Efficacy of Bimin Decoction on patients with perennial allergic rhinitis: an open-label non-inferiority randomized controlled trial

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Research

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Abstract

Background: Allergic rhinitis (AR) is a common allergic disease which affects people worldwide and traditional Chinese medicine is getting popular among AR patients for definite clinical effect and less adverse reactions. Lung qi deficiency and cold syndrome (LQDCS) is a frequent type of AR, and Chinese herbal medicine Bimin Decoction (BMD) was generated for AR patients with LQDCS. This study aimed to compare the clinical efficacy of BMD for AR patients with LQDCS to conventional medicine loratadine and fluticasone nasal spray. Methods/Design: The study was designed as an open-label, non-inferiority, randomized controlled trial. A total of 108 AR patients with LQDCS aged 19 to 60 were 1:1 randomly allocated to BMD group and control group by central computer system in Beijing Hospital of Traditional Chinese Medicine from January 2017 to April 2018. 98 completed the study (n=51; n=47). Patients in BMD group received Bimin Decoction while the control group received fluticasone nasal spray and loratadine tablets for a 4-week treatment. The primary outcome was change of the Total Nasal Symptom Score (TNSS) at baseline and the end of treatment. Alterations in Rhinoconjunctivitis Quality Life quality Questionnaire (RQLQ), nasal resistance (NR) and acoustic rhinometry parameters were second outcomes. Any side effect of treatment was observed and recorded. Results: After the 4-week treatment the TNSS total score was significantly reduced in both groups from baseline (P < 0.05), no significant between-groups differences were observed for the changes of TNSS scores [-0.298 (95% CI -0.640 to 0.140)], which was within the defined non-inferiority margin. RQLQ in both groups decreased significantly (P < 0.001) from baseline and more obvious reduction in BMD group was observed (P < 0.001). There was no significant difference in the nasal resistance, the nasal volume and the nasal minimum cross-sectional area after treatment between groups (P > 0.05). Conclusions: These findings indicated that BMD helps relieve PAR symptoms and improve rhinitis-related life quality. Our study indicated that BMD is non-inferior to loratadine tablets and fluticasone nasal spray for AR patients with LQDCS. Trial registration: Chinese Clinical Trial Registry, ChiCTR-INR-16010063. Registered on 2 December, 2016 Keywords: Perennial allergic rhinitis, Chinese traditional medicine, Randomized controlled trial, Clinical efficacy

Background

Allergic rhinitis (AR) is a common allergic disease which is divided into perennial AR(PAR) and intermittent AR [1]. Therapy of AR mainly include allergens avoidance, pharmacotherapy, immunotherapy and patient education; however, each has its limitations [2]. The most effective way for AR is to prevent from exposure to allergens, but those in the air are often difficult to avoid. Immunotherapy is still less popular for its long therapy cycle (recommended for 3~5 years) and unsatisfactory results among patients [3]. Therefore, pharmacotherapy is still the main approach for AR. Although antihistamines and intranasal corticosteroids are rapid and accurate in alleviating symptoms, they can't fully regulate the patients’ immune status and sometimes cause unfavorable side effects [4]. Increasingly patients are turning to explore complementary and alternative medicines and traditional Chinese medicine (TCM) has gained popularity [5].
Syndrome pattern is a term used in TCM to define a series of symptoms in medical condition and the lung qi deficiency and cold syndrome (LQDCS) is a type frequently observed in PAR. Our department has been devoted to TCM on AR for several decades and formed empirical herbal formula Bimin Decoction (BMD), which is composed of saposhnikovia divaricata (fangfeng), astragalus (huangqi), asarum heterotropoides (xixin), radix peoniae alba (baishao), atractylodes (baizhu), cassia twig (guizhi), prunus mume (wumei), fructus chebulae (hezi), licorice (gancao), schisandra chinensis (wuweizi) and herba ephedrae (mahuang). BMD contains substances which demonstrate anti-inflammatory and immune regulation functions [6-9], and it is generated for AR patients with LQDCS. The current study aimed to compare the clinical efficacy of BMD for PAR patients with LQDCS to conventional medicine loratadine and fluticasone nasal spray.

