±0.47	1.74±0.39▲	1.67±0.33▲
Joint swelling and pain	Observation	60	2.89±0.45•	1.76±0.38▲•	0.91±0.23▲■
	Control	60	2.86±0.44	1.75±0.37▲	1.69±0.31▲
Joint activity	Observation	60	2.48±0.39•	1.61±0.31▲•	0.77±0.24▲■
	Control	60	2.51±0.41	1.64±0.34▲	1.65±0.35▲
Skin temperature and skin color	Observation	60	2.62±0.71•	1.68±0.54▲•	0.86±0.41▲■
	Control	60	2.64±0.72	1.71±0.58▲	1.67±0.53▲
Systemic symptoms	Observation	60	2.73±0.62•	1.71±0.45▲•	0.79±0.32▲■
	Control	60	2.71±0.61	1.72±0.47▲	1.68±0.44▲

Note: •P>0.05, vs. control group at the same time point; ▲P<0.05, vs. before treatment in the same group; ■P<0.05, vs. control group at the same time point

Table 2: Comparison of VAS of two groups before and after treatment (x±S, *n*=60)

Item	Group	*n*	0 weeks	6 weeks	12 weeks
VAS	Observation	60	8.01±1.63•	5.24±1.15▲•	1.51±0.45▲■
	Control	60	7.99±1.61	5.32±1.21▲	3.07±0.83▲

Table 3: Comparison of the serum levels of UA and XOD in two groups before and after treatment (x±S, n=60)

Item	Group	*n*	0 weeks	6 weeks	12 weeks
UA	Observation	60	532.27±39.85•	443.18±27.76▲•	324.57±18.53▲■
($\mu mol.L^{-1}$)	Control	60	530.86±38.62	442.71±27.11▲	368.49±21.39▲
XOD	Observation	60	59.14±6.37•	29.35±4.81▲•	13.86±2.37▲■
($ng.mL^{-1}$)	Control	60	58.98±6.29	30.18±4.83▲	28.54±4.64▲

Table 4: Comparison of the levels of vascular endothelial function indexes of two groups before and after treatment (x±S, n=60)

Item	Group	0 weeks	6 weeks	12 weeks
NO	Observation	36.25±7.57•	45.14±8.18▲•	57.91±9.33▲■
($mmol.L^{-1}$)	Control	36.18±7.41	44.42±8.05▲	46.08±8.14▲
ET-1	Observation	51.63±6.17•	41.47±5.78▲•	30.09±3.71▲■
($ng.L^{-1}$)	Control	50.99±6.11	40.89±5.71▲	38.95±6.54▲
VEGF	Observation	33.51±6.49•	21.63±4.84▲•	13.09±3.21▲■
($ng.L^{-1}$)	Control	33.56±6.52	22.49±4.71▲	20.98±4.32▲
vWF	Observation	456.47±34.83•	213.12±24.17▲•	109.46±13.23▲■
($\mu.L^{-1}$)	Control	453.99±32.99	217.01±24.51▲	211.88±19.48▲

Table 5: Comparison of the serum levels of inflammatory factors in two groups before and after treatment (x±S, n=60).

Item	Group	0 weeks	6 weeks	12 weeks
CRP	Observation	35.26±7.28•	25.17±5.13▲•	10.91±2.73▲■
(mg/L)	Control	35.08±7.11	24.49±5.02▲	22.78±4.74▲
TNF-α	Observation	71.53±11.27•	51.45±10.08▲•	29.08±7.61▲■
(pg/mL)	Control	71.49±11.14	50.99±10.05▲	47.95±8.94▲
IL-1β	Observation	63.61±8.48•	44.53±7.04▲•	33.09±5.11▲■
(pg/mL)	Control	62.96±8.42	43.97±7.01▲	40.97±5.82▲
NALP3	Observation	12.65±2.82•	8.82±1.87▲•	5.25±0.93▲■
(ng/L)	Control	12.68±2.89	8.79±1.81▲	8.58±1.38▲

