

Acupuncture as an add-on therapy to sublingual allergen-specific immunotherapy for patients with allergic rhinitis

Jiang-hua Li, MM^a, Lin-hong Yang, MD^a, Ying Chen, MM^b, Zong-xian Fan, MM^{a,*}

Abstract

This study retrospectively analyzed the effectiveness of acupuncture as add-on therapy (AAOT) to sublingual allergen-specific immunotherapy (SASIT) for patients with allergic rhinitis (AR). A total of 120 eligible cases of adult patients with AR were included in this retrospective study. Of these, 60 patients received AAOT plus SASIT and were assigned to a treatment group, while the other 60 subjects underwent SASIT only, and were assigned to a control group. Primary outcome was AR symptoms. The secondary outcome was quality of life, as evaluated by the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). In addition, adverse events were also recorded during the study period. All outcomes were assessed before and after 8 weeks treatment. After 8 weeks treatment, patients in the treatment group had much better effectiveness in symptoms relief ($P < .05$), and quality of life improvement (activity domain, $P = .04$; practical domain, $P = .03$), compared with patients in the control group. In addition, although patients in the treatment group reported more mild pain at local area after the treatment than that in the control group ($P < .01$), no patients stopped the treatment. The results of this study showed that AAOT plus SASIT achieved more benefits in patients with AR than SASIT alone.

Abbreviations: AAOT = acupuncture as an add-on therapy, AR = allergic rhinitis, RQLQ = Rhinoconjunctivitis Quality of Life Questionnaire, SASIT = sublingual allergen-specific immunotherapy.

Keywords: acupuncture, allergic rhinitis, effectiveness, sublingual allergen-specific immunotherapy

1. Introduction

Allergic rhinitis (AR) is a very common health disorder worldwide.^[1–3] This IgE-mediated chronic inflammatory condition often manifests with sneezing, rhinorrhea, nasal and throat itching, nasal congestion, and postnasal drip.^[4,5] It has been reported that the global incidence rate ranges from 10% to 25% and still increasing year by year.^[6] In the USA, it affects about 60 million people and results in 3.5 million days of lost work productivity, as well as the 2 million days of school absenteeism every year.^[7,8] In China, it has been reported that the average self-reported prevalence rate of AR was 11.1%.^[9] If this disorder cannot be treated effectively and timely, it greatly affects the quality of life in patients with AR.^[10,11]

Sublingual allergen-specific immunotherapy (SASIT) is reported to treat this condition safely and effectively, especially for AR and asthma.^[12–15] It has disease-modifying properties

to potentially cure allergies, and do not have systematic complication.^[16–19] However, if an additional therapy is supposed to add to this therapy, more encouraging outcome results may be achieved.

Alternative therapy is a very powerful intervention to help relieve AR symptoms, such as Chinese herbal medicine,^[20–23] and acupuncture.^[24–26] Of these, acupuncture is reported to be specifically associated with down-regulation of allergen-specific IgE for house dust mite, and also with the significant relief of nasal itch, eye itch, and sneezing after acupuncture treatment, which may be account for the regulation of transient receptor potential vanilloid 1.^[26] However, no data are available to support the idea that acupuncture as add-on therapy (AAOT) to SASIT may benefit more for patients with AR. Therefore, this study hypothesized that the effectiveness of AAOT to SASIT would be superior to SASIT alone for the treatment of adult patients with AR.

2. Methods and materials

2.1. Ethical statement

This study was approved by the Ethical Committees of First Affiliated Hospital of Jiamusi University. However, the informed written consent from subjects was waived because this retrospective study just analyzed their medical records.

2.2. Design

The present study was designed as a retrospective study. It analyzed the data of 120 eligible patient cases with AR. Of these cases, 60 patients received AAOT plus SASIT and were assigned to the treatment group. The other 60 subjects underwent SASIT alone and were assigned to the control group. No randomization and blinding procedures were applied to this study, except the data analyst was masked. Patients in both groups were treated for

Editor: Qinzhong Zhang.

L-HY and J-HL contributed equally to this study.

