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Acupoint herbal patching for allergic rhinitis: a systematic review and meta-analysis of randomised controlled trials

Zhou F. [1, 2], Yan L.-J.[3], Yang G.-Y. [1], Liu J.-P.[1]

[1]Center for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing, China,[2]School of Nursing, Beijing University of Chinese Medicine, Beijing, China, [3]Department of Neurology, Guangdong Province Traditional Chinese Medicine Hospital, Guangzhou, China.
Correspondence: Liu J.-P. Center for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, 11 Bei San Huan Dong Lu,Chaoyang District, Beijing 100029, China. Tel.: +86 10 64286760; Fax: +86 10 64286871; e-mail: jianping_l@hotmail.com

Abstract

Background: Acupoint herbal patching (AHP) is extensively used in treatment of allergic rhinitis in China. However, existing systematic review is insufficient.

Objective of review: To evaluate the effectiveness and safety of AHP in treating allergic rhinitis.

Search strategy: We searched seven electronic databases for RCTs from inception until August 2014.

Evaluation method: Two authors selected studies, extracted data and evaluated risk of bias independently. The Cochrane risk of bias tool was applied to assess

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the methodological quality of the included trials and RevMan 5.2 software was utilised to perform data analysis.

Results: Twenty RCTs involving 2438 participants were included. Most of them were evaluated as high risk of bias. AHP significantly decreased the recurrence rate at six months compared with western medicine (RR 0.52; 95% CI 0.42 to 0.64), and similar effect was found for AHP plus western medicine versus western medicine (RR 0.53; 95% CI 0.44 to 0.65). AHP appeared to be more effective than placebo in improving total clinical symptoms and signs after treatment and at 6 months, and in improving quality of life at less than 3 months and over 3 months. No severe adverse effects were found in the AHP groups.

Conclusions: AHP alone or combined with western medicine appears to be more effective than placebo or western medicine respectively. AHP seems to be a safe treatment. However, the findings should be interpreted with caution. Further large-scale, rigorously designed trials are warranted to confirm the findings.

Keypoints

- Currently, there appears a potential effect for acupoint herbal patching in allergic rhinitis treatment.

- A systematic review of the available literature showed that acupoint herbal patching alone may reduce the recurrence rate at six months.

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- Acupoint herbal patching appeared to be more effective than placebo in improving quality of life for short-term and long-term.
- More rigorous multicenter, larger, adequately powered randomised trials that evaluate acupoint herbal patching for different types of allergic rhinitis on patient important outcomes are warranted.

Background

Allergic rhinitis (AR) is a symptomatic disorder of the nose induced after exposure, which is characterized by nasal congestion and discharge, sneezing, nasal itching.[1] It is subdivided into intermittent and persistent AR, and the prevalence ranges from 1% to 40% and 1% to 13% worldwide, respectively.[2] In China, the prevalence of AR varies from 8.7% to 37.9% and has increased in adults and children over the last two decades.[3]

AR is associated with significantly impaired quality of life, sleep, hearing, and reduces productivity.[4-8] It is estimated that about 200 million AR may represent an early stage of asthma.[9] According to the Agency for Health Care Research and Quality and the National Center for Health Statistics of United State, the direct cost of AR was 6.1 billion dollars in 2000 and almost doubled in 2005, and the indirect cost was inestimable.[10]

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Current conventional symptomatic treatment of AR includes intranasal corticosteroids, antihistamines, decongestants, cromolyn, and leukotriene receptor antagonists and most of them have adverse effects.[11] If medications appear to be inadequate, immunotherapy can be alternative choice.[12] However, this therapy is inconvenient, with a few standardized allergens and risk of systemic anaphylactic reactions.[13]

Acupoint herbal patching (AHP), also known as *xueweitiefu*, is defined as an external application of the processed medicinal herbal preparations directly to specific portions of the body to produce therapeutic effects through skin absorption and/or stimulating the meridians and acupoints.[14] Here, acupoints are the specific sites through which the *qi* of *zang-fu* organs and meridians (pathways in which the *qi* and blood of the human body are circulated) is transported to the body surface. Herbal patches are applied on acupoints to regulate the functional activities of body, strengthen body resistance so as to prevent and treat disease.[15] AHP is firstly recorded in the Formulae for Fifty-two Disease (*Wu Shi Er Bing Fang*，the oldest prescription of traditional Chinese Medicine, written around the fourth century BC.).[16] AHP used in AR treating was formulated in *Zhang Shi Yi Tong* (*Qing* Dynasty, 1644-1912).[17] Nowadays, according to the seasons, AHP can be classified into *sanfu* AHP (only applied during *sanfu* period) and non *sanfu* AHP (applied without a specific time frame). In the Chinese Lunar Calendar, *sanfu* refers to the hottest

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period of the year between mid-July to mid-August. This period of time is of special significance in TCM in treating AR when *yang* in human body is the strongest.

Use of AHP is very popular in China, and 653 medical institutions applied *sanfu* AHP in Beijing according to the year 2014's official data.[18] The Beijing Daily reported 19,000 people in 2009 and 27,000 people in 2010 used *sanfu* AHP in only one TCM general hospital.[19]

Many preclinical and clinical studies showed the promising effect of AHP in treating AR.[20–26] In 2013, a systematic review included 8 randomised controlled trials (RCTs) published in Chinese focused on AHP for AR, which showed a potential benefit.[27] However, it only has involved the outcome of effectiveness rate and didn't evaluate the safety of AHP. The objective of this review is to evaluate the effectiveness and safety of AHP for AR, using recurrence rate, specific symptoms and quality of life as primary outcomes.

Methods

Protocol and registration

This systematic review was registered in an international prospective register of systematic reviews, with the registration number CRD42013006358 (Available from

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http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42013006358).

Eligibility criteria

RCTs testing the effect of AHP for AR with no limitations on language, publication type or blinding were eligible.

Participants: patients with any types of AR regardless of gender, age, ethnic group, severity, diagnosed with international criteria or TCM diagnosis criteria. Trials including participants complicated with asthma, or sinusitis were excluded.

Intervention: AHP was defined as pasting herbal plaster on some acupoints of patient's body regardless of herb regimen, acupoints selected, patching season or treatment sessions.

Control: placebo, no treatment, western medicine (referred by AR and its impact on asthma workshop report)[1] and immunotherapy were considered eligible. Combination of AHP and western medicine or immunotherapy compared with same western medicine or immunotherapy was also included.

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Outcomes: Primary outcome measures were recurrence rate of AR, improvement of clinical symptoms and signs including sneezing, rhinorrhea, stuffiness, itchy nose evaluated by scoring criteria, and quality of life measured by a validated instrument or tool such as RQLQ (Rhinoconjunctivitis Quality of Life), SF-36 (36-item Short Form Health Survey). Secondary outcome measures included biomarkers and adverse effects.

Study identification and selection

We searched RCTs which could be published, unpublished and ongoing. All the following electronic databases from their inception to August 2014: PubMed, EMBASE, Cochrane Central Register of Controlled Trials in the Cochrane Library, China National Knowledge Infrastructure, Chinese Science and Technology Periodical Database, Chinese Biomedical Literature Database, and Wanfang Database. And reference lists of all full text papers were hand-searched in case of additional relevant trials. The ongoing trials were searched from mainstream registries. Details of the mainstream registries and search strategies for each database could be found in the supplementary files.