Note: •P>0.05, vs. control group at the same time point; ▲P<0.05, vs. before treatment in the same group; ■P<0.05, vs. control group at the same time point

Table 6: Comparison of clinical efficacy between two groups (%, *n*=60)

Group	*n*	Recovery	Significantly effective	Effective	Ineffective	Total effective rate
Observation	60	14	28	14	4	93.33%
Control	60	4	20	26	10	83.33%

Table 7: Comparison of adverse reactions between two groups (%, *n*=60)

Type of adverse reactions	Observation group	Control group
Nausea and vomiting/*n*	2	2
Allergy/*n*	0	0
Abdominal pain and diarrhea/*n*	0	2
Myelosuppression/*n*	0	2
Incidence of adverse reactions	3.33%	10.00%

Comparison of clinical efficacy of the two groups
The total effective rate was significantly higher in the observation group (93.33%) than in the control group (83.33%) ($P<0.05$; table 6).

Comparison of adverse reactions between the two groups
The incidence of adverse reactions was 3.33% in the observation group, and 10.00% in the control group. Using the $\chi 2$ test, the difference in the incidence of adverse reactions was statistically significant between the two groups ($P<0.05$; table 7).

DISCUSSION

GA belongs to the category of "bi-syndrome" and "severe and migratory arthralgia" in the traditional Chinese medicine. Chinese medicine has an early understanding of this disease. *Basic Questions* propounded that limb pain is mostly rheumatic, which is caused by phlegm flowing into meridians and collaterals. *On Inquiring the Properties of Things* propounded that gout patients will feel pain in their limbs when they walk, which is the wind syndrome of severe and migratory arthralgia. According to the etiology and pathogenesis of CGA described by doctors of past dynasties, the internal cause of CGA is that the spleen is not healthy and the fat, sweet and thick taste is too much; the exogenous dampness and heat and evil toxin cause the internal dampness and turbidity, stagnation into phlegm, block the meridians and joints, and pain occurs when it is blocked. For many years, we have treated GA according to three stages of acute attack, intermittent and chronic stages. We think that the syndrome of phlegm dampness obstructing collaterals is more common in CGA. The pathogenesis of CGA is due to spleen deficiency. Phlegm stasis and internal resistance is the key to the pathogenesis of CGA. For the treatment of CGA with phlegm dampness obstructing collaterals, the root causes and symptoms should be treated simultaneously. Gouty Tea used in this study originated from the theoretical basis of traditional Chinese medicine, and combined with many years of clinical experience. In this prescription, *Rhizoma Atractylodis*, *Radix Codonopsis*, *Rhizoma Atractylodis Macrocephalae* and *Radix Glycyrrhizae* can invigorate spleen, replenish *qi* and dry dampness. *Radix Angelicae Sinensis*, *Radix Gentianae Macrophyllae* and *Ramulus Cinnamomi* can remove wind and dampness, promote blood circulation and relieve pain. *Radix Cyathulae* and *Cortex Phellodendri* can clear away the dampness and heat of the lower Jiao. *Rhizoma Smilacis Glabrae*, *Rhizoma Alismatis* and *Rhizoma Dioscoreae Septemlobae* can facilitate urination and excrete dampness. *Rhizoma Cimicifugae* and *Radix Puerariae* are pungent and can induce *qi* to rise and disperse rheumatism among muscles. Throughout the whole prescription, the compatibility of Gouty Tea is reasonable, which has the effect of strengthening spleen and removing dampness, dredging collaterals and relieving pain.