The authors have no conflicts of interest to disclose.

^a Department of Otolaryngology, ^b Department of Intensive Care Unit, First Affiliated Hospital of Jiamusi University, Jiamusi, China.

* Correspondence: Zong-xian Fan, Department of Otolaryngology, First Affiliated Hospital of Jiamusi University, No. 348 Dexiang St, Xiangyang District, Jiamusi, Heilongjiang, 154003, China (e-mail: lnhong005@yeah.net).

Copyright © 2019 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

Medicine (2019) 98:1(e13945)

Received: 21 November 2018 / Accepted: 10 December 2018

<http://dx.doi.org/10.1097/MD.0000000000013945>

a total of 8 weeks. All primary and secondary outcomes were measured at baseline and after 8 weeks treatment.

2.3. Patients

Patients with confirmed diagnose of moderate or severe persistent AR aged 18 to 70 years old were included.^[27] In addition, all patients had a history of at least 2 years of typical AR symptoms, and positive skin prick test result, as well as the positive radioallergosorbent test result to house dust mite or Bermuda grass.

Subjects were excluded if they had allergic symptoms of AR less than 2 years; respiratory diseases, such as asthma, infectious diseases, chronic obstructive respiratory diseases, and nasal polyposis; any other medications or interventions, including acupuncture and SASIT 2 month before the study, or other treatments during the study; pregnancy or breast-feeding; and incomplete data.

2.4. Treatment schedule

Patients in both groups received SASIT (Dermatophagoides farinae drops; Wolwopharma Biotechnology, Zhejiang, China), 1 drop (333 µg/mL) daily for a total of 8 weeks. The sublingual drops were applied based on the introduction, recommended by the manufacturer.^[28]

In addition, patients in the treatment group also received add-on acupuncture treatment. Four acupoints were utilized to treat AR by using Hwato single-use disposable needles (0.22 mm width × 30 mm length, Suzhou Medical Appliance Factory, Jiangsu Province, China). Acupuncture therapy was applied to bilateral Yingxiang (LI 20, beside the wing of the nose, at the meeting point with the nasolabial line), Fengchi (GB 20, at the top of the sternocleidomastoid muscle which runs from the back of the head down to the front of the shoulders at the clavicle), Hegu (LI 4, on the dorsum of the hand, between the first and second metacarpal bones, approximately in the middle of the second metacarpal bone on the radial side), and Yintang (MHN-3, at the forehead, at the midpoint between the two medial ends of the eyebrow) for 30 minutes daily with 3 times manipulation to make sure patients felt deqi after each manipulation. All patients were treated 2 times daily for a total of 8 weeks.

2.5. Outcome measurements

Primary outcome was AR symptoms.^[29] It includes 6 allergic symptoms and 4 rhinitis symptoms. Each item varies from 0, no symptoms to 3, severe symptoms. The secondary outcome was quality of life. It was assessed with Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ).^[30] It has 7 domains presented with 28 items. Each item ranges from 0 to 6, with higher score indicating lower poor quality of life. In addition, any adverse events were also recorded during the study period. All outcomes were measured before and after 8 weeks treatment.

2.6. Statistical methods

All data were analyzed by SPSS Statistics 19.0 (IBM Corp., Armonk, NY). The distributions of the samples were checked by one-sample Kolmogorov–Smirnov test. Chi-square test or Fisher exact test was used to analyze the categorical data; while the *t* test or Mann–Whitney *U* test was applied to analyze the continuous data. The value of *P* < .05 was defined as having statistical significance.

Based on the results of the previous study, the effect size in this study was calculated by using data of symptom severity relief at the end of treatment.^[31,32] Thus, the desired sample size for this study is 60 subjects each group, with 90% power, 2-tailed significance level of 5%. Therefore, a total of 120 patients were sufficient to assess the effectiveness of AAOT to SASIT.

3. Results

The demographics and characteristics of all enrolled patients in both groups are summarized in Table 1. No significant differences regarding all these values were detected between 2 groups.