Zhou F and Yan LJ identified studies for eligibility and checked against inclusion criteria independently. Through screening titles and abstracts, we removed obviously irrelevant trials; then downloaded full texts if they met the eligibility criteria.

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Data extraction

Zhou F and Yan LJ independently extracted data on patient characteristics, details of the intervention and control, outcome measures, and results. We resolved different opinions by discussion or consultation with Liu JP.

Methodological Assessment

Zhou F and Yan LJ assessed the methodological quality of the included studies independently using the risk of bias tools according to the Cochrane Handbook version 5.1.0.[28] Any disagreements happened, a third author (Liu JP) was involved. Six bias items were: selection bias, performance bias, detection bias, attrition bias, reporting bias and others, and each was categorized as low, high and unclear risk. [28]

Statistical analysis

We performed statistical analysis using RevMan 5.2. Dichotomous data were expressed as risk ratio (RR) with 95% confidence interval (95% CI); while the continuous data were presented as mean difference (MD) with 95% CI. If different measurement scales were used, standardized mean difference (SMD) was performed. Heterogeneity was assessed using the I^2 statistic. I^2 value equal or greater than 50% was considered as indicative of substantial heterogeneity,[28] and a random-effect model was applied. Funnel plots were generated to detect publication bias if more than 10 trials were identified to report the same outcomes.

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For outcomes observed at the multiple time points, data were analyzed as subgroups, i.e. improvement of symptoms and signs, within 3 months and over 3 months.

Results

Trial Selection

The flow chart of search process and study selection is shown in Figure 1.

Trial Characteristics

Twenty included trials were conducted in China[29-48], of which 19 published in Chinese, only one conducted in Taiwan and published in English.[29] In total, 2438 participants with AR were involved in the 20 trials, aged between 5 to 65 and the duration of disease varied from 0.5 to 28 years. Five trials involved participants younger than 18 years, [31,32,35,36,48] and one trial involved only children.[35] Detailed characteristics of the trials are listed in Table 1.

Seventeen Chinese herbs and 23 acupoints were applied for the AHP intervention. Although some of the ingredients of AHP were different among the included trials, the main properties and flavor of the herbs were similar: acrid-warm and penetrating; and majority of the formulae of the herbal patches had same purpose to warm *yang* for dispelling cold, and benefit *qi* for promoting spleen *yang*. Thus, they were considered as the same orientation. All

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the main constituents of herb ingredients and locations of selected acupuncture points are listed in the supplement Table 1.

Eighteen trials reported the participants with total improvement of clinical symptoms and signs (i.e. *cure, markedly effective, effective*).[49-52] Four trials reported scores of several single symptoms and signs (the lower the score, the milder the symptom).[49,50]. Only four trials reported information about adverse events.[29,35,39,40,46] The characteristics of AHP therapy and outcome measures are listed in Table 2.

Methodological Quality

According to the predefined quality assessment criteria, the included trials were evaluated as high risk of bias (Fig. 2).

Seven trials (35%) used a random number table,[31,33,35,42,45-47] while one applied drawing lots,[40] one conducted computer randomization,[29] 11 trials did not report any details about randomization. No trial mentioned the allocation concealment. Three trials applied the single blinding to patients,[29,37,47] while two trials used the blinding to patients, evaluators and statistician.[31,42] Only two trials reported the number of dropouts.[31,42] No trial provided trial registration information. Six trials published as postgraduate theses were appraised as low risk of bias[33,35,39,42,47,29] No trial performed estimation of sample size. Comparable baseline characteristics were described in 19 trials.

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Effects of interventions

The overall effect estimates of AHP were shown in the Table 3.

Recurrence rate of AR during follow up

Of two trials reported this outcome.[35,41] Compared with western medicine, AHP significantly decreased recurrence rate at sixth months (RR 0.52; 95% CI 0.42 to 0.64).[35] Similar finding was also found in AHP plus western medicine compared with the same western medicine (RR 0.53; 95% CI 0.44 to 0.65).[41]

Clinical symptoms and signs improvement

(1)Total improvement rate of clinical symptoms and signs

AHP versus placebo Meta-analysis of two trials showed that AHP was better than placebo at ≤3 months (RR 4.61; 95% CI 2.61 to 8.14).[42,47] Mi's trial reported AHP has a better effect than placebo at third month (RR 4.85; 95% CI 3.42 to 6.89) and sixth month (RR 6.33; 95% CI 4.23 to 9.49).[37]

AHP versus western medicine Seven trials were available for a meta-analysis,[30,35,38,39,43,45,46] which demonstrated no significant difference at ≤3 months (RR 1.04; 95% CI 0.92 to 1.17). However, meta-analysis of five trials showed AHP was superior to western medicine at ＞ 3 months (RR 1.35; 95% CI 1.22 to 1.49).[32,34,43,45,48] Wen's trial reported a better effect of AHP than western medicine at 12 month (RR 1.50; 95% CI 1.18 to 1.91).[43]

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AHP plus western medicine versus western medicine A meta-analysis of four trials demonstrated that AHP plus western medicine improved symptom and signs at ≤3 months (RR 1.22; 95% CI 1.12 to 1.33).[33,40-44] However, another meta-analysis of two trials showed no significant difference at ＞3 months (RR 1.62; 95% CI 0.96 to 2.73).[33,36]

(2) Improvement of individual symptoms and signs

AHP versus placebo A meta-analysis of two trials showed AHP had lower scores in sneezing (SMD -0.52; 95% CI -0.97 to -0.11), rhinorrhea (MD -0.44; 95% CI -0.81 to -0.07) and stuffiness (MD -0.54; 95% CI -0.82 to -0.25), but not in itchy nose at ≤3 months (MD -0.46; 95% CI -1.00 to -0.08).[29,42] In addition, Wang's trial demonstrated AHP decreased the scores in sneezing at sixth month (MD -0.41; 95% CI -0.77 to -0.05).[42]

AHP versus western medicine Shi's trial reported reduced score of sneezing of AHP (MD -0.73; 95% CI -1.13 to -0.33), but not for the other three symptoms at ≤3 months.[39]

AHP plus western medicine versus western medicine Song's trial showed that the combination therapy was better in decreasing the scores of four common clinical symptoms at ≤3 months (sneezing: MD -0.32; 95% CI -0.54 to -0.10; rhinorrhea: MD -0.37; 95% CI -0.57 to -0.17; stuffiness: MD -0.37; 95% CI -0.64 to -0.10; itchy nose: MD -1.04; 95% CI -7.14 to -5.06).[40]

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Quality of life

Two trials reported quality of life using RQLQ (higher scores reflecting lower quality of life) [31,42] Two meta-analyses demonstrated that AHP improved the quality of life compared with placebo at ≤3 months (MD –8.92; 95% CI -13.39 to -4.45) or at ＞3 months (MD -9.03; 95% CI -13.58 to -4.49). Furthermore, Hsu's trial reported no significant difference between AHP and placebo on SF-36.[29]

