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Systematic Review

Acupuncture for allergic rhinitis: a systematic review and meta analysis

针刺治疗过敏性鼻炎系统评价和 meta 分析

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Abstract

Objective: To analyze and review the clinical efficacy of acupuncture (including electroacupuncture) alone for allergic rhinitis (AR) and to compare its efficacy with antihistamines and Chinese patent medicine *Bi Yan Kang* Tablet.

Methods: The search strategy, inclusion and exclusion criteria were made according to the principle of evidence-based medicine. We performed a systematic search on China National Knowledge Infrastructure (CNKI), Wanfang Academic Journal Full-text Database (Wanfang), Chongqing VIP Database (CQVIP), Chinese Biomedical Literature Database (CBM), PubMed, Excerpta Medica Database (EMBASE), Web of Science, Cochrane Library, and Cochrane Central Register of Controlled Trials (CENTRAL) for randomized controlled trials (RCTs) of acupuncture for allergic rhinitis between January 1990 and December 2015. The quality was evaluated by Cochrane Handbook for Systematic Reviews of Interventions Version 5.1, and the meta-analysis was conducted by RevMan 5.3 version.

Results: Twenty eligible RCTs were included into the meta-analysis after selection. Compared with antihistamines, the meta-analysis showed RR＝1.24＞1, 95%CI[1.15, 1.33], *P*＜0.00001, indicating that acupuncture achieved a better total effective rate for AR than antihistamines; MD＝–0.93＜0, 95%CI[–1.22, –0.63], *P*＜0.00001, indicating that acupuncture is better than antihistamines in decreasing the total nasal symptom score (TNSS) in AR patients; and MD＝1.46＞0, 95%CI[–10.84, 13.75], *P*＝0.82, indicating that there was no statistical difference between acupuncture and antihistamines in regulating immunoglobulin E (IgE) in AR patients. Compared with *Bi Yan Kang* Tablet, the meta-analysis has shown RR＝1.50＞1, 95%CI[1.30, 1.73], *P*＜0.00001, indicating that acupuncture achieved a better total effective rate for AR than Chinese patent medicine *Bi Yan Kang* Tablet.

Conclusion: Acupuncture alone can achieve a better total effective rate for AR than antihistamines and *Bi Yan Kang* Tablet. It is also better than antihistamines in improving clinical symptom scores; however, whether acupuncture is better than *Bi Yan Kang* Tablet needs further proof. As far as current data are concerned, there was no statistical difference between acupuncture and antihistamines in improving serum IgE; further study is needed in this regard. The risk of bias due to absent randomization methods or blinding implementation decreased the evidence level of the overall conclusion.

Keywords: Acupuncture Therapy; Electroacupuncture; Rhinitis, Allergic; Randomized Controlled Trial; Systematic Review; Meta-analysis

【摘要】目的：分析评价单纯针刺(包含单纯电针)对过敏性鼻炎(AR)的临床疗效，并与抗组胺药物治疗以及中成药鼻炎康片治疗进行对照观察。**方法：**按照循证医学的要求，制定原始文献的检索策略、纳入标准及排除标准，检索中国知网(CNKI)、万方学术期刊全文数据库(Wanfang)、重庆维普数据库(CQVIP)、中国生物医学文献数据库(CBM)、PubMed、荷兰医学文摘 (EMBASE)、科学网、Cochrane 图书馆和 Cochrane 随机对照试验注册中心中 1990 年 1 月至 2015 年 12 月间针刺治疗 AR 的随机对照(RCTs)临床研究文献,以 Cochrane 系统评价手册 5.1 进行质量评价，采用 RevMan 5.3 对纳入文献进行 meta 分析。**结果：**共 20 篇文献符合纳入标准。meta 分析显示，针刺与抗组胺药物比较，合并 RR＝1.24＞1, 95%CI[1.15, 1.33], *P*＜0.00001, 提示针刺治疗 AR 临床总有效率优于抗组胺药物;合并 MD＝–0.93＜0, 95%CI[–1.22, –0.63], *P*＜0.00001, 提示针刺降低 AR 患者鼻部症状评分的效果优于抗组胺药物; 合并 MD＝1.46＞0, 95%CI[–10.84, 13.75], *P*＝0.82, 提示针刺对 AR 患者血清免疫球蛋白 E (IgE)的影响与抗组胺药物无统计学差异。针刺与中成药鼻炎康片比较，合并 RR＝1.50＞1, 95%CI[1.30, 1.73], *P*＜0.00001, 提示针刺治疗 AR 临床总有效率优于口服鼻炎康片。**结论：**单纯针刺治疗 AR 临床总有效率优于抗组胺药物治疗和中成药鼻炎康治疗，同时对于改善 AR 患者临床症状评分也优于抗组胺药物治疗，但从现有数据无法得知是否优于中成药鼻炎康

