Original Article

Efficacy and safety of Sanfeng Tongqiao Diwan in the treatment of upper airway cough syndrome: a randomized, double-blind, placebo-controlled clinical study

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Background: Sanfeng Tongqiao Diwan has shown the potential to alleviate acute, recurrent, and chronic rhinitis in adults based on available studies. However, the evidence for its application in upper airway cough syndrome (UACS) is unclear. The purpose of this study was thus to investigate the efficacy and safety of Sanfeng Tongqiao Diwan in the treatment of UACS.

Methods: This was a single-center, randomized, double-blind, placebo-controlled clinical trial. A total of 60 patients who satisfied the inclusion criteria were randomly divided into experimental and placebo groups in a 1:1 ratio. The experimental group was given Sanfeng Tongqiao Diwan, and the placebo group was given a simulant for 14 consecutive days. The follow-up period was 15 days. The primary outcome was the total effective rate. The secondary outcomes included clinical efficacy, Visual Analogue Scale (VAS) of related symptoms, and Leicester Cough Questionnaire in Mandarin-Chinese (LCQ-MC) scores before and after the treatment. Additionally, the safety was also evaluated.

Results: The total effective rate in the experimental group was 86.6% (26/30), which was significantly higher than the 7.1% (2/28) in the placebo group (difference 79.6; 95% CI: 57.0 to 89.1; P<0.001). Nasal congestion, runny nose, cough, postnasal drip, and overall symptoms in the experimental group were significantly lower than those in the placebo group after treatment (3.7±1.5 *vs.* 5.0±1.1, 3.6±1.3 *vs.* 5.9±1.1, 3.8±1.2 *vs.* 6.8±1.3, 3.5±1.4 *vs.* 6.1±1.5, 3.8±2.0 *vs.* 7.3±1.4, respectively; all P values <0.001). After treatment, the LCQ-MC score in the experimental group was significantly higher than that in the placebo group (all P values <0.001). The blood eosinophil count in the placebo group was significantly higher after treatment than before treatment (P=0.037). No abnormalities were found in liver or renal indicators during the treatment period in the 2 groups, and no adverse reactions occurred.

Conclusions: Sanfeng Tongqiao Diwan improved the symptoms and living quality of patients with UACS and showed acceptable safety. The results of this trial represent rigorous clinical evidence for the application of Sanfeng Tongqiao Diwan and further support a new option in UACS treatment.

Trial Registration: Chinese Clinical Trial Registry ChiCTR2300069302.

Keywords: Upper airway cough syndrome (UACS); Sanfeng Tongqiao Diwan; efficacy; safety; clinical trial

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Introduction

Upper airway cough syndrome (UACS) refers to a clinical syndrome characterized by chronic cough as the main manifestation due to nasal disease-causing secretions flowing into the back of the nose and throat, directly or indirectly stimulating cough receptors. The main underlying diseases are allergic rhinitis and chronic rhinosinusitis, but UACS may also be related to throat disorders. The main clinical manifestations of UACS are cough, expectoration, and symptoms in the nose and pharynx (1). In Western medicine, etiological treatment and symptomatic treatment are the main therapeutic approaches for UACS and can include anti-inflammatory, antiallergy, and anti-cough medications; expectorants; nasal irrigation; and other treatments. The clinical symptoms often recur. The treatment of UACS with traditional Chinese medicine (TCM) is still in the exploratory stage. Related research indicates that UACS belongs to the "cough" category, mostly due to pathogenic wind invading the lungs (2). The lungs and nose are heterogeneous and of the same category, their pathogenesis is the same, their diseases are caused by mutual interactions, and their symptoms are interreferential; therefore, treatment should be based on the principles of dredging collaterals, dispelling wind, promoting the lungs, and relieving asthma. Sanfeng Tongqiao Diwan contains *Scutellaria baicalensis* (Huang qin), *Schizonepeta tenuifolia* (Jing jie), *Asarum sieboldii* (Xi xin), and *Notopterygium incisum* (Qiang huo). It has the actions of clearing heat and dispelling wind, dispelling cold, and opening orifices and can significantly improve the symptoms of acute sinusitis and allergic rhinitis, with no drug-related adverse reactions being observed in related studies (3,4). In this study, 60 patients with UACS were selected as the research participants to evaluate the clinical efficacy and safety of Sanfeng Tongqiao Diwan in the treatment of UACS and to provide new approaches for the treatment of UACS with prepared TCM. We present the following article in accordance with the CONSORT reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-433/rc).