Biomarkers

Three trials reported serum-IgE at ≤3 months.[46,29,35] Liu's trial reported decreased the level of serum-IgE by AHP compared with western medicine.[35] Zhang's trial didn't show any difference between AHP and sublingual specific immunotherapy;[46] and Hsu's trial found no significant difference between AHP and placebo in decreasing the level of serum-IgE.[29]

Adverse events

Four trials mentioned adverse events of AHP therapy. [35,39,40,46] Three trials reported none.[35,39,46] One trial reported obvious burning pain in the patching areas, and redness around it in two patients but these symptoms gradually disappeared after half an hour.[40] Although Hsu's trial didn't mention the adverse events, it reported two participants' withdrew due to the occurrence of local pain and blisters.[29]

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Discussion

Summary of main results

This review of 20 RCTs found that either within 3 months or more than 3 months, AHP appeared to be more effective than placebo on total improvement rate of clinical symptoms and signs. However, it's difficult to translate into clinical language due to compound several indicators. On other hand, the improved degree of mean score of RQLQ was obvious, which is enough for raising the AR patients' symptoms from severely impaired level to moderately impaired or from moderately to mildly impaired. Although AHP applied alone or in combination with western medicine appeared to be more efficacious in reducing recurrence rate at 6 months, we could not draw clinical conclusion due to only one individual trial with high risk bias. No serious adverse events were reported. Thus, AHP might be safe for AR.

Overall completeness and applicability of evidence

The evidence of this review covered different groups of people with AR, including adolescents, adults and the elderly, with different length of disease course. So, the extrapolation of this review can be acceptable in various populations.

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However, inadequate reporting information hindered us to make clear judgment of the quality of included trials and draw conclusions for clinical practice. For example, 17 trials didn't report the type and severity of AR, 16 trials failed to offer TCM diagnosis (syndrome differentiation).

Quality of evidence and potential biases in review

The poor methodological quality of included trials indicated high risk of bias. Selection bias could happen because only half of trials reported randomization methods and no trial offered information about allocation concealment. Besides, 15 trials didn't apply any blinding directly inducing the potential performance bias and detection bias. Deficiency of sample-size calculation was also a defect because statistical power cannot be guaranteed. Above existing possible biases may lead to deviation from the true value of evaluated intervention.

Three of 11 meta-analyses showed moderate degree of heterogeneity. Poor methodological quality might partly be the reason. Other reasons might be the complexity of the usual treatment in the real clinical scenario, such as the disease type of participants, different western medicines, acupoints selected, herbs selected. Therefore, the findings must be interpreted prudently.

Comparison with other reviews

A previous review published in Chinese by Shen et al. [27] assessed AHP for AR found that AHP appeared to have a potential effect. Similarly, our review involving doubled participants than Shen's review also demonstrated AHP

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appeared to be effective. However, Shen's review had only two comparisons (AHP versus western medicine and AHP plus western medicine versus same western medicine), our review added the comparison of AHP with placebo. In addition, Shen's review only reported the total improvement rate of clinical symptoms and signs, while our review evaluated the potential effect of AHP using patient important outcomes, such as the recurrence rate of AR, individual symptoms and quality of life.

Implications for clinical practice

We inferred that AHP may be safe and can be applied for people with AR. AHP alone or combined with western medicine may decrease the recurrence rate of AR and improve the quality of life. Due to insufficient evidence, the value for laboratory biomarkers is still unclear.

For the formula of AHP and selected acupoints, we sorted the top five ingredients of AHP and selected acupoints. The top five herb ingredients were *semen sinapis, herba asari, radix kansui, rhizoma corydalis, rasix aconiti peaparata*. According to TCM, all the properties and flavor of them are acrid-warm and penetrating which could benefit *qi*, dispel cold, reduce swelling, dissipate blood stasis.[53] Most of the top five selected acupoints (DU14, BL13, BL20, BL23, BL12) belong to bladder meridian. Pasting AHP on these acupoints could help warm *yang*, free nasal orifices, ventilate *lungs*, invigorate

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spleen and dissolve sputum.[15] Hence, for the clinical health professionals, using them as the basic herbs and basic acupoints for AR treatment is suggested.

Due to small total number of trials included, we failed to compare *sanfu* with non*sanfu* AHP for the effectiveness. Thus, we could not infer the better pasting season of AHP for health professionals.

Implications for research

We have following suggestions for future research:

(1) Improving Methodology Quality It is highly recommended to register the protocols of trials and report the registration in their publications to avoid selective outcome reporting. Besides, sample size calculation should be done in trial design and be reported. Detailed randomization and allocation concealment should be reported. Although using blinding for medical professionals is still a challenge on AHP, it is possible to blind outcome assessor and/or statistician. In addition, we suggest to conducting intention-to-treat analysis, especially for evaluating long term effect of AHP treatment. Though no serious adverse events were reported in the included trials, we suggest further research could conduct large-scale long-term observational study or survey to investigate the safety of AHP.

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(2) Selecting Patient Important Outcomes We found few trials reporting recurrence rate of AR, and individual symptoms which are important concerns of patients with AR. Accordingly, we suggest further research select patient important outcomes such as recurrence rate of AR, specific clinical symptom and quality of life.

(3) Taking the Characteristics of AR Itself into Account Unfortunately, there were few included trials reporting information about the AR itself in this review, which makes the reader need to understand the findings more cautiously. It is advisable to take the characteristics of AR itself into account during study, such as AR type, allergen, and onset seasons. First, AR type should be classified clearly. Mixing them up will only lead to confusion. Moreover, researchers need to set follow up time long enough according to different onset seasons, at least to cover the next onset season to evaluate the effectiveness of AHP for AR.

(4) Clearly Reporting of AHP Trials In this review, many information were not clearly reported. Clear, transparent, and sufficiently detailed information related to RCTs are important for readers. Future trial reports should comply with the Consolidated Standards of Reporting Trials Statement (CONSORT)[54] and Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA),[55] considering AHP involving both Chinese medical herbs and acupuncture points. In addition, the Chinese medicine syndrome diagnostic

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criteria used in the trials should be elaborated clearly, which could provide more information for potential users' evaluation and application. Future trial could follow the TCM professional syndrome diagnostic criteria such as criteria of diagnosis and therapeutic effect of TCM and clinical guideline of new drugs for TCM.[51,52]

Conclusion

AHP alone or combined with western medicine appears to be more effective than placebo or medication alone in managing patients with AR. AHP seemed to be a safe intervention. However, due to poor methodological quality, the findings should be interpreted with caution. Further large, rigorously designed trials are warranted to confirm the findings.

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Author Contributions

Conceived and designed the review: Zhou Fen and Liu Jian-Ping; Searched trials: Zhou F and Yan Li-Jiao; Appraised trials: Zhou F, Yan LJ and Liu JP; Extracted data: Zhou F and Yan LJ; Synthesized and analyzed date: Zhou F and Liu JP; Wrote the paper: Zhou F, Liu JP, Yang Guo-Yang.

Conflicts of Interest

None declared.