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片。在改善血清 IgE 方面，目前数据显示，单纯针刺效果与抗组胺药物治疗无统计学差异，有待进一步研究。在所纳入的随机对照临床文献中，随机方法不详，盲法实施缺失，造成一定的偏倚风险，因此降低了整体结论的证据级别。

【关键词】针刺疗法；电针；鼻炎，变应性；随机对照临床试验；系统评价；meta 分析
【中图分类号】R246.8　　【文献标志码】A

1 Background

1.1 What is allergic rhinitis (AR)

AR, also known as hay fever, is a chronic non-infectious condition that occurs when the immune system overreacts to allergens in the air. The underlying mechanism involves immunoglobulin E (IgE) antibodies attaching to the allergen and causing the release of inflammatory chemicals such as histamine from mast cells. Signs and symptoms include a stuffy or itchy nose, sneezing, rhinorrhea and sneezing[1]. Allergic rhinitis may be seasonal (triggered by pollen), perennial (triggered by dust mites) or episodic (triggered by pet hair).

With its prevalence and persistence, AR can affect patients' social life and work performance. In addition, nasal sinusitis, bronchial asthma and other comorbidities often coexist in AR patients. According to the data in *Allergic Rhinitis and its Impact on Asthma* (ARIA, 2008 update)[2-3], AR affects about 500 million people worldwide, including 100 million in Europe and North America, 150 million in Asia-Pacific Region, 100 million in India, Pakistan and neighboring area, 75 million in South and Central America, 30 million in Africa and 50 million in other countries. The self-reported prevalence of AR in major cities across China has shown that more than 50 million people suffer from AR[4].

1.2 What're the interventions for AR

According to the treatment guidelines for AR in China (2009, Wuyishan)[5], it's essential to avoid the allergen, oral or nasal antihistamines (preferred), intranasal corticosteroids, and drug combination. These measures are same as those in the *Clinical Practice Guideline: Allergic Rhinitis* issued by American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNSF)[6]. The guidelines in China mentioned that Chinese medicine can alleviate AR symptoms. The updated AAO-HNSF guidelines in 2015[7] recommended acupuncture treatment (a low quality of evidence), but did not mention the use of Chinese medicine.

1.3 Why it is important to do this review

A systematic review is highly helpful to provide more clinical evidences and improve the levels of quality evidence for acupuncture in AR treatment. Although systematic reviews have been conducted by some scholars in China[8-10], they failed to provide reliable quality levels of evidence because of update absence, mix of acupuncture interventions, input error and outdated criteria for assessing risk of bias in included studies. It is therefore essential to improve the quality in systematic review.

To better complete this systematic review, we've raised two issues to address. One is to further classify intervention methods. *Zhen Jiu* (in Chinese pinyin, acupuncture-moxibustion) consists of two parts: needling and moxibustion; and needling and moxibustion contain a variety of methods such as needling alone, electroacupuncture (EA), warming needle, warm moxibustion, ginger-partitioned moxibustion, crude herb moxibustion and thunder-fire moxibustion. However, clinical trials on acupuncture for AR published in international journals only mentioned acupuncture (a general concept) as the invention, with an absence of specific invention or classification. Consequently, detailed intervention methods were reported in this systematic review to minimize the heterogeneity in intervention methods. The other is to select a rational control group. As for published clinical trials on acupuncture for AR, sham acupuncture is often used in control group[11-16], major differences may occur due to difficult design and different methods in sham acupuncture. Oral antihistamines were employed as a control medicine in this trial, because it is currently the most preferred treatment for AR in Western medicine. Since Chinese medicine was not mentioned in American clinical practice guidelines for allergic rhinitis, commonly used Chinese patent medicine *Bi Yan Kang* Tablet was used as a control medicine to compare the efficacy between acupuncture and Chinese patent medicine.