Methods And Design

Study design

An open-label, non-inferiority, randomized controlled trial was carried out to investigate the efficacy of BMD on symptoms, life quality and nasal resistance (NR) in PAR patients. All participants were recruited from the Otorhinolaryngology Department of Beijing Hospital of Traditional Chinese Medicine (BJHTCM). The study design and protocol were approved by the Ethics Committee of Beijing Hospital of Traditional Chinese Medicine affiliated to Capital medical University (code 2016BL-047). The study was conducted in accordance with the principles of the Declaration of Helsinki (2004) and the Medical Research Involving Human Subjects Act (WMO). Registration in China Clinical Trial Registry Center (ChiCTR-INR-16010063) was completed on 2 December 2016. This article will be reported according to the Consolidated Standards of Reporting Trials (CONSORT) 2010 guidelines [10].

Participants

Recruitment information was posted in Beijing Hospital of Traditional Chinese Medicine and publicized through the Internet. Participants with PAR volunteered for the study were selected from January 2017 to April 2018 by physicians of otorhinolaryngology clinics. All the participants should meet the Western medicine diagnostic criteria for AR and the TCM syndrome diagnostic criteria for LQDCS. Syndrome differentiation was determined by two independent qualified TCM otolaryngologists independently.

Inclusion criteria:

(1) patients aged 18 to 65 years, no sex limitation (2) symptoms including sneezing, rhinorrhea, nasal obstruction and itching, occurred at least 4 days per week and lasted more than 4 weeks [11], with positive skin prick test to house dust mites (+++ or more, ALK reagent) according to the Allergic Rhinitis and its Impact on Asthma criteria (ARIA, 2008); (3)the syndrome differentiation corresponded with LQDCS which contains a light pink tongue with thin white coating and weak pulse [12]; (4) patients who signed the informed consent form volunteered to participate in the study; (5) patients without allergy to Chinese herbal medicine.
Exclusion criteria:

(1) women who were pregnant or ready to conceive in past 6 months, or during lactation; (2) patients with nasal polyps, rhinosinusitis, obvious deviated nasal septum, or upper respiratory tract infection; (2) patients who were undergoing treatment for AR; (3) those who have serious disorders such as vascular malformation, hypertension, hematologic diseases, diabetes mellitus, malignant tumor, or mental disorders.

Randomization and blinding

The physicians were responsible for recruitment and therapeutic assessment of the patients. Participants recruited were randomly allocated into either the BMD group ($n = 54$) or the control group ($n = 54$) in a 1:1 ratio by a computer-generated random sequence in Good Clinical Practice Office of BJHTCM after a 7-day washout period, and the sequence could not be viewed by the physicians. The investigators were responsible for the distribution of drugs. All research team members were required not to communicate with the participants regarding their allocation. The flow chart and the study period are listed below (Fig. 1 and table 1).

**Fig 1 (additional file 1)**

**Table 1 Study design schedule**

<table>
<thead>
<tr>
<th>Week</th>
<th>-1 Baseline</th>
<th>0 Treatment and follow-up phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient enrollment</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Medical history</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Skin prick tests</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Informed consent</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>Randomization</td>
<td>√</td>
<td></td>
</tr>
<tr>
<td>TNSS</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>RQLQ</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Adverse event</td>
<td>√</td>
<td>√</td>
</tr>
</tbody>
</table>

TNSS, Total Nasal Symptoms Score;

RQLQ, Rhinoconjunctivitis Quality of Life Questionnaires.

**Intervention**

All the patients completed the Total Nasal Symptom Score (TNSS), the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), nasal resistance and acoustic rhinometry under instruction. The participants in BMD group received BMD while the control group received fluticasone furoate spray (Flixonase, 50μg*120press, Glaxo Wellcome, S.A) and loratadine tablets (Clarityne, Shanghai Schering plough Pharmaceutical Co. Ltd.). Ingredients and dosage of BMD are presented below in table 2. Herbal
medicines involved in the study were all produced by Beijing Institute of Traditional Chinese Medicine in the same batch. Every dose was decocted twice. All the herbals should be soaked in cold water for 1 hour before decoction. The first decoction was boiled over high heat and remained boiling with low heat for 30 minutes, then filtered and reserved the liquid. The second decoction was boiled over high heat with cold water and then remained boiling with low heat for 15 minutes. Liquid was filtered and combined with that of the first decoction and the total volume added up to 400ml approximately. Patients took 200ml orally at 30 minutes after breakfast and dinner respectively for 4 weeks. According to the step-up therapy recommended by ARIA [13], the participants in control group were given fluticasone furoate spray 2 press per nostril and loratadine tablets 10mg per night. No other medicine or spicy, fishy, cold food was allowed during treatment for all participants.