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Legends

Figure 1. Flow diagram of study searches and selection.

Figure 2. Risk of bias graph. Presentation of the risk of bias graph of the review author's judgments about each risk of bias item presented as percentages across all included trials.

Table 1. Characteristics of included trials.

Table 2. Characteristics of AHP therapy and outcome measures of included trials.

Table 3. Estimate effect of AHP for improving clinical outcomes of patients with allergic rhinitis.

Figure S1. Risk of bias summary. Presentation of the risk of bias summary of the review author's judgments about each risk of bias item for each included trials.

Table S1. The list of main constituents of herb ingredients and locations of selected acupoints.

File S1. Mainstream registries and research strategies.

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Table 1. Characteristics of included trials

Study ID[Ref.]	Sample (R/A)	Age (yr) Range or Mean±SD	Diagnostic criteria	Classify of AR: no. subjects	Severity of AR: no. subjects	History (yr) Range or Mean±SD (Years)	CM Syndrome Differentiation
Hsu 2010 [29]	T:18/18 C:15/15	Total:22.6±6.3	Symptoms for over 2 years, specific allergen identified with elevated T-IgE, elevated ECP[#]	NR	NR	NR	NR
Hu 2010[30]	T:60/60 C:60/60	T:8~60 C:9~64	WDC: Chinese Journal of Otorhinolaryngology-1997[49]	NR	NR	T: 0.5~19 C:1~17	NR
Hu 2012[31]	T:30/27 C:30/21	T:26±7 C:23±2	WDC: Chinese Journal of Otorhinolaryngology-1997[49]	NR	NR	NR	NR
Kong 2010[32]	T:82/82 C:75/75	T:8~69 C:9~64	WDC: Chinese Journal of Otorhinolaryngology-1997[49]	NR	NR	T: 0.5~19 C:1~17	NR
Liao 2008[33]	T:38/38 C:38/38	T:30.52±9.53 C:31.23±10.56	WDC: Chinese Journal of Otorhinolaryngology-1997[49] CDC: Medicine Science and Technology Press of China[52]	NR	T:Mild 16, Moderate17, Severe 5. C:Mild 18, Moderate 13, Severe 7.	T:7.13±1.52 C:6.92±1.64	T: Lung *qi* deficiency and pathogenic wind attacking the superficies type (18) Lung and spleen *qi* deficiency type (10) Insufficiency of the kidney *yang* type (10)

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C: Lung *qi* deficiency and pathogenic wind attacking the superficies type (14)
Lung and spleen *qi* deficiency type (16)
Insufficiency of the kidney *yang* type (8)

Study ID[Ref.]	**Sample(R/A)**	**Age (yr) Range or Mean±SD**	**Diagnostic standard**	**Classify of AR: no. subjects**	**Severity of AR: no. subjects**	**History (yr) Range or Mean±SD (Years)**	**CM Syndrome Differentiation**
Lin 2013[34]	T:30/30 C:30/30	T:37.27±11.40 C:37.20±10.81	WDC: Chinese Journal of Otorhinolaryngology-2004[50] CDC: State Administration of Traditional Chinese Medicine -1995[51]	NR	NR	T:4.24±2.64 C:4.26±2.87	NR
Liu 2011[35]	T:152/152 C:150/150	T:8.25±4.32 C:8.16±4.43	WDC: Chinese Journal of Otorhinolaryngology Head and Neck Surgery-2004[50] CDC: State Administration of Traditional Chinese Medicine -1995[51]	NR	Clinical symptom scores [50] T:10.05±1.27 C:10.08±1.09	T:0.5~14 C:0.5~13.5	NR
Ma 2012[36]	T:60/60 C:60/60	T:8~65 C:6~62	CDC: State Administration of Traditional Chinese Medicine -1995[51]	Perennial/seasonal AR: 45/75 in total	NR	T:0.5~15C:1~17	NR

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Mi 2010[37]	T:158/158 C:158/158	T:36±12 C:36±13	WDC: Chinese Journal of Otorhinolaryngology-1997[49] CDC: State Administration of Traditional Chinese Medicine -1995[51]	NR	NR	T:4.7±2.2 C:4.2±2.8	T:Lung deficiency related cold type (48),Deficiency weakness of spleen *qi* type (59),The kidney *yang* deficiency type (51) C:NR
Mi 2011[38]	T:49/49 C:44/44	T:37.14±13.627 C:NR	WDC: Chinese Journal of Otorhinolaryngology-1997[49]	NR	Clinical symptom scores[49] T:11.53±2.451 C: 11.73±2.518	Total:0.5~15	NR

Study ID[Ref.]	**Sample(R/A)**	**Age (yr) Range or Mean±SD**	**Diagnostic standard**	**Classify of AR: no. subjects**	**Severity of AR: no. subjects**	**History (yr) Range or Mean±SD (Years)**	**CM Syndrome Differentiation**
Shi 2011[39]	T:30/30 C:30/30	T:20~56 C:19~58	WDC: Chinese Journal of Otorhinolaryngology Head and Neck Surgery-1997[49]	NR	NR	T:2~6 C:2~6	NR
Song 2013[40]	T:35/35 C:35/35	T:42.15±10.31 C:43.68±11.67	WDC: Chinese Journal of Otorhinolaryngology Head and Neck Surgery-2004[50] CDC: State Administration of Traditional Chinese Medicine -1995[51]	Perennial/seasonal AR T: 9/26 C: 11/23	NR	T: 9.02±2.61 C:8.34±2.98	Lung deficiency related cold type

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Sun 2007[41]	T:155/155 C:153/153	T:34±13.5 C:32±14	WDC: Chinese Journal of Otorhinolaryngology Head and Neck Surgery-2004[50]	NR	NR	T: 0.5±20 C:0.5±25	NR
Wang 2013[42]	T:30/28 C:30/26	T:28.36±13.35 C:33.19±16.71	WDC: Chinese Journal of Otorhinolaryngology-1997[49]	NR	NR	T:7.43±6.53 C:6.04±3.50	NR
Wen 2007[43]	T:118/118 C:118/118	T:18~56 C:18~54(range)	WDC: Chinese Journal of Otorhinolaryngology-1997[49]	All belonged to perennial AR	NR	T:2~25 C:2~28	NR
Wu 2013[44]	T:42/42 C:42/42	NR	WDC: Chinese Journal of Otorhinolaryngology Head and Neck Surgery-1997[49]	NR	NR	NR	NR
Xu 2012[45]	T:45/45 C:45/45	T:18~49 C:16~51(range)	WDC: Chinese Journal of Otorhinolaryngology Head and Neck Surgery-2004[50]	NR	NR	T:1~21 C:1~22	NR

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Study ID[Ref.]	Sample(R/A)	Age (yr) Range or Mean±SD	Diagnostic standard	Classify of AR: no. subjects	Severity of AR: no. subjects	History (yr) Range or Mean±SD (Years)	CM Syndrome Differentiation
Zhang 2012[46]	T:30/30 C:30/30	T:10.25±2.56 C:11.12±2.12	WDC: Chinese Journal of Otorhinolaryngology-1997[49] CDC: State Administration of Traditional Chinese Medicine -1995[51]	NR	NR	NR	Total:Lung deficiency related cold type
Zhang 2007[47]	T:30/30 C:30/30	NR	CDC: State Administration of Traditional Chinese Medicine -1995[51]	NR	NR	NR	NR
Zhu 2010[48]	T:47/47 C:44/44	T:5~55 C:8~50(range)	CDC: State Administration of Traditional Chinese Medicine -1995[51]	NR	NR	T:0.5~21 C:0.6~20	NR

[#]:Although this trial didn't offer the name of diagnostic criteria, it followed the western medicine diagnostic criteria.