Highlight box

Key findings

- In this study, Sanfeng Tongqiao Diwan significantly improved the cough, postnasal drip, nasal congestion, runny nose, and overall symptoms of patients with upper airway cough syndrome (UACS) in the test group according to the Leicester Cough Questionnaire in Mandarin-Chinese (LCQ-MC) score, with a total effective rate of 86.6%.

What is known and what is new?

- To our knowledge, there has been considerable progress and a theoretical basis has been established for the treatment of UACS with traditional Chinese medicine (TCM). Sanfeng Tongqiao Diwan has shown the potential to alleviate acute, recurrent, and chronic rhinitis in adults.
- Our study demonstrated that Sanfeng Tongqiao Diwan alleviates the symptoms of UACS, improves the quality of life (QoL) of patients with UACS, and has good safety.

What is the implication, and what should change now?

- The results represent rigorous clinical evidence for the application of Sanfeng Tongqiao Diwan and may further support new TCM options in UACS treatment.

Methods

Research participants

The patients aged 18–65 years with UACS treated at the Department of Allergy and Clinical Immunology of the First Affiliated Hospital of Guangzhou Medical University were enrolled. This was a randomized, double-blind (blind to the patients and the investigators), placebo-controlled trial established by The First Affiliated Hospital of Guangzhou Medical University-Yangtze River Pharmaceutical Group Co., Ltd. (Taizhou, China). Sixty patients were divided equally into a placebo group and experimental group using the block randomization method. The random sequence was generated by independent statisticians through SAS 9.4 software (SAS Institute, Cary, NC, USA). In the experimental group, Sanfeng Tongqiao Diwan (38 mg/20 pills) was taken 3 times a day with warm boiled water after meals (tid); the treatment period was 14 days. The placebo group was given a simulant granule, mainly composed of starch and dextrin. Food colorants and flavoring agents were added to mimic the color, fragrance, taste, and texture of Sanfeng Tongqiao Diwan pills. Both

Sanfeng Tongqiao Diwan and the simulant were provided by Yangtze River Pharmaceutical Group Co., Ltd. (Taizhou, China), and the dosage was the same for both groups. For the purpose of successful blinding, the test drug and the placebo were packed in sealed box with a drug number printed on the outside. During the treatment period, the 2 groups were not given other antihistamines or TCMs, and dextromethorphan oral disintegrating tablet (30 mg) was prescribed as needed (tid). The study was approved by the Medical Ethics Committee of The First Affiliated Hospital of Guangzhou Medical University (No. GYFYY-2020-170) and conducted in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from all the patients.

Study protocol

During the whole research process, the participants were required to complete a series of questionnaires including symptom relief score, Visual Analogue Scale score (VAS), and Leicester Cough Questionnaire in Mandarin-Chinese (LCQ-MC). At baseline, clinical investigators obtained inform consent and recorded demographic and general characteristics, including age, gender, height, weight, medical history, chest X-ray, spirometry, bronchial provocation test, allergen skin prick test, and induced sputum was performed as standard investigation in all patients. At baseline and treatment end point (15 days), laboratory and imaging examinations were conducted, including routine blood testing, liver and kidney function test, and 12-lead electrocardiogram (ECG) to evaluate safety. In addition, vital signs and adverse events (AEs) were monitored throughout the study. The primary outcome was total effective rate. The secondary outcomes included clinical efficacy, the change of VAS of clinical symptoms, and LCQ-MC scores before and after the treatment. If AEs occurred, the clinical investigators were required to record the symptoms and signs, abnormal laboratory indicators, the time of onset and end, the relationship with the test drug, the severity, the intervention, and prognosis of the event.