For participants who withdrew or were excluded, information were recorded and the medicines were returned to investigators immediately. Patients who completed the study were followed up by the physicians and required to fulfill the TNSS score, RQLQ score, nasal resistance and acoustic rhinometry at the end of the treatment.

Table 2 The ingredients, dosage and actions of herbal medicines in *Bimin Decoction* (Every 7 dose)

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Dosage (g)</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saposhnikovia divaricata root (fangfeng)</td>
<td>10</td>
<td>Dispelling wind-cold to prevent muscular interstices from invasion of exogenous pathogenic factors</td>
</tr>
<tr>
<td>Astragalus root (huangqi)</td>
<td>15</td>
<td>Strengthening the defense and removing edema</td>
</tr>
<tr>
<td>Atractylodes root (baizhu)</td>
<td>10</td>
<td>Consolidating the exterior and enhancing immunologic function</td>
</tr>
<tr>
<td>Cassia twig (guizhi)</td>
<td>6</td>
<td>Warming <em>yang</em> and dispelling cold</td>
</tr>
<tr>
<td>Radix paeoniae alba root (baishao)</td>
<td>10</td>
<td>Astringing the acid to nourishing <em>yin</em> of the body</td>
</tr>
<tr>
<td>Prunus mume fruit (wumei)</td>
<td>6</td>
<td>Astringing lung <em>qi</em> to consolidate the base of life</td>
</tr>
<tr>
<td>Fructus chebulae fruit (hezi)</td>
<td>6</td>
<td>Astringing lung <em>qi</em> to consolidate the base of life</td>
</tr>
<tr>
<td>Asarum heterotropoides root (xixin)</td>
<td>3</td>
<td>Eliminating wind to dispersing cold and removing edema</td>
</tr>
<tr>
<td>Schisandra chinensis fruit (wuweizi)</td>
<td>6</td>
<td>Astringing lung <em>qi</em> to consolidate the base of life</td>
</tr>
<tr>
<td>Herba ephedrae stem (mahuang)</td>
<td>3</td>
<td>Relieving exterior and eliminating wind to dispersing cold</td>
</tr>
<tr>
<td>Licorice root (gancao)</td>
<td>6</td>
<td>Reconciling all the other herbals</td>
</tr>
</tbody>
</table>

Main outcome
The main outcome of this study was the change of TNSS. The measurement was based on four nasal symptoms including sneeze, rhinorrhea, itchy nose and nasal obstruction, each was scored from 0 to 3 (0 = none, 1 = mild, 2 = moderate, and 3 = severe).

Secondary outcomes

The authorized and Sinicized RQLQ was applied. RQLQ consists of 28 questions on a 7-point scale (0 = not impaired at all, 6 = severely impaired) in 7 domains: activity limitations, sleep problems, nose and eye symptoms, non-nose/eye symptoms, practical problems, and emotional functions [14]. Total score and seven domain scores between groups were compared.

All participants rested for 20~30 minutes and required to clean up nasal secretions before nasal resistance (NR) and acoustic rhinometry measurements (model: NR-6, British GM). Bilateral exhalation and inhalation resistance, total nasal resistance and nasal minimum cross-sectional area (NMCA) were analyzed. The nasal volume (NV) was set between 0 and 7cm. Each patient underwent 4 times measurements on each side and the average was calculated for data analysis.

Sample size

The sample size was evaluated with SAS 9.3 software (SAS Institute Inc., Cary, NC, USA) in the Clinical Evaluation Center of Beijing Hospital of TCM. The mean change in TNSS pre-and post-treatment was set as the indicator in the calculation. Results from our previous studies showed that the mean TNSS change of the BMD group was $6.62 \pm 2.84$ and that of the control group was $5.79 \pm 2.18$ [15], considering a power of 80%, alpha of 0.05, an acceptable delta of 0.2, a non-inferiority margin of 0.77 [15], a clinically important difference can be detected by a sample size of at least 49 in each group. This number was then increased to 59 each group (total of 108) to allow for a predicted 20% dropout rate.

