

Qingfeijianpi therapy for persistent allergic rhinitis

A randomized, positive-controlled clinical trial

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Abstract

This study aims to investigate the effectiveness and safety of Qingfeijianpi therapy for persistent allergic rhinitis (AR).

A total of 101 patients with persistent AR were included into the study. These patients were randomly divided into 2 groups: treatment group, in which patients were given Qingfeijianpi decoction (1 dose/day for 4 weeks); control group, in which patients were given an oral dose of loratadine (tablet, 10 mg/time, once per day for 4 weeks). A total of 96 patients completed the 16-week course of treatment. The nasal symptom and traditional Chinese medicine syndrome were scored to evaluate symptom improvement, and the Rhinoconjunctivitis Quality of Life Questionnaire was used to assess the quality of life of patients. Furthermore, the 4-week clinical treatment effect and 16-week follow up were evaluated.

After the 4-week treatment, the mean difference in symptom score in the treatment group was similar to that in the control group. However, during the follow-up, the decrease in symptom score was better with the Qingfeijianpi therapy than with loratadine.

Compared to loratadine, the Qingfeijianpi decoction exhibited a significant benefit in symptom improvement of persistent AR.

Abbreviations: AR = allergic rhinitis, CI = confidence interval, PAR = persistent allergic rhinitis, RQLQ = Rhinoconjunctivitis Quality of Life Questionnaire, SD = standard deviation, SEM = standard error of the mean, TCM = traditional Chinese medicine.

Keywords: Chinese herbs, effect, persistent allergic rhinitis, Qingfeijianpi method, traditional Chinese medicine syndrome

1. Introduction

Allergic rhinitis (AR) has become one of the most common chronic health problems due to its prevalence and impact on quality of life, performance at work, and school activities. AR occurs in over 500 million people around the world, and this number continuously increases.^[1] Furthermore, high prevalence rates were found in many countries in recent years.^[2–7] For its prevalence in adults in China, a research in Guangzhou, which is the third major city in China, revealed a prevalence rate of 6.24%; and its prevalence was significantly higher in the urban area (8.32%) versus the rural area (3.43%).^[8] A population-based study in 11 major cities in China has shown that the prevalence of AR ranged from 8.7% in Beijing in East China to

24.1% in Urumqi in West China. These were based on 38,203 telephone interviews validated by questionnaires, adjusted for age, and gender. Moreover, among these cases, 74.4% were diagnosed with intermittent AR and 25.6% were diagnosed with persistent AR.^[9]

The classical symptoms of AR are nasal itching, sneezing, rhinorrhea, and nasal congestion. In addition, ocular symptoms are also frequent such as itching and redness of the eyes and tearing.^[10] Persistent AR (PAR) is defined as nasal symptoms that occur in more than four days a week, and occur in more than 4 weeks within the last 12 months.^[1]

Pharmacologic agents have become more effective and fast-acting in relieving symptoms. However, these do not have long-term benefits, symptoms generally recur. Chinese herbal medicine has long been used to treat AR, and it has been considered to improve traditional Chinese medicine (TCM) syndrome and holistic convalescence by preventing recurrence. Syndrome is a special term for TCM. TCM syndrome differentiation is a process in which the etiology, nature, site of the patterns and relationship between the immune system and pathogenic factors are identified according to the 4 diagnostic methods, inspection, listening and smelling, inquiry, pulse-taking. Hence, research on the relationship between TCM syndrome and AR is continuously being conducted.^[11,12] Although Chinese herbal medicine has shown its immediate effects,^[13–15] its long-term effects have not been studied to date. The Qingfeijianpi therapy has been used in clinic for 10 years, but no scientific study has been conducted. Qingfeijianpi therapy is a therapeutic method to cure damp-heat syndrome. It means clearing away the lung-heat and tonifying spleen at the same time. For the damp-heat syndrome of AR, lung-heat and spleen-dampness are key factors for the disease, so herbs which can clear away the lung-heat and tonify spleen are used to treat it. This research will focus on the 16-week improvement of nasal symptoms, TCM syndrome and the quality of life of PAR patients with 4-week medicine.

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2. Materials and methods

2.1. Participants

The present study was conducted from June 2015 to June 2016 at the Department of TCM, Tongren Hospital.