Eligible criteria

Patients who were diagnosed with UACS were eligible to participate in the trial if they were 18–65 years old and signed the informed consent form. The following diagnostic criteria for UACS were obtained from the *Chinese National Guideline on Diagnosis and Management of Cough (2021)* as revised by the Asthma Group of the Chinese Thoracic Society and the epidemiologic research on causes of chronic cough in China (5,6): (I) episodic or persistent cough for at least 8 weeks, mainly during the day, with fewer events after falling asleep, accompanied by nasal obstruction, runny nose, dry pharynx with foreign body sensation, and repeated clearing of the pharynx; (II) clinical manifestations and medical history of nose or (and) throat diseases; (III) auxiliary examinations supporting the diagnosis of nose or (and) throat diseases, including obvious hyperplasia of the posterior pharyngeal follicles and mucous or purulent secretion or occasional cobble-like changes; (IV) normal spirometry without airway hyper-responsiveness; (V) normal eosinophil percentage in induced sputum; and (VI) cough resolving after etiological treatment.

Patients were excluded for the following reasons: (I) patients with chronic obstructive pulmonary disease (COPD), cough-variant asthma, gastroesophageal reflux cough, eosinophilic bronchitis, bronchiectasis, or congenital respiratory diseases and other diseases causing chronic cough; (II) patients with severe heart, liver, kidney, mental diseases, or tumors; (III) patients who were pregnant, lactating, or planning for pregnancy; (IV) patients with known allergies to the study drug or drug composition; (V) patients unable to self-administer the drugs, potentially affecting the efficacy evaluation, or patients who had participated in clinical trials of other drugs; and (VI) patients who were smokers or alcoholics.

Patients could quit the study if they withdrew informed consent, or had adverse events and did not want to continue participating in the study, or did not comply with the protocol and/or the investigator's instructions.

Primary efficacy indicators

Symptom relief score

The total curative effect of UACS symptoms was calculated using the nimodipine method as follows: total curative effect index = (pretreatment score – posttreatment score)/pretreatment score × 100%. "Completely recovered" was defined as the disappearance of clinical symptoms and signs, and the curative effect index was ≥95%; "significantly effective" was defined as significantly improved clinical symptoms and signs, and the curative effect index was ≥70%; "effective" was defined as improved clinical symptoms and signs, and the curative effect index was ≥30%; and "ineffective" was defined as no improvement or

even aggravation of clinical symptoms and signs, and the curative effect index was <30%.

VAS score

A straight 10-cm line with a mark every 1 cm was used to assess the severity of the main symptoms, namely, cough, sputum, postnasal drip, nasal congestion, and runny nose: 0 indicated no symptoms, and 10 indicated the most severe level of symptoms. The higher the value was, the more severe the symptoms.

LCQ-MC score

This scale includes 3 dimensions: social function, physical condition, and psychological function. There are a total of 19 items, each of which is scored on a scale that ranges from 1 to 7 points. The scores of 3 dimensions are summed to give a total score. The higher the total score was, the better the quality of life (QoL) (7).

Routine blood and biochemical tests

For both groups, blood was collected before and after treatment. Within 1 hour of collection, 1 mL of whole blood was placed into a K2EDTA vacuum tube (BD Biosciences, Franklin Lakes, NJ, USA), and leukocytes, erythrocytes, eosinophils, and other cells were detected with a Beckman Coulter LH750 (Beckman Coulter, Brea, CA, USA). Then, 5 mL of blood was placed into a blood collection tube containing heparin anticoagulant, allowed to stand for 30 minutes, and centrifuged at 1,200 ×g for 10 minutes at 20 ℃. The supernatant was collected, and a reagent (AU5800 analyzer, Beckman Coulter) was used to assess renal function and liver function.

Routine urine tests

Before and after treatment, urine was obtained from the participants in the 2 groups. A total of 5 mL fresh midstream urine was collected, and within 1 hour, urine biochemical analyses were conducted using a Sysmex UF1000i (TOA Medical Electronics, Kobe, Japan).

Statistical methods

Based on a 2-sided significance level of 0.05, 27 participants in each group could achieve 90% power to detect a difference between the group proportions of 40% in total efficacy rate. The test statistic was the Z test with unpooled variance. The total sample size was 30 patients per group according to a 10% shedding rate.

All analyses were based on the intention-to-treat (ITT) principle. The full analysis set (FAS) included all patients who took medication and had postmedication evaluation at least once after randomization. Missing data were imputed by last-observation-carried-forward (LOCF) method in FAS. Patients without major protocol violations in FAS were included in the per protocol set (PPS). The safety set (SS) was composed of the patients who received study treatment and safety assessment at least once during the trial.