This systematic review was written in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* to address aforementioned issues and better complete the review.

2 Objectives

This systematic review aims to analyze and review the clinical efficacy of acupuncture (including EA) alone for AR and compare its efficacy with oral antihistamines and Chinese patent medicine *Bi Yan Kang* Tablet.

3 Methods

This systematic review analyzed the efficacy of acupuncture (including EA) alone for AR and compared its efficacy with oral antihistamines and Chinese patent medicine *Bi Yan Kang* Tablet.

3.1 Criteria for considering studies for this review

3.1.1 Types of studies

Randomized controlled trials (RCTs) published between January 1990 and December 2015 were included, including journal papers, conference papers and dissertations; no limitation of blinding method; prospective studies only; and the papers were published in Chinese or English.

3.1.2 Types of participants

Those who aged ＜70 years old (no gender limitation) and met one of the following diagnostic criteria for AR: *Criteria of Diagnosis and Therapeutic Effects of Diseases and Syndromes in Traditional Chinese Medicine*[17]; *Practical Otolaryngology*[18], *Clinical Otolaryngology of Integrated Chinese & Western Medicine*[19], *Diagnosis and Efficacy Evaluation Criteria for Allergic Rhinitis* (1997, Haikou)[20], *Diagnosis, Treatment and Recommended Protocol for Allergic Rhinitis* (2004, Lanzhou)[21], *Diagnosis and Treatment Guidelines for Allergic Rhinitis* (2009, Wuyishan)[5], *Allergic Rhinitis and Its Impact on Asthma* (ARIA), 2008 update[2]; *Allergic Rhinitis and Its Impact on Asthma* (ARIA) *Guidelines*: 2010 revision[22]; and *Consensus Statement on the Treatment of Allergic Rhinitis*[23]. In addition, there were reasonable inclusion and exclusion criteria. There were no limitations on AR classifications (seasonal, perennial, episodic, intermittent or persistent).

3.1.3 Types of interventions

Acupuncture (including EA) alone was used for in the treatment group, excluding moxibustion, point application, bloodletting, ear point sticking, cupping and other combined therapies. There were no limitations on acupuncture points, needling technique, needle-retaining time, needle specifications, acupuncture frequency and treatment sessions. Two groups having different needling technique, acupuncture points and treatment timing were considered one group of same research subjects, using Review Manager Version 5.3. The control group remained unchanged. As for studies involving simple acupuncture group and other therapies that should be excluded, data on simple acupuncture were included only. The control group remained unchanged.

Participants in the control group only took oral antihistamines. These include Cetirizine, Loratadine, Terfenadine and Tranilast. There were no limitations on pharmaceutical preparation, drug content, manufacturers, administration time and doses, and treatment sessions. Alternatively, participants in the control group only took Chinese patent medicine *Bi Yan Kang* Tablet, and there were no limitations on manufacturers, administration time and doses, and treatment sessions.

3.1.4 Types of outcome measures

Included studies contained one of the following outcomes. Primary outcomes: clinical efficacy evaluation, including the total effective rate, recovery and significant improvement rate or recurrence rate (long-term effective rate), total nasal symptom score (TNSS). Secondary outcomes: immunological markers in serum (e.g., IgE contents), eosinophils (EOS), rhinoconjunctivitis quality of life questionnaire (RQLQ) and total non-nasal symptom score (TNNSS).

3.2 Search methods for identification of studies

3.2.1 Electronic searches

The first search started in June 2015 and updated in January 2016. The time range was between January 1990 and December 2015. The studies were written in Chinese or English. The following databases were searched: China National Knowledge Infrastructure (CNKI), Wanfang Academic Journal Full-text Database, (Wanfang), Chongqing VIP Database (CQVIP), Chinese Biomedical Literature Database (CBM), PubMed, Excerpta Medica Database (EMBASE), Web of Science, Cochrane Library and Cochrane Central Register of Controlled Trials (CENTRAL). Take PubMed for example, the search strategies are listed in Table 1.