2.1.1. Inclusion criteria. Inclusion criteria included: Patients who meet the PAR diagnostic criteria of Western medicine and the TCM damp-heat syndrome differentiation standard; patients who are 18 to 60 years old; patients who voluntarily participate in this study, and terminate all other treatments which may affect the assessment of the drug; and patients who provided a signed informed consent form.

2.1.2. Exclusion criteria. Exclusion criteria included: Patients who received oral administration of steroids in the past 2 weeks and oral administration of antihistamine drugs or topical steroids 1 week prior to enrollment; patients with severe deviation of nasal septum and hypertrophic rhinitis; patients with asthma; patients with severe primary diseases such as diseases in the cardiovascular, cerebrovascular, liver, kidney, and hematopoietic systems; patients with mental illness; patients who are allergic to the drug; patients who are pregnant, lactating, or planning a pregnancy; patients who do not meet the inclusion criteria or prescribed medication, or have incomplete data; and patients treated for less than 28 days.

2.2. Study design

This study had obtained approval from the medical ethics committee from Beijing Tongren Hospital affiliated to Capital Medical University (No: TRECKY2015-005). Every participant signed informed consent when enrolled in the study.

This study is a randomized controlled trial. Participants were randomly selected using an envelope with a computer-generated random number before treatment. The trial involved a 4-week treatment period and a 12-week follow-up period.

2.3. Treatment

The author is the successor of Professor Kong Sibō, a Chinese medicine “Peking School” representative doctor, who is experienced in using gypsum. Hence, we put forward the Qingfeijianpi therapy of treatment for persistent AR damp-heat syndrome, which has been used in clinic for 10 years. Loratadine tablets were chosen as the positive drug, which is a typical oral H1-antihistamine effective for AR with little impairment or side effects.^[16]

Patients in the treatment group were given Qingfeijianpi decoction (1 dose/day for 4 weeks) and patients in the control group were given oral loratadine tablets (10 mg/time, once a day for 4 weeks). After treatment, the follow-up period for all patients was 12 weeks. The whole course lasted for 16 weeks.

Herbs: 1 g of *Ephedra*, 30 g of gypsum, 10 g of *Scutellaria*, 10 g of *Morus alba*, 10 g of *Prunella*, 10 g of *Magnolia*, 5 g of fried *Xanthium*, 20 g of raw semen coicis, 15 g of poria, and 0.6 g of antelope horn powder; prescription drugs used by Beijing Tcmages Pharmaceutical Co. Ltd. in granule form.

2.4. Outcome measures

2.4.1. Primary measures. Primary outcome was a change from baseline in 4 nasal and 2 eye symptoms in participants in the herbal treatment group. Throughout the study, 4 nasal symptoms (nasal congestion, sneezing, rhinorrhea, and nasal itching) and 2 eye symptoms (itching, redness and tearing) were self-assessed

daily and recorded in a diary by participants. The participants were given the scoring standard with a 4-point scale: 0 = none; 1 = slight, the symptom is clearly present but is not troublesome; 2 = moderate, the symptom is present and is troublesome, but not disabling or insufferable; 3 = severe, the symptom is severe or insufferable.^[17] The daily symptom score was expressed as the sum of the nose and eye scores. The weekly symptom score was the mean value of the daily symptom scores.

2.4.2. Secondary measure. The TCM syndrome and Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores were obtained. Scores were assessed at eight time points: first, W1, W2, W3, W4, W8, W12, and W16. RQLQ was developed to specially evaluate the quality of life of patients with AR.^[18] This was divided into 7 domains: sleep, non-hay fever symptoms, practical problems, nasal symptoms, eye symptoms, activities, and emotions. Each domain was scored between 0 (no impairment on quality of life) and 6 (severe impairment). The total score of all 7 domains was calculated as the overall RQLQ life score.

TCM syndrome: 4 main symptoms: nasal congestion, sneezing, rhinorrhea, and nasal itching. Six secondary symptoms: irritability, dry mouth, dry stool, red tongue, yellow greasy coating, and slippery pulse. Two main symptoms with 2 secondary symptoms are required to establish the syndrome.^[19,20] The 2-point scale (0=none, 1=yes) was used as the scoring standard of irritability, dry mouth and dry stool. The 4-point scale (0=none; 1=slight; 2=moderate; 3=severe) was used as the scoring standard of other symptoms.