R:number subjects randomized; A: number subjects analyzed; CM: Chinese medicine; WDC:Western medicine diagnostic criteria; CDC:Chinese medicine diagnostic criteria; SD: standard deviation; T:treatment group; C: control group; NR:not reported.

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Table 2.Characteristics of AHP therapy and outcome measures of included trials

Study ID[Ref.]	Comparison Type	Acupoints Selected	Herbal Components	Excipient	Pasting Time	Frequency and Duration of AHP	Control Interventions	Outcome Observation Time	Outcome Measures
Hsu 2010[29]	Non *sanfu*, AHP vs Placebo	DU14,BL12, BL13,EX-B 1	Semen Sinapis,Radix Kansui,Rhizoma Corydalis	Succus Rhizomatis Zingiberis	Non *sanfu*	Once weekly, keep patching 3 hours ,3 times	Flour, water and edible pigments	1 week after treatment finished	Clinical symptom, QoL-SF-36, T-IgE, ECP
Hu 2012[31]	Non *sanfu*, AHP vs Placebo	DU14,BL12, BL13,BL23, BL43,BL52	Semen Sinapis, Herba Asari,Radix Kansui,Rhizoma Corydalis	Succus Rhizomatis Zingiberis	Non *sanfu*	Once per ten days, keep patching 2~6 hours,5 times	Strach with ginger juice	6 months after treatment finished	Qol-RQLQ
Lin 2013[34]	Non *sanfu*, AHP vs WM	BL13,BL43, BL23,DU14, BL12,BL20, RN17	Semen Sinapis,Herba Asari,Radix Kansui,Rhizoma Corydalis,Flos Caryophylli,Radix Angelicae Dahuricae	Ginger juice	Non *sanfu*	Once per 10 days, keep patching 2 hours ,9 times	Loratadine, 5mg, qd, 30days	3months after treatment finished	Clinical symptom score-2004,ER-2004[50]
Mi 2011[38]	Non *sanfu*, AHP vs WM	BL13,BL21, BL20, BL12 ,BL43,BL23 ,EX-B1,BL15	Semen Sinapis,Herba Asari,Radix Kansui,Rhizoma Corydalis	Ginger juice	Non *sanfu*	Once every 10 days, keep patching 1~2 hours, 9 times	Budesonide Nasal Spray (Rhinocort), Each nostril 1 spray, bid, 60 days	3 months after treatment finished	Clinical symptom score-1997,ER-1997[49]

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Wen 2007[43]	Non s*anfu*, AHP vs WM	DU14, BL13 , BL20 , BL23	Semen Sinapis,Herba Asari, Radix Kansui	Ginger juice	Non *sanfu*	Once per 5~7days, keep patching 4~6 hours,6 times	BCG-Polysaccharide Nucleic Acid (BCG-PSN), 1ml, qd, im, 10 days	1 month, 6 month, 12 month after treatment finished	Clinical symptom score-1997,ER-1997[49]

Study ID[Ref.]	**Comparison Type**	**Acupoints Selected**	**Herbal Components**	**Excipient**	**Pasting Time**	**Frequency and Duration of AHP**	**Control Interventions**	**Outcome Observation Time**	**Outcome measures**
Ma 2012[36]	Non *sanfu*, AHP+WM vs WM	DU14,BL13, BL12,BL20, BL23,LI20	Semen Sinapis,Radix et Rhizoma Asari,Radix Kansui,Rhizoma Corydalis,Herba Ephedrae,Cortex Cinnamomi,Moschus	NR	Non *sanfu*	Bid, keep patching 2~6 hours,15 times	Loratadine, 10mg, qd, 10 days	3 months after treatment finished	ER-1995[51]
Shi 2011[39]	Non *sanfu*, AHP+WM vs WM	DU14,BL13, BL17,ST36	Grinding the Chinese herb (with properties of warm channel to expel cold, tonify deficinecy to support *yang*) first, then turning into paste in proportion	NR	Non *sanfu*	Once per *2~3day* ,15 days	Cetirizine, 10mg, qd	After treatment finished	Clinical symptom score-1997,ER-1997,[49] Adverse event

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Song 2013[40]	Non *sanfu*, AHP+WM vs WM	DU14, BL13, BL12	*Daiwenjiu* provided by a pharmaceutical company (Lot number: 1003021)	NR	Non *sanfu*	Once per day, keep patching 2~6 hours, 14 times	Cetirizine, 10mg, qd, 14 days	After treatment finished	Clinical symptom score-2004,ER-2004,[50] Adverse event
Mi 2010[37]	*Sanfu*, AHP vs Placebo	BL13,BL21, BL52,BL20, BL12,BL43, BL23,EX-B 1,BL15	Semen Sinapis, Herba Asari,Radix Kansui,Rhizoma Corydalis	Succus Rhizomatis Zingiberis	*Sanfu*,once in first *fu*,then once every 10 days, and Strengthen 2 months	Once per fu, keep patching 1~2 hours,1 *sanfu*+2months	Cattail Pollen, edible pigments with ginger juice	6 months after treatment finished	Clinical symptom score-1997,ER-1997[49]

Study ID[Ref.]	**Comparison Type**	**Acupoints Selected**	**Herbal Components**	**Excipient**	**Pasting Time**	**Frequency and Duration of AHP**	**Control Interventions**	**Outcome Observation Time**	**Outcome Measures**
Wang 2013[42]	*Sanfu*, AHP vs Placebo	BL13,BL20, BL23,DU14, BL12,BL43, BL52	Semen Sinapis, Herba Asari,Radix Kansui,Rhizoma Corydalis	Succus Rhizomatis Zingiberis	*Sanfu*,once ten days (enhance once on first *fu* and last *fu*)	Once per *fu*, keep patching 4~6 hours, 5 times	Buckwheat grind powder, with fresh ginger juice	6 months after treatment finished	Clinical symptom score-1997,ER-97,[49] Qol-RQLQ