SPSS 20.0 statistical software (IBM Corp., Armonk, NY, USA) was used for data analysis. Categorical data including gender, number of underlying diseases, and clinical efficacy are expressed as the percentage of positive results and were analyzed with the chi-squared (χ^2) test. The Newcombe-Wilson method was used to calculate the rate difference between 2 groups and its 95% CI. Measurement data including age, body mass index (BMI), disease duration, serum indicators of liver and renal function, cell counts of routine blood test, VAS, and LCQ-MC are expressed as the mean ± standard deviation (SD) or median (P25–P75) and were compared using independent-samples *t*-test or Mann-Whitney test based on the results of the Shapiro-Wilk test. Intragroup comparisons of measurement data before and after intervention were performed with a paired *t*-test or paired-samples Wilcoxon signed-rank test according to the results of normality test. A 2-sided P value <0.05 was considered statistically significant.

Results

Demographic data

A total of 60 patients with UACS from July 2021 to July 2022 were enrolled. In the first visit of the trial, 2 patients in the placebo group withdrew from the study because they failed to complete the blood test and refused to take any medication (*Figure 1*). There was no significant difference in age, sex, BMI, disease course, or underlying diseases between the 2 groups, and the data between the 2 groups were comparable (*Table 1*).

Clinical efficacy

On the 15th day after treatment, the total effective rate for the experimental group was significantly higher than that for the placebo group, and the difference was statistically significant (79.6; 95% CI: 57.0 to 89.1; P<0.001; *Table 2*). Details about

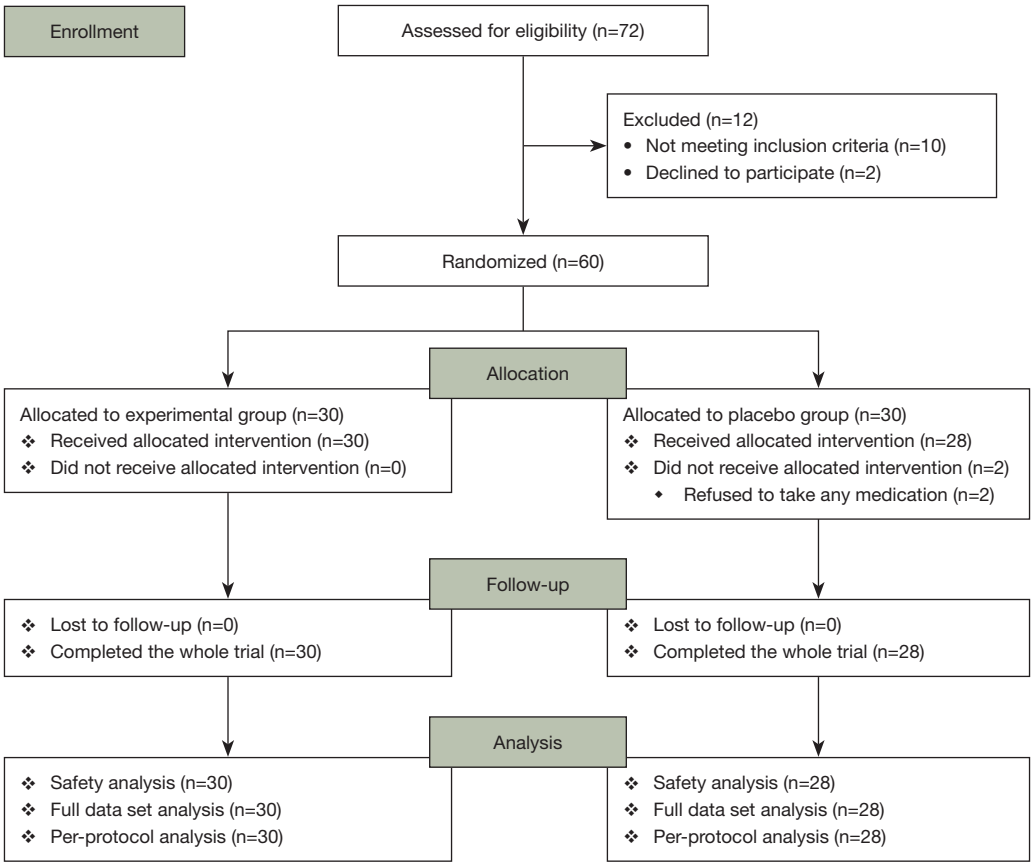

Figure 1 Flowchart of the study.