This study indicated that the therapeutic method in the observation group can significantly down-regulated the levels of UA and XOD and the VAS in patients with CGA and the efficacy is better than that of the control group. In terms of improving the single score of TCM symptoms, the efficacy is better in the observation group than that of the control group. After 12 weeks of treatment, it was found that the clinical total effective rate of the observation group was significantly better than that of the control group. The observation group was better than the control group in improving the levels of UA and XOD and the single score of TCM symptoms. Moreover, with the prolongation of treatment time, the efficacy of the observation group was more significant. We believe that on one hand, Gouty Tea improves the internal environment of the organism by invigorating the spleen and removing dampness and promoting the excretion of uric acid; on the other hand, Gouty Tea can relieve the pain of patients by dredging collaterals and mitigating pain. The abnormal high level of serum UA is a very important cause of GA. The degree of joint damage can be alleviated by urate crystal in joint and surrounding tissues, activating phagocytes and various inflammatory factors simultaneously. UA is the final product of purine catabolism in human body and XOD is the most important enzyme in its metabolic pathway. XOD can catalyze xanthine and hypoxanthine to generate UA.

When XOD activity is increased, it will lead to excessive production of UA, resulting in the increase of blood UA level (Tang *et al.,* 2019). Our results indicate that both groups can significantly reduce UA level, and the effect of observation group is better, which may be related to that Gouty Tea can markedly inhibit XOD activity and effectively suppress UA synthesis. Modern pharmacological studies have shown that *Cortex Phellodendri* inhibits the synthesis of UA by inhibiting XOD activity (Liang *et al.,* 2018). *Rhizoma Dioscoreae Septemlobae* has the effects of promoting UA excretion, anti-inflammation and improving immunity (Li *et al.,* 2020). *Rhizoma Smilacis Glabrae* is diuretic, promotes UA excretion, has anti-inflammatory and analgesic effects (Jin *et al.,* 2018). *Radix Gentianae Macrophyllae* extract can directly decrease the release of prostaglandin E2 from phagocytes, an can also inhibit the activity of cyclooxygenase 2 to reduce the release of prostaglandin E2 at the inflammatory site and play an anti-inflammatory and analgesic effect (Nie *et al.,* 2017). *Ramulus Cinnamomi* had obvious antipyretic, analgesic and diuretic effects (Li *et al.,* 2018). *Radix Achyranthis Bidentatae* can reduce the degree of joint swelling and promote the absorption of inflammatory substances in gout (Chen *et al.,* 2017).

Hyperuricemia can affect the function of vascular endothelial cells (VEC) release and metabolism, resulting in vascular endothelial dysfunction (Britnell *et al.,* 2018). VEC plays a variety of physiological functions by secreting and regulating bioactive substances, growth factors and cytokines. The physiological functions of VEC mainly include the following aspects: 1) regulating vasodilation: secreting endothelium-derived vasodilator such as ET-1 and NO; in hyperuricemia, local oxidative stress is formed, ET-1 level is increased, NO level is decreased, and imbalance of ET-1 and NO levels leads to vascular endothelial dysfunction (Kadiyoran *et al.,* 2019). 2) Regulating cell growth and proliferation: regulating the synthesis and secretion of VEGF and other growth factors, VEGF plays an extremely important role in maintaining vascular permeability and fluid balance (Yessica *et al*., 2019). 3) Releasing and regulating various bioactive substances such as vWF: More than 90% of vWF in blood circulation is synthesized and released by VEC. When VEC is damaged and dysfunctional, the release of vWF increases. VWF can be used as a sensitive biological index to reflect vascular endothelial function and hypercoagulability. This study demonstrated that the levels of NO, ET-1, VEGF and vWF in CGA patients were significantly improved in the observation group, and the efficacy was better in the observation group than that of the control group. After 12 weeks of treatment, it was found that the observation group was better than the control group in improving the level of NO, ET-1, VEGF and vWF. With the prolongation of treatment time, the efficacy of the observation group was more significant, indicating that Gouty Tea could effectively improve the vascular endothelial function of patients, is conducive to maintaining the intravascular environment, which is related to the inhibition of UA synthesis and activation of VEC. Modern pharmacological studies have shown that *Radix Angelicae Sinensis* and *Radix Puerariae* can reduce blood viscosity and improve vascular endothelial function (Zuo *et al.,* 2012, Zhang *et al.,* 2017); *Radix Achyranthis Bidentatae* can expand blood vessels, promote blood circulation, and improve vascular endothelial function (Chen *et al.,* 2017).