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Zhang 2007[47]	*Sanfu*, AHP vs Placebo	DU14,BL12, BL13,BL23, DU4	Semen Sinapis, Herba Asari,Ramulus Cinnamomi,Radix Aconiti Lateralis Praeparata,Fructus Perillae	Succus Rhizomatis Zingiberis	*Sanfu*, first day of each *fu*	Once per *fu*, keep patching 1~1.5 hours	100% flour with boiled water	After treatment finished	Clinical symptom score-1997,ER-1997[49]
Kong 2010[32]	*Sanfu*, AHP vs WM	BL12,BL13, BL43,BL20, BL23, DU9	Semen Sinapis, Herba Asari,Radix Kansui,Rhizoma Corydalis, Moschus	Ginger juice	*Sanfu*, first day of each *fu*	Once per *fu*, keep patching 4~6 hours	Cetirizine, 10mg, qd, 15 days	3 months after treatment finished	ER-1997[49]
Hu 2010[30]	*Sanfu*, AHP vs WM	BL43,DU14, BL12,BL13, EX-HN15,BL20,BL17,BL23	Semen Sinapis, Herba Asari,Radix Kansui,Rhizoma Corydalis, Radix Scutellariae	Succus Rhizomatis Zingiberis	*Sanfu*, first day of each *fu*	Once per ten days, keep patching 2~6 hours, 3 times	Cetirizine (Zyrtec), 10mg, qd. Beclometasone Dipropionate Aqueous Nasal Spray (Beconase), 2 sprays daily, tid, 10 days	After treatment fininshed	Clinical symptom score-1997[49]

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Study ID[Ref.]	Comparison Type	Acupoints Selected	Herbal Components	Excipient	Pasting Time	Frequency and Duration of AHP	Control Interventions	Outcome Observation Time	Outcome Measures
Liu 2011[35]	*Sanfu*, AHP vs WM	BL13,LU7, DU14,BL10, BL20	Herba Asari,Herba Centipedae,Mylabris,Herba Agastachis	NR	*Sanfu*, first day of each *fu*	Keep patching 3~4 hours,3 *fu*s	Antihistamine (Clarityne), 10mg, qd +Budesonide Nasal Spray (Rhinocort), bid, 14~28 days	3months(only for recurrence rate) after treatment finished	Recurrence rate, Clinical symptom score-2004,ER-2004, [50] IgE Adverse event
Xu 2012[45]	*Sanfu*, AHP vs WM	DU14,BL43, BL13,BL20, BL23	Semen Sinapis,Herba Asari,Radix Kansui,Rhizoma Corydalis	Ginger juice	*Sanfu*, first day of each *fu*	Once per *fu*, once every 10 days, keep patching 8 hours ,3 *fu*s	Antihistamine (Clarityne), 10mg, qn + Budesonide Nasal Spray (Rhinocort), bid, 7 days	1 month and 12 months after treatment finished	Clinical symptom score-2004 ER-2004[50]

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Zhu 2010[48]	*Sanfu*, AHP vs WM	DU14,RN17 ,BL12,BL13 ,BL20,BL23	Semen Sinapis,Herba Asari,Radix Kansui,Rhizoma Corydalis,Rhizoma Pinelliae	Dimethyl sulfoxide	*Sanfu*, first day of each *fu*	Once per *fu*, once every 10 days, keep patching 4~6 hours ,3 *fu*s	Cetirizine, 10mg, qd + Beclometasone Dipropionate Aqueous Nasal Spray (Beconase), 2 sprays once, tid,10 days	3 months after treatment finished	ER-1995[51]

Study ID[Ref.]	**Comparison Type**	**Acupoints Selected**	**Herbal Components**	**Excipient**	**Pasting Time**	**Frequency and Duration of AHP**	**Control Interventions**	**Outcome Observation Time**	**Outcome Measures**
Liao 2008[33]	*Sanfu*, AHP+WM vs WM	DU14,BL13, BL23, PC6	Semen Sinapis,Herba Asari,Radix Kansui,Radix Angelicae Dahuricae,Radix Aconiti Preparata	Ginger juice	*Sanfu*, before and after three days of each *fu*	Once per *fu*,3 *fu*s	Desloratadine Tablets (Xinminting), 5mg,qd + Triamcinolone Acetonide Nasal Spray (Xinruike), Each nostril 1 spray, daily, 1 month	11~12months after treatment finished	ER-[52]

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Sun 2007[41]	*Sanfu*, AHP+WM	vs WM	BL13,RN17, DU14,BL17, BL20,BL23	Semen Sinapis,Herba Asari,Radix Kansui, Radix Angelicae Dahuricae,Cortex Cinnamomi,Flos Caryophylli	Ginger juice	*Sanfu*, first day of each *fu*	Once per *fu* (first day of *fu*), keep patching 3~6 hours, *3 fus*	Azelastine hydrochloride tablet (Minqipian) with 1% Dexamethasone droplets of ephedrine nasal fluid and 2% Sodium Cromoglicate Nass Drops, alternatively	6 months after treatment finished	Recurrence rate, Clinical symptom score-2004, ER-2004[50]

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Study ID[Ref.]	Comparison Type	Acupoints Selected	Herbal Components	Excipient	Pasting Time	Frequency and Duration of AHP	Control Interventions	Outcome Observation Time	Outcome Measures
Wu 2013[44]	*Sanfu*, AHP+WM vs WM	BL43,DU14, BL12,BL13, BL20,BL23, ST36，BL26, BL24	Semen Sinapis,Herba Asari,Radix Kansui,Herba Ephedrae,Radix Scutellariae	Ginger juice	*Sanfu*, first day of each *fu*	Once per *fu* (first day of *fu*), keep patching 2~6 hours, *3 fu*s	Loratadine, 10mg, qd + Beclometasone Dipropionate Aqueous NasalSpray, 3 tid, 10 days	After treatment finished	Clinical symptom score-1997,ER-1997[49]
Zhang 2012[46]	*Sanfu* AHP vs WM-sublingual SIT	DU14,BL13, BL20, LI4	Radix Astragali,Flos Magnoliae Liliflorae, Fructus Gleditsiae,Semen Sinapis,Herba Asari,Rhizoma Corydalis	Succus Rhizomatis Zingiberis	*Sanfu*, first day of each *fu*	Once per *fu*, keep patching 2~4 hours, 3 *fu*s	fenchenmandiji (changdi), by sublingual, one year	After treatment finished	ER-1997[49], IgE, EOS, Adverse event

Ref.:reference; WM:western medicine; Qol:quality of life; ER:clinical manifestation improvement effectiveness rate; RQLQ:Rhinoconjunctivitis Quality of Life; SF-36: the 36-item Short Form Health Survey.

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Table 3. Estimate effect of AHP for improving clinical outcomes of patients with allergic rhinitis.