3.2.2 Searching other resources

We used manual search for inaccessible abstracts or full texts through electronic database. We also manually searched the following journals: C*hinese Acupuncture and Moxibustion*, *Shanghai Journal of Acupuncture and Moxibustion*, *Journal of Clinical Acupuncture and Moxibustion*, *Acupuncture Research*, *Journal of Acupuncture and Tuina Science* (English) and *World Journal of Acupuncture-Moxibustion*.

3.3 Data collection and analysis

3.3.1 Selection of studies

We first summarized the retrieved bibliography and abstracts to remove duplicates. Then we read the titles and abstracts to exclude ineligible articles for failing to meet the inclusion criteria. For eligible articles, we obtained the full texts and completed literature screening. The literature screening was independently conducted by two reviewers Liu Jie and Hong Jue. Differences were settled by discussion or the third reviewer Zhang Cui-hong. For overlapping publications on the same content by the same author, only the first article was included. For two publications on similar content by the same author (for example, same research project with different subgroups or same research project with same subgroups but different outcome measurements), the two papers were included as one study if there were sufficient evidences proving that the two articles were from the same research project.

Table 1. Search strategies

Search terms and databases
Search terms are free text terms unless otherwise stated. MeSH＝Medical subject heading (Medline medical index term); exp＝Exploded MeSH; the dollar sign ($) or asterisk (*)＝Any character(s); the question mark (?) ＝To substitute for one or no characters; ab＝Abstract; adj＝Adjacent; ot＝Original title; pt＝Publication type; sh＝MeSH; ti＝Title; tw＝Text word; tiab＝Title and Abstract; mp＝Title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier
PubMed
#1 acupuncture. mp.
#2 acupuncture *. mp.
#3 $acupuncture. mp.
#4 acupoint. mp.
#5 needling. mp.
#6 or/#1-#5
#7 exp allergic rhinitis
#8 exp seasonal rhinitis
#9 exp perennial rhinitis
#10 or/#7-#9
#11 allergen. tw.
#12 rhinitis. tw.
#13 #11 and #12
#14 #10 or #13
#15 #6 and #14
#16 randomized controlled trail. pt.
#17 controlled clinical trial. pt.
#18 randomized. ab.
#19 randomly. ab.
#20 trial. ab.
#21 groups. ab.
#22 or/#16-#21
#23 #15 and #22
#24 meta-analysis. pt.
#25 exp meta-analysis
#26 exp technology assessment, biomedical/
#27 exp meta-analysis as topic
#28 or/#24-#27
#29 #23 not #28
#30 (comment or editorial or historical-article). pt.
#31 #29 not #30
#32 (animals not (animals and humans)). sh.
#33 #31 not #32

3.3.2 Data extraction and management

Two reviewers (Liu Jie and Hong Jue) independently extracted data, including types of studies, types of participants, types of interventions, types of outcome measures and methodology (e.g., random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias). The data consistency was validated by the third reviewer Wu Ling-xiang. We contacted primary authors when relevant information was not reported.

3.3.3 Assessment of risk of bias in the included studies

The study quality assessment was conducted using the Cochrane Collaboration's tool for assessing risk of bias in *Cochrane Handbook for Systematic Reviews of Interventions*[24]. The assessment was performed independently by two reviewers (Liu Jie and Hong Jue). Differences were settled by the third reviewer Huang Qin-feng.

3.3.4 Measures of treatment effect

We summarized the outcome data of the included studies. For studies containing three or more groups, only eligible groups were included. Alternatively, different groups were merged and included upon statistical analysis on outcomes. The Review Manager Version 5.3 (provided by the Cochrane Collaboration) was used for combining effect size. For consistency checking between different studies, the heterogeneity was assessed by Cochran Q statistic, $P > 0.1$ and $I^2 < 50\%$ indicated no statistically significant heterogeneity between studies and therefore allow for direct combining effect and a selection of fixed effect model; $P \leqslant 0.1$ and $I^2 \geqslant 50\%$ indicated statistically significant heterogeneity between studies and therefore sources of heterogeneity needs to be investigated. When the source of heterogeneity cannot be explained by clinical and methodological heterogeneity, the fixed effect model can be replaced by random effect model. The enumeration data were analyzed using dichotomous data and presented as relative risk (RR) and 95% confidence intervals (CI). The measurement data were analyzed using continuous data and presented as weight mean difference (WMD) and 95% CI.