After 8 weeks treatment, patients in the treatment group achieved more promising effect in symptoms relief (*P* < .01, Table 2), and quality of life improvement, as measured by RQLQ scale (activity domain, *P* = .04; practical domain, *P* = .03; Table 3), compared with patients in the control group.

After 8 weeks treatment, patients in both groups reported mild adverse events, and no patient quitted the treatment because of the adverse events (Table 4). No significant differences of all adverse events were found between 2 groups, except the number of patients in the treatment group who experienced mild pain at local area was much higher than that in the control group (*P* < .01, Table 4).

4. Discussion

Previous studies have assessed the efficacy of the SASIT for the treatment of patients with AR.^[12–15] Most of them achieved promising efficacy and few adverse events.^[16–19] However, its

Table 1
Demographic characteristics at baseline.

Characteristics	Treatment group (n=60)	Control group (n=60)	P value
Mean age (year)	34.8 (8.1)	35.6 (7.7)	.45
Gender			
Male	35 (58.3)	31 (51.7)	.46
Female	25 (41.7)	29 (48.3)	.46
Ethnicity (Asian Chinese)			
Han	55 (91.7)	52 (86.7)	.38
Korean	5 (8.3)	8 (13.3)	.38
Body mass index (kg/m ²)	23.2 (2.1)	23.5 (2.3)	.46
Smoking status	9 (15.0)	7 (11.7)	.59
AR duration (year)	3.1 (1.4)	2.8 (1.6)	.27
Type of AR			
Moderate persistent	26 (43.3)	29 (48.3)	.58
Severe persistent	34 (56.7)	31 (51.7)	.58

Data are present as mean ± standard deviation or number (%); AR = allergic rhinitis.

Table 2
Comparison of symptoms after treatment.

Outcome measurements	Treatment group (n=60)	Control group (n=60)	P value
Runny nose	1.78 (0.53)	2.01 (0.48)	<.01
Blocked nose	1.62 (0.58)	1.89 (0.46)	<.01
Sneezing	1.73 (0.44)	1.93 (0.39)	<.01
Itchy nose	1.67 (0.61)	1.98 (0.56)	<.01
Gritty feeling/red/itchy eyes	1.20 (0.78)	1.56 (0.71)	<.01
Watery eyes	1.04 (0.70)	2.12 (0.63)	<.01

Data are present as mean ± standard deviation.

Table 3**Comparison of quality of life after treatment.**

RQLQ	Treatment group (n=60)	Control group (n=60)	P value
Activity domain	6.01 (5.37)	7.96 (4.98)	.04
Practical domain	6.34 (4.92)	8.23 (4.37)	.03

Data are present as mean \pm standard deviation; RQLQ = Rhinoconjunctivitis Quality of Life Questionnaire.

Table 4**Adverse events related to the treatment.**

Adverse events	Treatment group (n=60)	Control group (n=60)	P value
Gastrointestinal reactions	3 (5.0)	2 (3.3)	.65
Pain at needling area	15 (25.0)	1 (1.7)	.005
Numbness at local area	2 (3.3)	0 (0)	.29
Weakness at local area	2 (3.3)	0 (0)	.29
Tired	1 (1.7)	0 (0)	.50
Headache	1 (1.7)	1 (1.7)	1.00
Low mood	1 (1.7)	2 (3.3)	.57
Constipation	2 (3.3)	1 (1.7)	.57

Data are present as number (%).

efficacy is still limited in some patients. Acupuncture therapy has also been reported to have satisfied outcome results just by using it alone.^[24–26] Thus, it is very necessary to apply AAOT to SASIT for treating patients with such condition.

To our best knowledge, no study specifically focused on assessing the effect of AAOT to SASIT for the treatment of AR. Therefore, the present study firstly explored the combination effectiveness of AAOT plus SASIT for AR and has achieved more promising effectiveness than SASIT alone. These results may provide very helpful and valuable evidence for the clinical practice and future studies for treating AR.

The results of the present study found that patients who received AAOT plus SASIT exerted much better outcome results, both in symptoms relief and quality of life improvement than patients who underwent SASIT alone. The results indicated that the effects of AAOT plus SASIT are superior to the SASIT alone for the treatment of patients with AR.