In addition to metabolic factors, inflammation is the main factor in the pathogenesis of GA, and NALP3 is the main inflammatory mediator in the inflammatory reaction. When exogenous ATP, potassium ion outflow, reactive oxygen species and lysosome lysis occur, the inflammatory pathway of NALP3 can be activated and proinflammatory factors such as IL-1β can be released. The combination of IL-1β and specific receptor IL-1R can trigger a cascade of inflammatory reactions and promote the release of inflammatory factors including TNF-α, IL-6 and IL-8, aggravating the inflammatory reaction (Ma *et al.,* 2018). As an inflammatory activator, urate crystals can induce the production of reactive oxygen species, which are the main molecules in the activation of NALP3 inflammatory pathway (Zhou *et al.,* 2019). NALP3 and IL-1β are the key factors for inflammation in GA, and their levels are positively correlated with the severity of disease (Ma *et al.,* 2018, Zhou *et al.,* 2019). This study exhibited that the therapeutic method in the observation group significantly reduced the levels of CRP, TNF-α, IL-1β and NALP3 in CGA patients, and the efficacy was better than that of the control group. After 12 weeks of treatment, it was found that the observation group was better than the control group in reducing the levels of CRP, TNF-α, IL-1β and NALP3. With the prolongation of treatment time, the efficacy of the observation group was more significant, which shows that Gouty Tea can fundamentally inhibit the formation of urate crystal and effectively downregulate inflammatory response. The previous basic research of our team has confirmed that Gouty Tea has obvious anti-inflammatory effect on rabbit GA induced by microcrystalline sodium urate (Wang *et al.,* 2007). A clinical study shows that Gouty Tea can reduce the levels of serum IL-1, IL-6, IL-18 and CRP in patients with acute GA (Liu *et al.,* 2019). Modern pharmacological studies have shown that *Cortex Phellodendri* can effectively inhibit inflammatory reaction by enhancing the function of phagocytes in immunologic process, and its active substances, such as phellodendrine can decrease the production of IL-1 and TNF-α (Liang *et al.,* 2018). Selina-4(14), 7(11)-dien-8-one and atraactylenolide in *Rhizoma Atractylodis* can enhance non-specific immunity and improve anti-inflammatory activity (Yu *et al.,* 2017). *Ramulus Cinnamomi* has anti-inflammatory and anti-allergic effects (Li *et al.,* 2018).

During this study, there were 2 cases of nausea and vomiting, 2 cases of abdominal pain and diarrhea in the control group. After symptomatic treatment, the symptoms disappeared. In addition, there were 2 cases of mild myelosuppression in the control group. In the observation group, there were only 2 cases of nausea and vomiting, but no special treatment, and the symptoms disappeared after 2 days. This may be related to the anti-gastric ulcer effect of *Rhizoma Smilacis Glabrae* (Jin *et al.*, 2018) and *Rhizoma Atractylodis* (Yu *et al.*, 2017) and the protection of *Rhizoma Atractylodis Macrocephalae* on digestive system (Wang *et al.*, 2018). The results from this study showed that based on the cognition that CGA is dominated by phlegm dampness blocking collaterals, the treatment of invigorating the spleen, removing dampness, dredging collaterals, and relieving pain is clinically effective and safe.

CONCLUSION

To sum up, Gouty Tea is safe and effective in the treatment of CGA. Gouty Tea can remarkably inhibit XOD activity and effectively inhibit UA synthesis, fundamentally improve purine metabolism disorder, effectively improve vascular endothelial function and inhibit inflammatory reaction, which may be one of the mechanisms of Gouty Tea in the treatment of CGA. However, the sample size is limited and the follow-up time is short in this study, which needs further discussion.

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