3.3.5 Assessment of reporting biases

The funnel plot was used to analyze the potential publication bias, using the RR (efficacy comparison between the observation group and control group obtained through meta-analysis) as x-axis and log RR as y-axis.

3.3.6 Sensitivity analysis

Sensitivity analysis was conducted using the following method when included studies were sufficient: Remove a low-quality study, re-estimate the combining effect size and compare with previous meta-analysis outcome; remove a study that contains significantly more cases than other studies, re-estimate the combining effect size and compare with the previous meta-analysis outcome. Then the consistency of combining effect was observed using different statistical methods. Insignificant change in combining effect size indicates a low sensitivity,

suggesting a reliable outcome; otherwise a high sensitivity suggests a low reliable outcome.

4 Results

4.1 Description of studies

A total of 535 articles were identified from electronic database and 6 articles from other sources. After removing duplicates, 289 potentially relevant titles and abstracts were initially screened, and 238 were excluded for failing to meet the inclusion criteria. We retrieved and reviewed 51 full-text articles, and 12 were excluded for failing to meet the inclusion criteria. We then retrieved and reviewed 39 articles regarding their research subjects, interventions, control group, and outcome measurement, and 19 were excluded. Twenty articles were eligible and included[25-44]. The flowchart of literature screening is shown in Figure 1.

We reviewed the 20 full-text articles and extracted the characteristic information including the title, research methodology, diagnostic criteria, AR type, subgroup intervention/cases/course of treatment and outcome measurement. The characteristics of included studies are shown in Table 2. Special data processing and consolidation have been performed during the data extraction. RCTs[33, 36] reported 3 groups: an acupuncture group, a Western drug group and another ineligible treatment group that did not meet the inclusion criteria. We've only analyzed relevant information of the acupuncture group and Western drug group. RCTs[31, 42] reported 3 groups: 2 groups of different acupuncture methods and a medication group. Since there is no limitation on needling technique, the two acupuncture groups were combined and included using the Review Manager Version 5.3. Primary data were extracted for the rest studies.

4.1.1 Description of participants

All participants in the included studies met the inclusion criteria. However, the following two issues can be summarized from Table 2. First, all included studies reported diagnostic criteria. About 73.7% studies in China employed the criteria by Otolaryngology Head and Neck Surgery Branch, Chinese Medical Association[5, 20-21]; however, many of these studies used the old edition instead of the updated one. Only 1 article used the WHO issued international criteria[22], suggesting a low adoption of international criteria in studies conducted in China. Second, in terms of allergens, AR can be classified as seasonal (pollen), perennial (dust mites) or episodic (pet hair). In terms of duration, AR can be classified as intermittent or persistent; in terms of severity, AR can be classified as mild, moderate and severe. Of included studies, 85% did not mention AR classifications and only 3 articles selected perennial AR.

4.1.2 Description of interventions

According to the inclusion criteria, antihistamines or *Bi Yan Kang* Tablet was used as intervention in the control group. As a result, two parts were included in this systematic review and meta-analysis: the comparison between acupuncture and antihistamines and the comparison between acupuncture and *Bi Yan Kang* Tablet.