Table 1 Comparison of the general conditions of patients with UACS in the 2 groups

Variable	Experimental group	Placebo group	P value
Number of cases	30	28	
Age (years), mean ± SD	33.7±4.2	32.5±3.9	0.549
Sex, n (%)			0.436
Male	17 (56.7)	13 (46.4)	
Female	13 (43.3)	15 (53.6)	
BMI (kg/m^2), mean ± SD	21.2±2.3	20.8±1.7	0.403
Disease duration (weeks), median [IQR]	17 [13–21]	15 [11–20]	0.054
History of underlying diseases, n (%)			0.770
Allergic rhinitis	20 (66.6)	18 (64.3)	
Chronic sinusitis	6 (20.0)	5 (17.9)	
Chronic pharyngitis	2 (6.7)	4 (14.3)	
Chronic tonsillitis	2 (6.7)	1 (3.6)	

UACS, upper airway cough syndrome; SD, standard deviation; BMI, body mass index; IQR, interquartile range.

Table 2 Comparison of the clinical efficacy in the 2 groups of patients with UACS

Clinical efficacy	Experimental group (n=30), n (%)	Placebo group (n=28), n (%)	Difference (95% CI)	P value
Completely recovered	1 (3.3)	0	3.3 (–9.0, 16.7)	0.330
Significantly effective	11 (36.7)	0	36.7 (17.6, 54.5)	<0.001
Effective	14 (46.7)	2 (7.1)	39.6 (16.9, 57.5)	<0.001
Total efficacy	26 (86.7)	2 (7.1)	79.6 (57.0, 89.1)	<0.001

UACS, upper airway cough syndrome.

Table 3 Comparison of VAS scores for the 2 groups of patients with UACS

Group	Time	Stuffy nose	Runny nose	Cough	Expectoration	Postnasal drip	General symptoms
Experimental group	Before treatment	5.1±2.1	5.4±2.1	7.3±1.5	3.1±1.6	6.1±1.8	7.0±1.5
	After treatment	3.7±1.5$^{\#*}$	3.6±1.3$^{\#*}$	3.8±1.2$^{\#*}$	2.6±1.3	3.5±1.4$^{\#*}$	3.8±2.0$^{\#*}$
Placebo group	Before treatment	4.9±1.6	5.2±1.8	6.7±1.0	3.1±1.9	6.0±1.1	7.3±1.2
	After treatment	5.0±1.1	5.9±1.1	6.8±1.3	3.0±1.5	6.1±1.5	7.3±1.4

Data are presented as mean ± SD. Compared with the experimental group before treatment, $^{\#}$, P<0.001; compared with the placebo group after treatment, *, P<0.05. VAS, Visual Analogue Scale; UACS, upper airway cough syndrome.

Table 4 Comparison of LCQ-MC scores before and after treatment in the 2 groups of patients with UACS

Group	Time	Physiological score	Social score	Psychological score	Total score
Experimental group	Before treatment	30.7±5.5	19.8±2.5	26.3±5.2	78.8±7.9
	After treatment	41.4±3.9$^{\#*}$	24.0±2.9$^{\#*}$	40.5±4.3$^{\#*}$	109.6±6.5$^{\#*}$
Placebo group	Before treatment	31.4±4.1	21.6±3.4	26.8±5.5	80.9±8.1
	After treatment	30.7±4.3	20.4±3.5	28.1±5.4	81.2±7.3

Data are presented as mean ± SD. Compared with the experimental group before treatment, $^{\#}$, P<0.001; compared with the placebo group after treatment, *, P<0.05. LCQ-MC, Leicester Cough Questionnaire in Mandarin-Chinese; UACS, upper airway cough syndrome.

the symptom relief scoring are available in Table S1.