Statistical analysis

All statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA; version 22.0) by qualified statisticians according to the intention-to-treat principle. We evaluated the baseline value and the corresponding outcomes. Descriptive statistics were used to compare baseline measures and patients’ characteristics between groups. Least-squares mean changes from baseline were evaluated using analysis of covariance (ANCOVA) models for the primary outcome.. The two-sample independent t test was used to compare the differences of secondary outcomes. Numeration data were assessed using Fisher's exact test. Level of $\alpha = 0.05$ was defined as statistically significant.

Results

A total of 108 cases met the criteria were randomized into the study, 4 cases were eliminated for common cold and 6 cases dropped out for personal reasons (Fig.1). There were 51 cases including 29 male and 22 female aged 19 to 60 years (mean, 36.8 years; SD, 11.6) in BMD group, and 47 cases including 26 male
and 21 female aged 22 to 59 years (mean, 37.9 years; SD, 10.2) in control group. No significant difference of the demographic characteristics between groups were detected (Table 3).

**TNSS**

Values for pretreatment TNSS were similar in both groups (Bimin decoction, 7.84 ± 1.46; fluticasone and loratadine, 8.43 ± 1.56; \( P = 0.062 \)). After the 4-week treatment, both groups reduced in TNSS total score: the BMD group from 7.84 ± 1.46 to 2.17 ± 1.26 \( (P = 0.019) \) and the control group from 8.43 ± 1.56 to 2.29 ± 0.93 \( (P = 0.021) \) (Table 3 and 4). The 95% confidence interval for group mean change difference was -0.640 to 0.140, which is within the defined non-inferiority margin of 0.77 (Table 4 and Fig. 2).

**Table 3** Homogeneity test for general characteristics and measurement variables at baseline (mean ± SD)

<table>
<thead>
<tr>
<th>Characteristics or variables</th>
<th>BMD group ((N = 51))</th>
<th>Control group ((N = 47))</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>36.8 ± 11.6</td>
<td>37.9 ± 10.2</td>
<td>0.523</td>
</tr>
<tr>
<td>Male/female</td>
<td>29/22</td>
<td>26/21</td>
<td>0.221</td>
</tr>
<tr>
<td>TNSS (score)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>7.84 ± 1.46</td>
<td>8.43 ± 1.56</td>
<td>0.062</td>
</tr>
<tr>
<td>Sneeze</td>
<td>2.22 ± 0.67</td>
<td>2.28 ± 0.71</td>
<td>0.608</td>
</tr>
<tr>
<td>Runny nose</td>
<td>2.06 ± 0.79</td>
<td>2.23 ± 0.76</td>
<td>0.265</td>
</tr>
<tr>
<td>Itchy nose</td>
<td>1.90 ± 0.94</td>
<td>2.19 ± 0.74</td>
<td>0.141</td>
</tr>
<tr>
<td>Nose obstruction</td>
<td>1.67 ± 0.95</td>
<td>1.72 ± 0.85</td>
<td>0.784</td>
</tr>
<tr>
<td>RQLQ (score)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>67.18 ± 8.19</td>
<td>66.81 ± 9.23</td>
<td>0.735</td>
</tr>
<tr>
<td>Activity limitations</td>
<td>9.04 ± 2.88</td>
<td>9.77 ± 3.10</td>
<td>0.226</td>
</tr>
<tr>
<td>Sleep problems</td>
<td>6.12 ± 2.42</td>
<td>6.36 ± 2.34</td>
<td>0.576</td>
</tr>
<tr>
<td>Eye symptoms</td>
<td>14.24 ± 2.95</td>
<td>13.94 ± 3.00</td>
<td>0.604</td>
</tr>
<tr>
<td>Nose symptoms</td>
<td>5.80 ± 3.02</td>
<td>4.85 ± 3.20</td>
<td>0.128</td>
</tr>
<tr>
<td>Non nose/eye symptoms</td>
<td>14.04 ± 3.48</td>
<td>13.72 ± 3.75</td>
<td>0.702</td>
</tr>
<tr>
<td>Practical problems</td>
<td>10.25 ± 2.54</td>
<td>11.04 ± 3.00</td>
<td>0.123</td>
</tr>
<tr>
<td>Emotional function</td>
<td>7.69 ± 2.67</td>
<td>7.13 ± 2.94</td>
<td>0.331</td>
</tr>
</tbody>
</table>