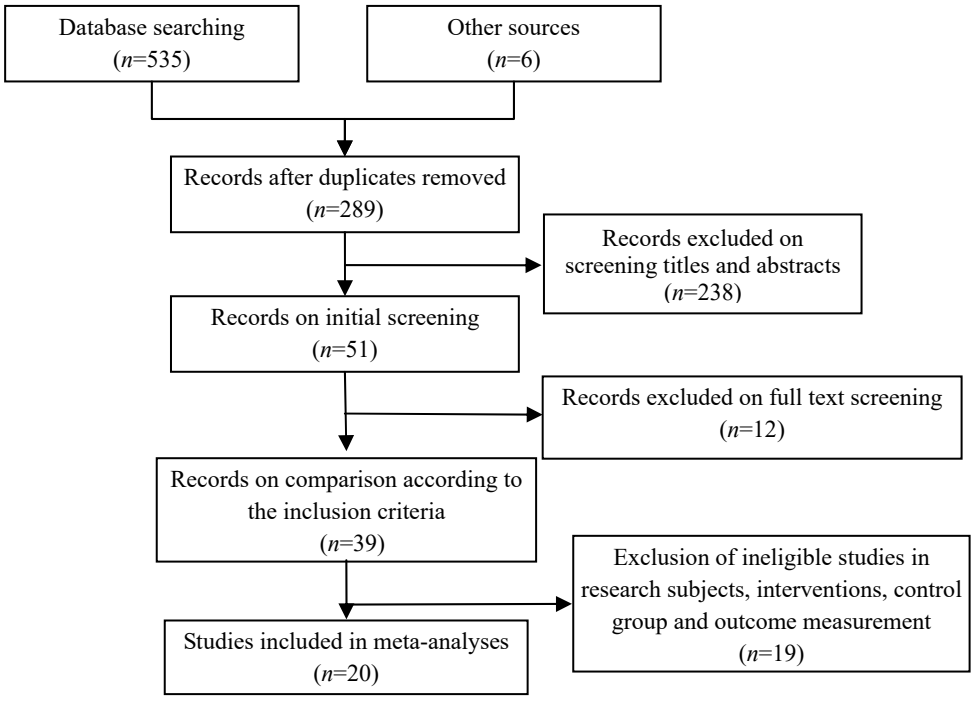

Figure 1. Literature screening and outcome

Table 2. Characteristics of the included studies

Study	Methodology	Diagnosis	RA type	Intervention method		Case		Session	Outcome
				Observation	Control	Observation	Control		
Bettina H 2014[25]	Randomized	A	Perennial	Acupuncture	Loratadine	15	9	4 week	TER, TNSS, IgE, IL-4
Du Y 2007[26]	Randomized	B	/	Acupuncture	Loratadine	34	35	4 week	TER, RR, TNSS, IAR
Huang M 2006[27]	Randomized	B	/	EA	Loratadine	30	30	10 d	TER, TNSS, EOS
Jin C 2013[28]	Randomized	B	/	Acupuncture	Loratadine	35	35	4 week	TER
Li YM 2003[29]	Randomized	B	Perennial	EA	Cetirizine	63	35	4 week	TER, RR
Li YM 2007[30]	Randomized	B	Perennial	EA	Cetirizine	50	50	4 week	TER, RR, EOS, IgE
Liang XQ 2008[31]	Randomized	C	/	EA	Loratadine	60	30	4 week	TER,TNSS, EOS
Liao QX 2015[32]	Randomized	D	/	Acupuncture	Loratadine	28	26	4 week	TER, RR
Liu C 2015[33]	Randomized	E	/	Acupuncture	Loratadine	22	22	4 week	TER, TNSS
Ni AM 2006[34]	Randomized	/	/	Acupuncture	Tranilast	195	191	4 week	TER
Qiao FY 2005[35]	Randomized	B	/	EA	Terfenadine	210	210	24 d	TER
Rao YQ 2006[36]	Randomized	B	/	Acupuncture	Cetirizine	47	46	4 week	TER, RR, TNSS, IgE
Shi ZH 2013[37]	Randomized	E	/	EA	Cetirizine	20	16	4 week	TNSS
Wang P 2013[38]	Multi-centered, randomized	F	/	EA	Cetirizine	27	28	4 week	TNSS, EOS, RQLQ, IgE, TNNSS
Xie H 2013[39]	Randomized	D, G	/	Acupuncture	Loratadine	30	30	4 week	TER
Xu WL 2015[40]	Randomized	H	/	Acupuncture	Cetirizine	34	34	20 d	TER, IAR
Zhang YC 2013[41]	Randomized, single-blinded	E	/	Acupuncture	Cetirizine	30	32	4 week	TNSS, IgE
Chen ZX 2007[42]	Randomized	B	/	Acupuncture	Bi Yan Kang	90	45	20 d	TER, RR
He TY 2006[43]	Randomized	B	/	Acupuncture	Bi Yan Kang	60	60	20 d	TER
Tian YP 2012[44]	Randomized	B, D	/	Acupuncture	Bi Yan Kang	50	50	10 d	TER