Comparison of the VAS scores for respiratory symptoms before and after treatment with Sanfeng Tongqiao Diwan

In the experimental group, the scores for nasal congestion, runny nose, cough, postnasal drip, and overall symptoms significantly decreased after treatment compared with those before treatment (all P values <0.05). The symptom scores in the placebo group did not change significantly after treatment. After treatment, the scores for nasal congestion, runny nose, cough, expectoration, postnasal drip, and overall symptoms were significantly lower in the experimental group than in the placebo group (all P values <0.05; *Table 3*).

Comparison of LCQ-MC scores before and after treatment with Sanfeng Tongqiao Diwan

Before treatment, there was no significant difference in LCQ-MC scores between the 2 groups. After treatment, the LCQ-MC score for the experimental group was significantly higher than that for the placebo group, and the difference was statistically significant (all P values <0.05; *Table 4*).

Comparison of the liver and renal functions of patients before and after treatment

There was no significant difference in serum alanine aminotransferase (ALT), r-glutamyl transpeptidase (r-GT), blood urea nitrogen (BUN), or creatinine (Cr) between the

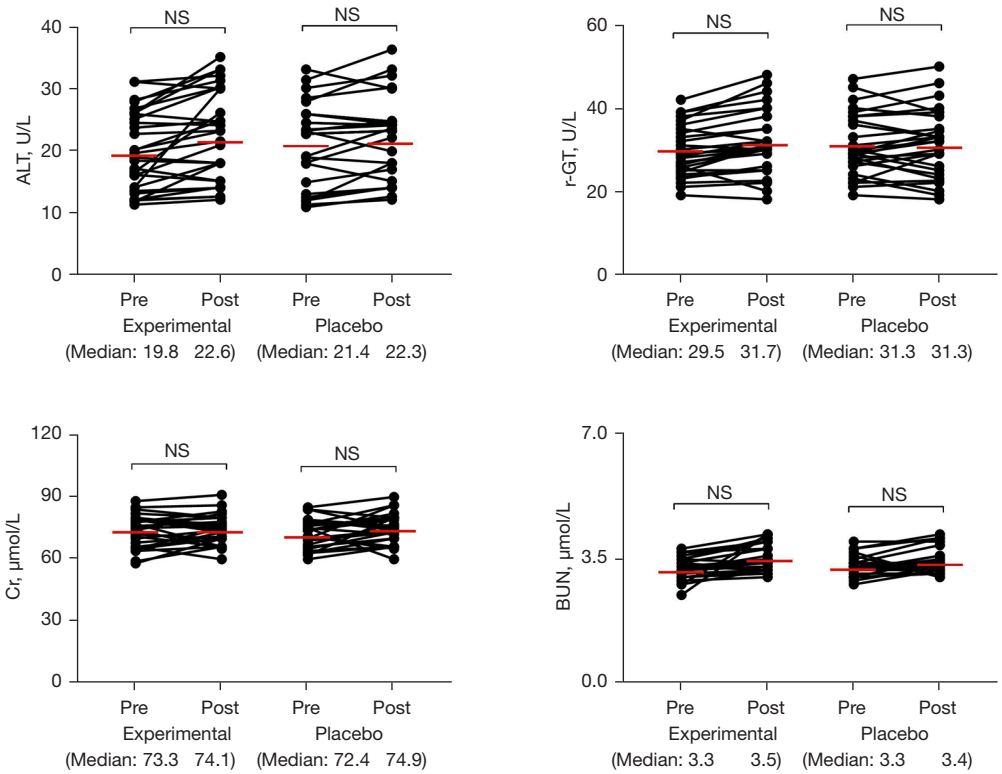

Figure 2 Comparison of liver function and renal function before and after treatment in the 2 groups of patients with UACS. The red bold line is the median. UACS, upper airway cough syndrome; ALT, alanine aminotransferase; r-GT, r-glutamyl transpeptidase; Cr, creatinine; BUN, blood urea nitrogen; NS, not significant.

2 groups before and after treatment, and no AEs or serious adverse events (SAEs) occurred (*Figure 2*).

Comparison of routine blood test results for patients before and after treatment

There was no significant difference in leukocyte, hemoglobin, or platelet counts between the 2 groups before and after treatment, but the blood eosinophil count in the placebo group was significantly higher after treatment than before treatment (P=0.037; *Figure 3*).

Discussion

This study found that single-drug treatment with Sanfeng Tongqiao Diwan significantly improved the clinical symptoms (cough, postnasal drip, and nasal congestion) and QoL of patients with UACS in the experimental group, but had no significant effect on liver function or renal function.