**Table 4** Effect of *Bimin* Decoction on allergic rhinitis symptoms
Characteristics or variables | Least squares mean change from baseline (± SE) | Mean difference (95% CI) | P value
---|---|---|---
| BMD group (N = 51) | Control group (N = 47) |

TNSS (score)  
Overall | 6.002 ± 0.149 | 5.997 ± 0.155 | -0.298 (-0.640 to 0.104) | 0.982 |
Sneeze | 1.742 ± 0.068 | 1.642 ± 0.071 | 0.066 (-0.182 to 0.314) | 0.316 |
Runny nose | 1.560 ± 0.072 | 1.605 ± 0.075 | -0.150 (-0.425 to 0.126) | 0.666 |
Itchy nose | 1.454 ± 0.074 | 1.422 ± 0.077 | -0.179 (-0.505 to 0.147) | 0.763 |
Nose obstruction | 1.252 ± 0.067 | 1.386 ± 0.070 | -0.169 (-0.466 to 0.128) | 0.171 |

Fig 2 (additional file 2)

RQLQ

After the treatment, the single and overall RQLQ in the two groups both reduced significantly: the BMD group from 67.18 ± 8.19 to 14.54 ± 3.56 (P < 0.001) and the control group from 66.81 ± 9.23 to 22.45 ± 4.70 (P < 0.001); RQLQ total score after treatment in groups was statistically significant (P < 0.001) (Table 5).

Table 5 Effect of Bimin Decoction on Rhinoconjunctivitis Quality of Life Questionnaire (mean ± SD)

<table>
<thead>
<tr>
<th>Characteristics or variables</th>
<th>BMD group (N = 51)</th>
<th>Control group (N = 47)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RQLQ (score)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>14.57 ± 3.56</td>
<td>22.45 ± 4.70</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Activity limitation</td>
<td>2.92 ± 1.56</td>
<td>2.81 ± 1.79</td>
<td>0.170</td>
</tr>
<tr>
<td>Sleep problems</td>
<td>0.90 ± 1.01</td>
<td>1.85 ± 1.16</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Nose symptoms</td>
<td>2.75 ± 1.75</td>
<td>4.26 ± 1.87</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Eye symptoms</td>
<td>1.20 ± 1.39</td>
<td>1.55 ± 1.64</td>
<td>0.319</td>
</tr>
<tr>
<td>Non nose/eye symptoms</td>
<td>3.71 ± 2.54</td>
<td>6.19 ± 2.74</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Practical problems</td>
<td>2.02 ± 1.49</td>
<td>3.79 ± 2.27</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Emotional function</td>
<td>1.08 ± 1.07</td>
<td>2.00 ± 1.63</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Nasal resistance and acoustic rhinometry

There was no significant difference in the NR, the NV and the NMCA between groups (P > 0.05) (table 6 and 7).
Table 6 Comparison of nasal resistance between groups after treatment Pa/cm\(^3\), mean ± SD additional file 3\(^a\)

Table 7 Comparison of acoustic rhinometry between groups after treatment ml, mean ± SD additional file 4\(^a\)

**Safety**

Both treatments were well tolerated. 7 patients (BMD, 5; fluticasone and loratadine, 8) reported a total of 13 adverse events: dry nose (2), sore throat (2), sleepiness (1) with BMD and dry nose (4), sore throat (3), cough (1) with fluticasone. Adverse events were not serious and were resolved with or without treatment.

**Discussion**

Modern drug treatment for PAR mainly includes antihistamines and intranasal corticosteroids [2]. These medicines play different roles in the prevention and therapy of allergic rhinitis. Although clear targets, rapid-acting and pronounced effects, they have different disadvantages of various degrees. For example, intranasal corticosteroids should be continuously used for several days to achieve the maximum effect and then gradually reduced to minimum dose to control symptoms, patients may discontinue when symptoms appear to relieve. Antihistamine drugs also have side effects such as cardiac toxicity, drowsiness, and operation disability [16]. As a result, more and more clinicians and patients are looking for complementary alternative medicines such as Chinese herbal to treat allergic rhinitis, which not only controls clinical symptoms but also regulates the constitution.