2.5. Adverse events

All participants were instructed to record any unexpected events throughout the trial in their diary. At W0 and W4, blood indexes ALT, AST, BUN, and Cr were recorded. Four vital signs including body temperature, respiration rate, blood pressure, and arterial pulse were recorded at W0 and W4.

2.6. Statistical analysis

The outcome data (nasal symptom, TCM syndrome and RQLQ scores) were analyzed using SPSS version 20.0 for Windows. Data were presented as mean ± standard deviation (SD) with 95% confidence interval (CI), or standard error of the mean (SEM); and comparisons between 2 groups were performed using the effect size estimates. The baseline characteristics of these 2 groups were evaluated using independent-sample *t*-test, gender was evaluated using χ^2 -test, and education level was evaluated using Wilcoxon rank sum test. For primary and secondary outcome measures, the difference between scores each week and at baseline was obtained. The mean differences at baseline and in follow-ups were evaluated using paired *t*-test in the same group or independent-sample *t*-test between 2 groups.

3. Results

3.1. Participants

A total of 101 patients were enrolled into the study, including 52 patients in the treatment group and 49 patients in the control group. Patients who completed the 4-week medication and telephone follow-up were regarded as patients who completed the study. Five patients did not complete the test. Among these 5 patients, 3 patients were from the treatment group and 1 patient was from the control group. These are mainly due to

Table 1
Participant characteristics compared between groups.

	Treatment group (n = 52)	Control group (n = 49)	P
Mean age in years, SD	42.42 (11.13)	40.55 (10.62)	.395
Male	30	22	.199
Female	22	27	
Degree of education			.585
illiteracy	1	0	
primary school	3	1	
middle school	11	11	
university	28	28	
postgraduate	9	9	

inconvenience, and these patients were only given 2 weeks of medicine once. Furthermore, among these 5 patients, 4 patients who withdrew from the study during the treatment period complained that it was not easy to ask to leave the hospital, while the remaining patient needed to move to another city.

3.1.1. Baseline data. There were no significant differences between the treatment and control groups in terms of age, gender ratio, and degree of education (Table 1).

3.2. Weekly symptom score

During W0-W4, the scores of both 2 groups decrease. There was significant reduction at W4 compared with W0 ($P < .05$) in 2 groups. Yet no significant difference was seen between treatment and control group at W4 ($P > .05$). During follow-up period, the symptom score of treatment group did not increase significantly at W16 compared with W4 ($P > .05$), while the symptom score of control group increased significantly at W16 compared with W4 ($P < .05$). Moreover, at W12, there was significant difference between 2 groups (Table 2).

3.3. TCM syndrome score

At W0, there was no significant difference between the 2 groups ($P > .05$). At W3 and W4, the TCM syndrome scores in treatment group decreased significantly compared with control group ($P < .05$). During the follow-up period, at W8, W12, W16, there were significant difference between the 2 groups ($P < .05$) (Table 3).

3.4. RQLQ score

There were no significant difference between the 2 groups before and after the treatment, at W0, W1, W2, W3, and W4 ($P > .05$).

Table 2
Comparison of symptom score between 2 groups.

Week	Treatment group (n = 49)	Control group (n = 47)	P
0	9.4 ± 3.75	9.38 ± 3.22	.967
1	7.67 ± 3.79	6.96 ± 3.89	.354
2	6.94 ± 3.27	5.73 ± 3.09	.060
3	6 ± 3.48	5.6 ± 3.22	.557
4	5.21 ± 3.17	5.29 ± 3.39	.903
8	5.19 ± 2.87	6.02 ± 3.58	.212
12	5.29 ± 2.82	6.79 ± 3.96	.03
16	5.63 ± 2.76	7.02 ± 4.36	.067

Table 3
Comparison of TCM syndrome score between 2 groups.

Week	Treatment group (n = 49)	Control group (n = 47)	P
0	13.6 ± 3.28	13.63 ± 2.81	.963
1	9.77 ± 3.22	10.46 ± 3.51	.308
2	8.73 ± 3.08	9.42 ± 3.60	.307
3	6.9 ± 3.08	8.48 ± 3.36	.016
4	5.96 ± 3.22	8 ± 3.48	.003
8	6.37 ± 2.58	8.1 ± 4.07	.015
12	6.69 ± 2.59	8.58 ± 4.21	.01
16	6.29 ± 2.80	8.81 ± 4.66	.002

While, during the follow-up period, at W12, W16, there were significant difference between the 2 groups ($P < .05$) (Table 4).