UACS is the most common cause of chronic cough, but its pathogenesis is still not completely clear. Currently, it is believed that the pathogenesis of UACS may involve a combination of multiple factors, including postnasal drip, airway inflammation, cough hypersensitivity, and neurogenic inflammation (8). Although there is no clear definition of UACS in TCM, UACS can be classified into the "cough", "allergic rhinitis (Bi Qiu)", and "nasal sinusitis (Bi Yuan)" categories on the basis of the symptoms, and the causes are summarized as wind, dampness, phlegm, heat, blood stasis, and deficiency. Among these, "pathogenic wind is the spearhead of all diseases" (9). Thus, the early onset of UACS is mostly caused by pathogenic wind invading the lungs. For the pathogenesis of UACS, pathogenic wind invades the lungs; the lungs lose their functions of diffusion, dispersion, purification, and descent; and fluid is not properly metabolized and stored, which over time condenses into phlegm and leads to cough. Therefore, clinical TCM treatment should follow the principles of dredging wind, opening orifices, clearing lungs, and clearing heat (10). Sanfeng Tongqiao Diwan clears away

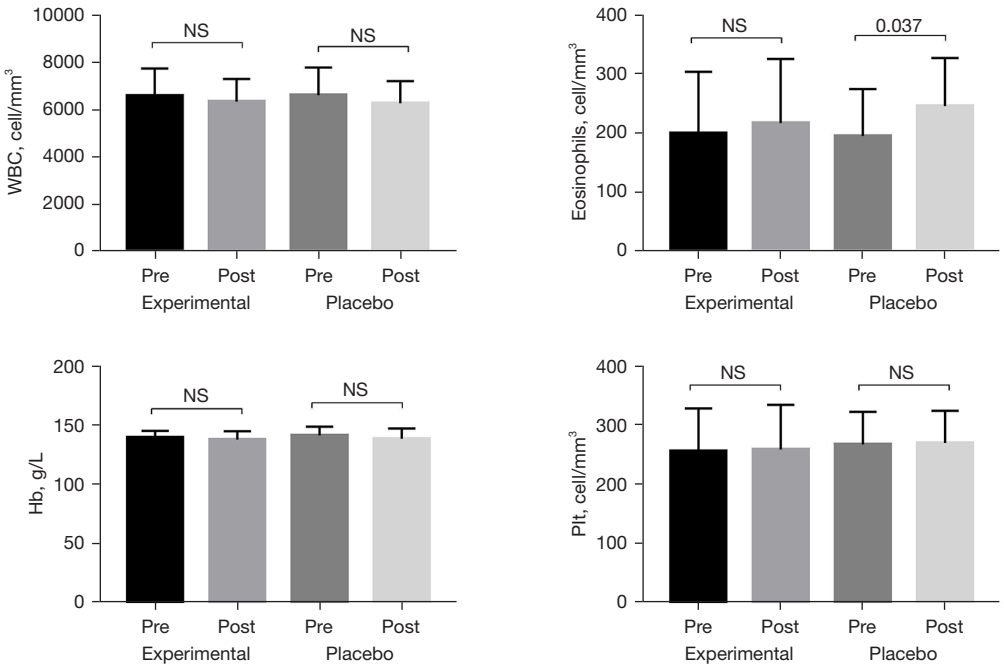

Figure 3 Comparison of routine blood test results for the 2 groups of patients with UACS before and after treatment. UACS, upper airway cough syndrome; WBC, white blood cell; Hb, hemoglobin; Plt, blood platelet; NS, not significant.