Trial ID	Total No. of participants		Effect Estimates ([95% CI])	*P* value
Outcome judgment time ⩽3 months				
1.Total clinical symptoms and signs improvement			RR ([95% CI])	
1.1AHP vs Placebo				
Wang 2013[42]	54		5.74 [1.86,17.46]	0.002
Zhang 2007[47]	60		4.14[2.16,7.95]	<0.0001
Pooling analysis 1.1(I^2 =0%)		114	4.61[2.61,8.14]	<0.00001
1.2AHP vs WM				
Hu 2010[30]	120		1.14[1.00,1.31]	
Liu 2011[35]	302		1.30[1.14,1.48]	
Mi 2011[38]	93		0.94[0.81,1.09]	
Shi 2011[39]	60		0.92[0.69,1.21]	
Wen 2007[43]	236		0.99[0.90,1.09]	
Xu 2012[45]	90		0.80[0.66,0.98]	
Zhang 2012[46]	60		1.25[0.93,1.69]	
Pooling analysis 1.2(I^2 =76%)	961		1.04[0.92,1.17] *Random	0.56
1.3AHP+WM vs WM				
Liao 2011[33]	76		1.09[0.94,1.26]	
Song 2013[40]	69		1.14[0.96,1.36]	
Sun 2007[41]	308		1.31[1.14,1.51]	
Wu 2013[44]	84		1.14[0.98,1.33]	
Pooling analysis 1.3(I^2 =0%)		537	1.22[1.12,1.33]	<0.00001
2.Syptom-sneezing score			**MD ([95% CI])**	
2.1AHP vs Placebo				
Hsu 2010[29]	33		-0.41[-1.10,0.29]	
Wang 2013[42]	54		-0.62[-1.16,-0.07]	
Pooling analysis 2.1(I^2 =0%)		87	-0.54[-0.97,-0.11] Std. Mean Difference	0.01
2.2AHP vs WM				
Shi 2011[39]	60		-0.73[-1.13,-0.33]	0.0004
2.3AHP+WM vs WM				
Song 2013[40]	69		-0.32[-0.54,-0.10]	0.005
3.Syptom-rhinorrhea score				
3.1AHP vs Placebo				
Hsu 2010[29]	33		-0.30[-0.99,0.39]	
Wang 2013[42]	54		-0.50[-0.94,0.06]	
Pooling analysis 3.1(I^2 =0%)		87	-0.44[-0.81,-0.07]	0.02

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Trial ID	Total No. of participants		MD ([95% CI])	*P* value
3.2AHP vs WM				
Shi 2011[39]	60		-0.03[-0.38,0.32]	0.87
3.3AHP+WM vs WM				
Song 2013[40]	69		-0.37[-0.57,5.-0.17]	0.0003
4.Syptom-stuffiness score				
4.1AHP vs Placebo				
Hsu 2010[29]	33		-0.56[-1.11,-0.00]	
Wang 2013[42]	54		-0.53[-0.86,-0.20]	
Pooling analysis 4.1(I^2 =0%)		87	-0.54[-0.82,-0.25]	0.0002
4.2AHP vs WM				
Shi 2011[39]	60		0.03[-0.33,0.39]	0.87
4.3AHP+WM vs WM				
Song 2013 [40]	69		-0.37[-0.64,-0.10]	0.007
5.Syptom-itchy nose score				
5.1AHP vs Placebo				
Hsu 2010 [29]	33		-0.16[-0.68, 0.37]	
Wang 2013[42]	54		-0.71[-1.11,-0.31]	
Pooling analysis5.1(I^2 =63%)		87	-0.46[-1.00,0.08]	0.10
5.2AHP vs WM				
Shi 2011[39]	60		0.04[-0.42,0.50]	0.86
5.3AHP+WM vs WM				
Song 2013[40]	69		-1.04[-7.14,5.06]	0.008
6.Sign-turbinate and nasal mucosa status score				
6.1AHP vs Placebo				
Wang 2013[42]	54		-0.90[-1.30,-0.50]	<0.00001
7.Sign-Nasal mucosa color score				
7.1AHP vs Placebo				
Wang 2013[42]	54		-0.67[-1.22,-0.12]	0.02
8.Quality of life				
8.1AHP vs Placebo				
Hu 2012 [31]	48		-8.00[-14.65,-1.47]	
Wang 2013 [42]	54		-9.73[-15.87,-3.59]	
Pooling analysis 7.1(I^2 =0%)		102	-8.92[-13.39,-4.45]	<0.00001
Hsu 2010(Physical function) [29]	33		0.67[-3.99,5.32]	0.78
Hsu 2010(Role limitation due to physical problems) [29]	33		1.85[-21.63,25.34]	0.88
Hsu 2010(Body pain) [29]	33		-5.34[-16.63,5.94]	0.35
Hsu 2010(General health) [29]	33		1.25[-9.15,11.64]	0.81
Hsu 2010(Vitality) [29]	33		-0.67[-12.13,10.80]	0.91

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Trial ID	Total No. of participants	MD ([95% CI])	*P* value
Hsu 2010(Social functioning) [29]	33	3.33[-5.80,12.47]	0.47
Hsu 2010(Role limitation due to emotional problems) [29]	33	7.04[-17.15,31.22]	0.57
Hsu 2010(Mental health) [29]	33	-4.13[-15.16,6.89]	0.46
9.Biomarker-IgE			
9.1AHP vs Placebo			
Hsu 2010(serum)[29]	33	136.23[-101.19,373.66]	0.26
9.2AHP vs WM			
Liu 2011(serum)[35]	302	-328.00[-329.18,-326.81]	<0.00001
Zhang 2012(serum)[46]	60	19.00[17.66,20.34]	<0.00001
10. Biomarker-EOS			
10.1AHP vs Placebo			
Hsu 2010(serum)[29]	33	-2.18[-136.80,-132.43]	0.97
10.2AHP vs WM			
Zhang 2012(nasal mucosa)[46]	60	2.42[1.67,3.17]	<0.00001
Outcome judgment time ＞3 months			
1.Recurrence rate of AR		RR ([95% CI])	
1.1AHP vs WM			
Liu 2011 [35]	302	0.52[0.42,0.64]	<0.00001
1.2AHP+WM vs WM			
Sun 2007 [41]	290	0.53[0.44,0.65]	<0.00001
2.Total clinical symptoms and signs improvement		RR ([95% CI])	
2.1AHP vs Placebo			
Mi 2010(3 months) [37]	316	4.85[3.42,6.89]	<0.00001
Mi 2010(6 months) [37]	316	6.33[4.23,9.49]	<0.00001
2.2AHP vs WM			
Kong 2010[32]	100	1.23[1.05,1.44]	
Lin 2013[34]	60	1.39[1.00,1.94]	
Wen 2007(6 months)[43]	236	1.31[1.10,1.57]	
Xu 2012(12 months)[45]	90	1.63[1.10,2.42]	
Zhu 2010[48]	91	1.37[1.11,1.70]	
Pooling analysis 2.2(I^2 =0%)		1.35[1.22,1.49]	<0.0001
Wen 2007(12 months)[43]	236	1.50[1.18,1.91]	0.001
2.3AHP+WM vs WM			
Liao 2008[33]	76	2.17[1.29,3.63]	
Ma 2012[36]	120	1.33[1.11,1.59]	
Pooling analysis 2.3(I^2 =74%)	196	1.62[0.96,2.73]Random	0.07