3.5. Adverse events

No adverse events occurred. Abnormal ALT, AST, BUN, and Cr were analyzed, but no clinical significance was found. And no one was found normal before treatment but abnormal after treatment. The four vital signs (body temperature, respiration rate, blood pressure, and arterial pulse) were analyzed, and the difference was not statistically significant.

4. Discussion

Chinese herbal medicine has been used for the treatment of AR for decades, especially in China.^[21-22] However, a few clinical studies have been conducted to confirm its effectiveness,^[13-15] but its post medication stage was not evaluated, which may be the potential advantage of Chinese herbs. This study was a randomized, positive-controlled trial that used the special qingfeijianpi prescription. Three main indicators, including daily symptom diary, RQLQ and TCM syndrome, were used to measure the clinical efficacy of the Qingfeijianpi therapy. This study confirms that the effect of Qingfeijianpi prescription is not worse than that of loratadine, especially in the long-term effect.

The Qingfeijianpi prescription consists of *Ephedra*, gypsum, *Scutellaria*, *M. alba*, *Prunella*, *Magnolia*, fried *Xanthium*, raw semen coicis, poria, and antelope horn powder. In TCM, the herbs in a prescription can be divided into Monarch, Minister, Assistant and Guide according to their functions. In this prescription, gypsum and antelope horn powder function as Monarch. Gypsum is cold and salty according to TCM theory, good at clearing away the lung-heat. Antelope horn powder is salty, cold, heavy, which can clear away lung-heat without

Table 4
Comparison of RQLQ score between 2 groups.

Week	Treatment group (n = 49)	Control group (n = 47)	P
0	78.42 ± 33.71	83.29 ± 34.89	.480
1	62.87 ± 29.39	63.63 ± 39.38	.913
2	58.81 ± 27.14	58.77 ± 37.93	.996
3	49.79 ± 27.38	55.5 ± 37.30	.388
4	43.9 ± 29.75	55.38 ± 37.90	.094
8	47.73 ± 25.33	58.96 ± 34.15	.070
12	42.19 ± 19.71	60.98 ± 36.90	.036
16	46.23 ± 17.60	62.23 ± 38.25	.038

suppressing the vital qi. Raw semen coicis, Poria, *Scutellaria*, *M. alba* function as Minister. Raw semen coicis is light, sweet, cool, functions in invigorating spleen and dehumidification. Poria is neutral, not cold not hot, which can fortify spleen and percolate dampness. *Scutellaria* and *M. alba* help Monarch to clear lung-heat. *Ephedra* and *Prunella* function as Assistant. *Ephedra*, spicy and warm, open the inhibited lung-energy, which assists other herbs, not helping lung-heat. *Prunella*, bitter and cold, functions in heat-clearing and damp-drying. *Magnolia* and fried *Xanthium* play role as Guide. The 2 herbs, spicy and warm, are good at clearing the nasal passages and guide all the herbs to the disease site.

For the symptom scores, there were no differences between the 2 groups after 4 weeks. However, during the follow-up period, we observed a stable improvement using the Qingfeijianpi therapy. The reduction of TCM syndrome and RQLQ exhibited the same trend as that in nasal symptoms. For the control group, there were no such changes. Even worse, the symptoms of PAR patients gradually returned to the initial state of the disease. The TCM syndrome scores between these 2 groups exhibited the largest difference, which may be an important factor for preventing recurrence. However, the pharmacological mechanism in western medicine remains unclear.^[2,3]

Consistent with the findings of previous TCM studies for PAR, we found that herbs of Qingfeijianpi therapy for the treatment of PAR exhibited a good immediate effect, as well as good long-term effects. Moreover, the TCM treatment was well-tolerated by patients and there were almost no adverse events.

We conclude that the Qingfeijianpi therapy may provide a safe and effective option for the treatment of PAR with damp-heat syndrome. However, there is possibility of potential bias or imprecision in this study. It is a non blind study of Western medicine and Chinese medicine. The main evaluation index is the symptom score which has the possibility of the subjective deviation of the patient, it may make the score difference of the treatment group more obvious.

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