heat and removes dampness, dispels wind and cold, clears the orifices, and relieves pain, and the main ingredients are *S. baicalensis*, *S. tenuifolia*, *A. sieboldii*, and *N. incisum*. Modern medical research shows that *S. baicalensis* has antiallergic, antiviral, antioxidant, and other effects. *S. baicalensis* can downregulate the expression levels of various inflammatory mediators, effectively inhibit the release of mast cell mediators in mice, and relax airway smooth muscle (11,12). *S. tenuifolia* is suitable for treating symptoms such as fever, nasal congestion, runny nose, nasal mucosal congestion, and headache caused by exopathic wind-cold and heat stagnating in the lungs, and pharmacological studies have shown that *S. tenuifolia* acts on the nuclear factor-κB (NF-κB) and interleukin (IL)-17 pathways and has an inhibitory effect on histamine release (13,14). *A. sieboldii* has strong ascending and dispersing effects in the theory of TCM, possessing anti-inflammatory, anti-allergic, analgesic, and antipyretic properties (3,15). *N. incisum* is also a TCM with a pungent flavor and warm nature and has a propensity to the lung and kidney meridians. *N. incisum* expels wind, dispels cold, promotes fluid circulation, opens the orifices, has antiallergic and immunosuppressive effects, and is a commonly used formula for treating allergic rhinitis and asthma (16,17).

However, there have been no studies on the treatment of UACS with Sanfeng Tongqiao Diwan. In this study, Sanfeng Tongqiao Diwan significantly improved the cough, postnasal drip, nasal congestion, runny nose, and overall symptoms and significantly improved the QoL, as determined from the LCQ score of patients with UACS in the experimental group, with a total effective rate of 86.6%. In the experimental group, treatment was ineffective for 4 patients, potentially because of the presence of inflammation involving multiple paranasal sinuses in these patients, presenting a relatively wide scope of inflammation. For such patients, herbal medicine combined with conventional treatment may be more effective than herbal alone (18). The resolution of 2 cases in the placebo group may be related to taking dextromethorphan as needed. In addition, we reported no significant change of metabolic parameters and no clinically relevant variation regarding liver or kidney function. No drug-related side effect was observed during the treatment period in the 2 groups. A previous study reported that the major AEs could include mild rash, with an incidence rate of 3.3%, which resolved without any intervention (4). The increase in blood eosinophils in the placebo group after 2 weeks was likely related to uncontrolled inflammation. The eosinophils in

the experimental group increased after treatment, but the difference was not statistically significant, suggesting that further research is warranted concerning the mechanism of action of Sanfeng Tongqiao Diwan against type 2 inflammation. The theoretical system of TCM is different from that of Western medicine, but specific groups of people who respond to treatment can still be identified through evidence-based medicine. For one, the clinical efficacy of TCM preparations is due to the synergistic effect of multiple TCMs. For another, a single drug has multiple action pathways (19). Therefore, the pharmacological effects of TCM preparations can be more complex than those of Western medicines.

The limitations of this study were the small sample size. Future related studies should include a larger sample size. In addition, the follow-up period was short, and the long-term treatment efficacy was not tracked and observed, and should thus be addressed in future studies.

Conclusions

Sanfeng Tongqiao Diwan significantly improved the cough, postnasal drip, and nasal symptoms of patients with UACS; improved QoL; and showed good safety. It thus represents a promising new option for the treatment of this condition.

Acknowledgments

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Footnote

Reporting Checklist: The authors have completed the CONSORT reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-433/rc

Trial Protocol: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-433/tp

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-433/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-433/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-433/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Medical Ethics Committee of The First Affiliated Hospital of Guangzhou Medical University (No. GYFYY-2020-170). Informed consent was taken from all the patients.

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Supplementary

Table S1 The symptom relief score in the two groups of UACS patients

Experimental-symptom relief score (N=30)			Placebo-symptom relief score (N=28)		
Pre	Post	Total curative effect index (%)	Pre	Post	Total curative effect index (%)
8	4	50	6	5	17
7	3	57	7	5	29
9	4	56	7	5	29
6	3	50	8	6	25
7	4	43	6	4	33
6	4	33	5	3	40
8	8	0	7	7	0
7	3	57	6	8	-33
8	2	75	5	6	-20
10	6	40	5	7	-40
7	1	86	6	6	0
6	2	67	5	5	0
4	2	50	8	7	13
5	1	80	8	8	0
6	2	67	10	8	20
8	3	63	9	7	22
9	4	56	6	5	17
9	5	44	7	7	0
3	0	100	9	9	0
7	7	0	5	4	20
8	2	75	4	4	0
8	2	75	3	5	-67
9	8	11	5	7	-40
5	1	80	6	6	0
9	2	78	7	6	14
4	6	-50	8	6	25
7	2	71	6	6	0
7	2	71	3	3	0
6	1	83			
5	1	80			

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