This study has 3 limitations. First, this retrospective study did not include follow-up assessment, thus, further studies should extend the study period to further evaluate the long-term effectiveness of AAOT plus SASIT. Second, the patients were not masked in this study, because all outcome data in this study were based on the completed medical records. Third, the lacking randomization of included cases was another limitation, which may increase risk of case selection in this study. Fourth, the lacking comprehensive outcomes was another limitation in this study, because all the outcome data were extracted from the completed medical records. Future studies should avoid all above limitations.

5. Conclusion

The results of this study demonstrated that the effectiveness of AAOT plus SASIT is superior to the SASIT alone for the treatment of patients with AR.

Author contributions

Conceptualization: Jiang-hua Li, Lin-hong Yang, Ying Chen, Zong-xian Fan.

Data curation: Jiang-hua Li, Ying Chen, Zong-xian Fan.

Formal analysis: Jiang-hua Li.

Investigation: Zong-xian Fan.

Methodology: Jiang-hua Li, Ying Chen.

Project administration: Lin-hong Yang, Zong-xian Fan.

Resources: Jiang-hua Li, Lin-hong Yang, Ying Chen, Zong-xian Fan.

Software: Jiang-hua Li, Ying Chen.

Validation: Jiang-hua Li, Lin-hong Yang, Ying Chen, Zong-xian Fan.

Visualization: Jiang-hua Li, Lin-hong Yang, Ying Chen, Zong-xian Fan.

Writing – original draft: Jiang-hua Li, Lin-hong Yang, Ying Chen, Zong-xian Fan.

Writing – review & editing: Jiang-hua Li, Lin-hong Yang, Ying Chen, Zong-xian Fan.

References

- Numminen J. Allergic rhinitis. *Duodecim* 2017;133:473–8.
- Shin YS, Jung CG, Park HS. Prevalence and clinical characteristics of local allergic rhinitis to house dust mites. *Curr Opin Allergy Clin Immunol* 2018;18:10–5.
- Hu QR, Li J. A brief introduction of local allergic rhinitis. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2018;32:1363–6.
- Cheng L, Chen J, Fu Q, et al. Chinese society of allergy guidelines for diagnosis and treatment of allergic rhinitis. *Allergy Asthma Immunol Res* 2018;10:300–53.
- Bao Y, Chen J, Cheng L, et al. Chinese guideline on allergen immunotherapy for allergic rhinitis. *J Thorac Dis* 2017;9:4607–50.
- Bousquet J, Van CP, Khaltaev N. Aria workshop group, World Health Organization allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;108:S147–233.
- Min YG. The pathophysiology, diagnosis and treatment of allergic rhinitis. *Allergy Asthma Immunol Res* 2010;2:65–76.
- Nathan RA. The burden of allergic rhinitis. *Allergy Asthma Proc* 2007;28:3–9.
- Han DM, Zhang L, Huang D, et al. Self-reported prevalence of allergic rhinitis in 11 cities of China. *Chin J Otorhinolaryngol Head Neck (Chin)* 2007;42:378–84.
- Ozdoganoglu T, Songu M, Inancli HM. Quality of life in allergic rhinitis. *Ther Adv Respir Dis* 2012;6:25–39.
- Meltzer EO. Allergic rhinitis: burden of illness, quality of life, comorbidities, and control. *Immunol Allergy Clin North Am* 2016;36:235–48.
- Mortuaire G, Michel J, Papon JF, et al. Specific immunotherapy in allergic rhinitis. *Eur Ann Otorhinolaryngol Head Neck Dis* 2017;134:253–8.
- Ismail NFF, Neoh CF, Lim SM, et al. The immediate effect of facial candling on inflammatory mediators, substance P, symptoms severity, and quality of life in allergic rhinitis patients: Study protocol for a randomized controlled trial. *Medicine (Baltimore)* 2017;96:e7511.
- Incorvaia C, Di Rienzo A, Celani C, et al. Treating allergic rhinitis by sublingual immunotherapy: a review. *Ann Ist Super Sanita* 2012;48:172–6.
- Han M, Chen Y, Wang M. Sublingual immunotherapy for treating adult patients with allergic rhinitis induced by house dust mite among Chinese Han population: a retrospective study. *Medicine (Baltimore)* 2018;97:e11705.
- Pipet A, Botturi K, Pinot D, et al. Allergen-specific immunotherapy in allergic rhinitis and asthma. Mechanisms and proof of efficacy. *Respir Med* 2009;103:800–12.
- Pfaar O, Klimek L. Specific immunotherapy for allergic rhinitis. Current methods and innovative developments *HNO* 2008;56:764–75.
- Caruso M, Cibella F, Emma R, et al. Basophil biomarkers as useful predictors for sublingual immunotherapy in allergic rhinitis. *Int Immunopharmacol* 2018;60:50–8.
- Wang ZX, Shi H. Single-allergen sublingual immunotherapy versus multi-allergen subcutaneous immunotherapy for children with allergic rhinitis. *J Huazhong Univ Sci Technolog Med Sci* 2017;37:407–11.
- Lee JA, Jang S, Jun JH, et al. Herbal medicine (Bojungikki-tang) for allergic rhinitis: a protocol for a systematic review of controlled trials. *Medicine (Baltimore)* 2018;97:e9551.