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Trial ID	Total No. of participants	MD ([95% CI])	*P* value
3.Syptom-sneezing score		**MD ([95% CI])**	
3.1AHP vs Placebo			
Wang 2013[42]	54	-0.41[-0.77,-0.05]	0.03
4.Syptom-rhinorrhea score			
4.1AHP vs Placebo			
Wang 2013[42]	54	-0.35[-0.89,0.19]	0.20
5.Syptom-stuffiness score			
5.1AHP vs Placebo			
Wang 2013[42]	54	-0.23[-0.62,0.16]	0.25
6.Syptom-itchy nose score			
6.1AHP vs Placebo			
Wang 2013 [42]	54	-0.38[-0.84,0.08]	0.10
7.Sign-turbinate and nasal mucosa status score			
7.1AHP vs Placebo			
Wang 2013 [42]	54	-0.80[-1.19,-0.41]	<0.0001
8.Sign-Nasal mucosa color score			
8.1AHP vs Placebo			
Wang 2013 [42]	54	-0.88[-1.42,-0.34]	0.001
9.Quality of life			
9.1AHP vs Placebo			
Hu 2012[31]	48	-7.20[-13.88,-0.52]	
Wang 2013[42]	54	-10.62[-16.83,-4.41]	
Pooling analysis 5.1(I^2 =0%)	102	-9.03[-13.58,-4.49]	<0.0001

Note: * random effects model; RR: risk ratio; MD: mean difference

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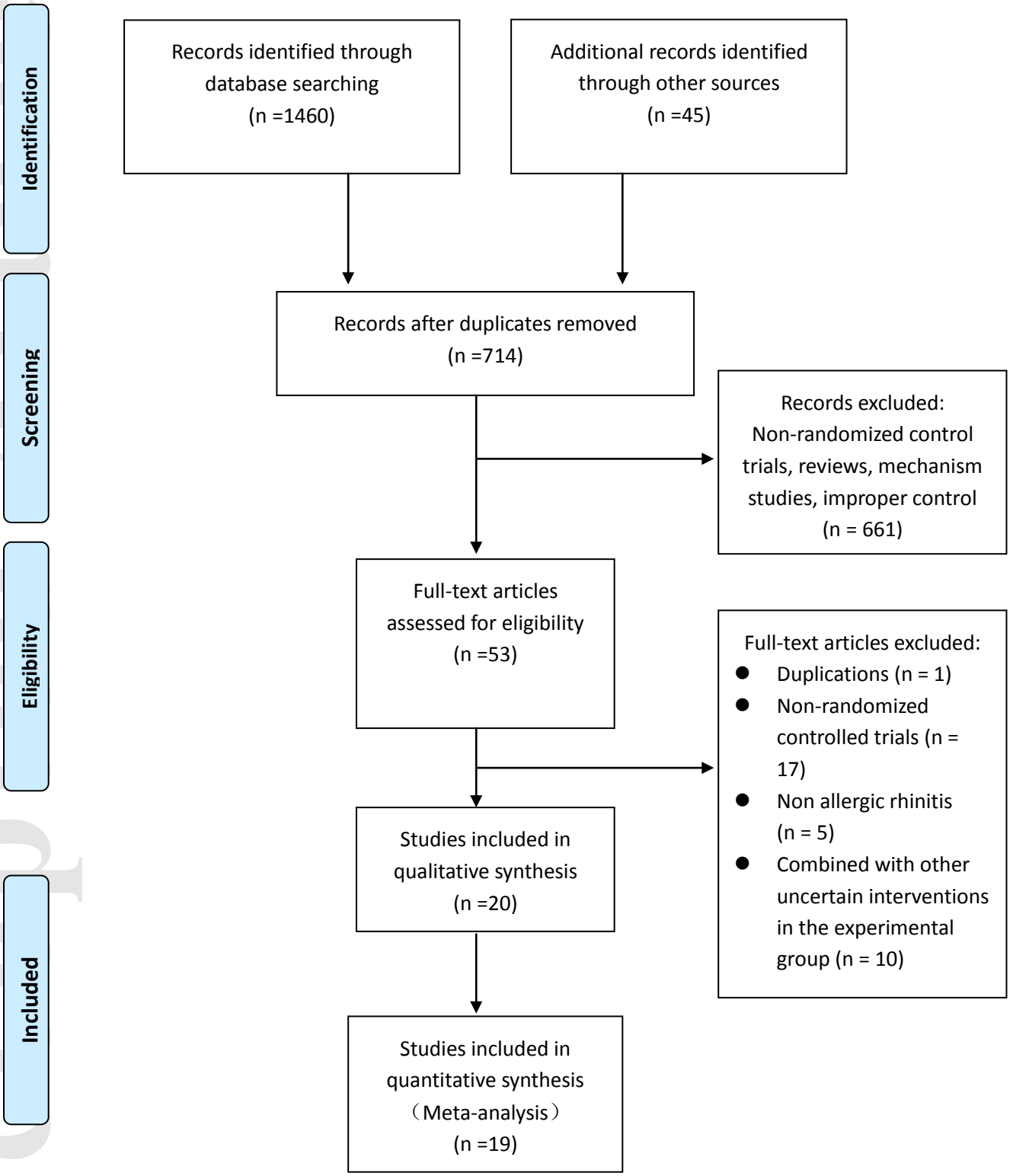

Figure 1. Flow diagram of study searches and selection.

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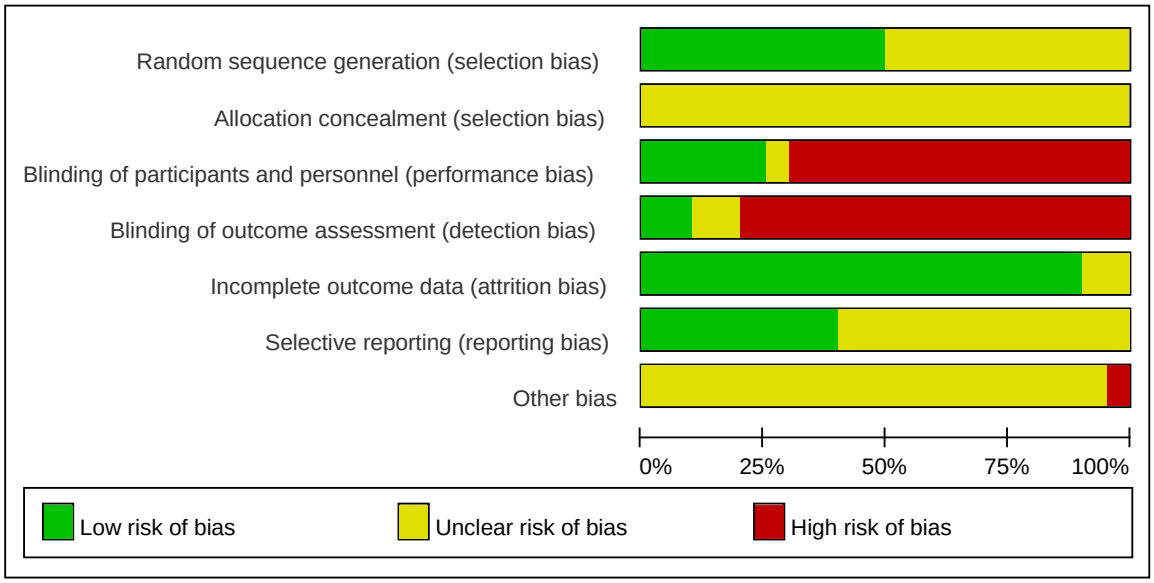

Figure 2. Risk of bias graph. Presentation of the risk of bias graph of the review author's judgments about each risk of bias item presented as percentages across all included trials.

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