AR is a dominant disease of traditional Chinese Medicine, which belongs to the concept of "Biqiu" (鼻鼽). TCM believes that AR is caused by specific constitution, organs consumption and exogenous pathogenic factors. Once the inducing factors are encountered, symptoms would be easy to attack. Treat AR using TCM has a long history. TCM is capable of regulating immune function to relieve symptoms and reduce the frequency of attacks. Researches showed that the ethanolic extract of asarum heterotropoides (xixin) reduces anaphylaxis, as well as the anti-histamine and anti-allergic effects [17]. Schisandra chinensis (wuweizi) increases the generation of lymphoblastic cells and enhances immune function to promote DNA synthesis of lymphocytes through its lung astringe and kidney nourishment function [18, 19]. Licorice root (gancao) shows glucocorticoids likely anti-inflammatory and anti-allergic effects and its main components such as flavonoids and licorice compounds alleviate cardiac toxic and side effects of antihistamines [19, 20].

Our study evaluated the efficacy of BMD and indicated that it is non-inferior to antihistamines and intranasal corticosteroids. Results showed that the difference of TNSS score in BMD group and control group after treatment were not statistically significant. The total score of RQLQ after treatment in BMD group was significantly reduced than that of the control group. The obvious improvements of sleep, work and overall feelings indicated advantages of BMD in improving systemic symptoms. No significant difference of total NR, nasal cavity volume and NMCA in groups after treatment was observed. We found
BMD alleviate mucosal hyperemia, edema and nasal turbinate swelling, leading to reduction of NR and increase of NMCA. Changes of lymphocytes in AR patients after BMD therapy need to be proved in our further researches.

Conclusions

Our research indicated that BMD was non-inferior to fluticasone nasal spray and loratadine in alleviating AR symptoms. Life quality of BMD group such as sleep, influence of work and overall comfort were improved significantly than the control. BMD may become an ideal alternative Medicine considering its satisfactory efficacy and life quality promotion for AR patients.

List Of Abbreviations

AR: Allergic rhinitis; BMD: *Bimin* Decoction; PAR: Perennial allergic rhinitis; TCM: Traditional Chinese medicine; LQWCP: Lung qi weak and cold pattern; TNSS: Total nasal symptom score; RQLQ: Rhinoconjunctivitis Quality of Life Questionnaire; NR: Nasal resistance; NMCA: Nasal minimum cross-sectional area; NV: Nasal volume.

Declarations

**Ethics approval and consent to participate**

The study design and protocol were approved by the Ethics Committee of Beijing Hospital of Traditional Chinese Medicine affiliated to Capital medical University (code 2016BL-047). All subjects signed informed consent before enrollment. The study was conducted in accordance with the principles of the Declaration of Helsinki (2004) and in accordance with the Medical Research Involving Human Subjects Act (WMO). The study was registered in the China Clinical Trial Registry Center (ChiCTR-INR-16010063) on 2 December 2016.

**Consent for publication**

All subjects who participated in the image acquisition signed ICFs. The patients agreed that his or her information in this study could be revealed for publication. Signed ICFs from the patients in this study are kept in the author’s institution and are available for review upon request from the Editor-in-Chief.

**Availability of data and materials**

Supporting data are available from the corresponding author on reasonable request.

**Competing Interests**

The authors declare that they have no competing interests.
Funding Statement

This trial was supported with funding from Beijing Natural Science Foundation (No. 7162081) and National Natural Science Foundation (No. 81674034)

Authors’ Contributions

JW designed the study, and JZ drafted the paper. HZ and HL made critical revisions. XY and JH were responsible for the statistical analysis of the trial and wrote portions of the statistical methods. JA, JG, SH and YW participated in the study as clinical research associates and revised the paper. All authors read and approved the final paper.

Acknowledgements

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References


Additional Files
Additional file 1.pdf: Fig 1 Study flow diagram.

Additional file 2.pdf: Fig 2 Mean of total nasal symptom score for the 4-week treatment period. *p < 0.05 compared with baseline.

Additional file 3.xlsx: Table 6 Comparison of nasal resistance between groups after treatment.

Additional file 4.xlsx: Table 7 Comparison of acoustic rhinometry between groups after treatment.

**Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

- AdditionalFile4.xlsx
- AdditionalFile2.pdf
- CONSORTChecklist.doc
- AdditionalFile1.pdf
- AdditionalFile3.xlsx