- [21] Qu J, Liu C, Lian HH, et al. Qingfeijianpi therapy for persistent allergic rhinitis: a randomized, positive-controlled clinical trial. *Medicine (Baltimore)* 2018;97:e10961.
- [22] Kim YE, Son MJ, Jung SY, et al. Socheongryong-tang for improving nasal symptoms associated with allergic rhinitis: a study protocol for a randomized, open-label, cetirizine controlled, clinical trial *Medicine (Baltimore)* 2018;97:e11812.
- [23] Lee M, Kim Y, Lee JA, et al. (Yupingfeng) for treating allergic rhinitis: a protocol for the systematic review of controlled trials. *Medicine (Baltimore)* 2018;97:e13227.
- [24] Adam D, Grabenhenrich L, Ortiz M, et al. Impact of acupuncture on antihistamine use in patients suffering seasonal allergic rhinitis: secondary analysis of results from a randomised controlled trial. *Acupunct Med* 2018;36:139–45.
- [25] Mi J, Chen X, Lin X, et al. Treatment of persistent allergic rhinitis via acupuncture at the sphenopalatine acupoint: a randomized controlled trial. *Trials* 2018;19:28.
- [26] McDonald JL, Smith PK, Smith CA, et al. Effect of acupuncture on house dust mite specific IgE, substance P, and symptoms in persistent allergic rhinitis. *Ann Allergy Asthma Immunol* 2016;116:497–505.
- [27] Gotoh M. Allergic rhinitis: diagnosis and treatment based on the guidelines. *Arerugi* 2012;61:1637–42.
- [28] Wang Z, Li W, Chen H, et al. Effect of sublingual immunotherapy on level of cytokines in PBMCs of patients with allergic asthma. *J Huazhong Univ Sci Technol Med Sci* 2011;31:376–8.
- [29] European Medicines Agency. Guideline on the clinical development of products for specific immunotherapy for the treatment of allergic diseases. London: European Medicines Agency; 2008. Doc. Ref. CHMP/EWP/18504/2006. Accessed October 1, 2018
- [30] Juniper E, Guyatt G. Development and testing of a new measure of health status for clinical trials in rhinoconjunctivitis. *Clin Exp Allergy* 1991;21:77–83.
- [31] Xue CC, English R, Zhang JJ, et al. Effect of acupuncture in the treatment of seasonal allergic rhinitis: a randomized controlled clinical trial. *Am J Chin Med* 2002;30:1–1.
- [32] Campbell MJ, Julious SA, Altman DG. Estimating sample sizes for binary, ordered categorical, and continuous outcomes in two group comparisons. *BMJ* 1995;311:1145–8.