Note: Diagnostic criteria [A=Consensus statement on the treatment of allergic rhinitis[23]; B=*Diagnosis and Efficacy Evaluation Criteria for Allergic Rhinitis* (1997, Haikou)[20]; C=*Diagnosis, Treatment and Recommended Protocol for Allergic Rhinitis* (2004, Lanzhou)[21]; D=*Criteria of Diagnosis and Therapeutic Effects of Diseases and Syndromes in Traditional Chinese Medicine*[17]; E=*Diagnosis and Treatment Guidelines for Allergic Rhinitis* (2009, Wuyishan)[5]; F=*Allergic Rhinitis and Its Impact on Asthma* (ARIA) *Guidelines*: 2010 revision[22]; G=*Practical Otolaryngology*[18]; H=*Clinical Otolaryngology of Integrated Chinese & Western Medicine*[19]. Outcomes (IAR =Incidence of adverse reactions; TER=Total effective rate; RR=Recurrent rate

4.1.3 Description of outcomes

As shown in Table 2, clinical efficacy was used as outcome measurement in 85% studies, TNSS as the outcome measurement in 45% studies and biochemical and immune parameters as the outcome measurement in only 35% studies. Apparently there were more subjective observation scores than objective indicators.

4.2 Risk of bias in the included studies

The risk of bias in the included studies was performed using the Cochrane Collaboration's tool for assessing risk of bias recommended in the *Cochrane Handbook for Systematic Reviews of Interventions*[24] (Figure 2-Figure 5).

4.2.1 Random sequence generation

Only 8 articles used and described the correct method of random sequence generation; and 3 articles used the wrong method of random sequence generation, for example, by the patients' consultation sequence. The rest articles did not mention the method of sequence generation, and we failed to get in touch with the author, these were therefore labeled as 'unknown'.

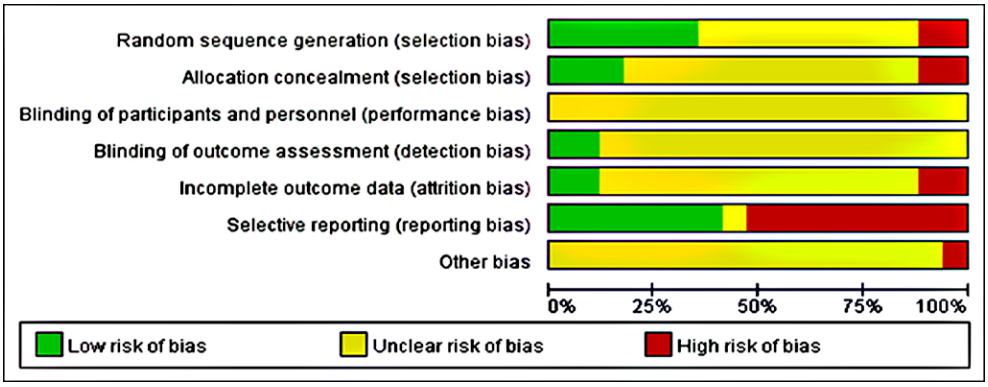

Figure 2. Risk of bias summary: acupuncture VS. antihistamine

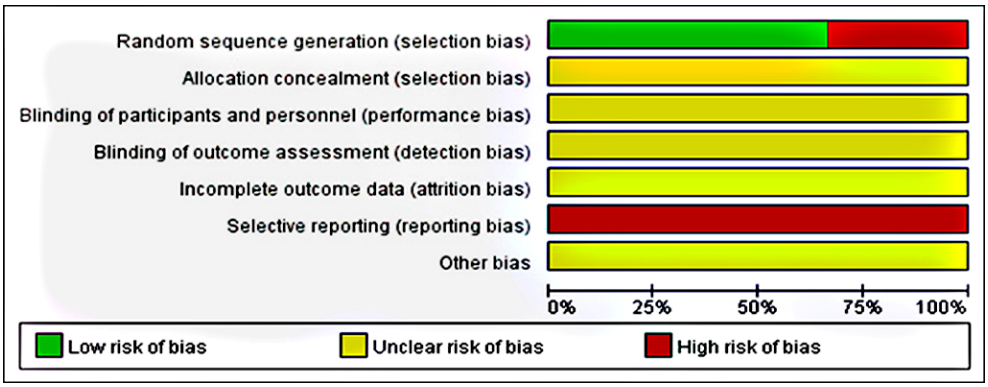

Figure 3. Risk of bias summary: acupuncture VS. *Bi Yan Kang* Tablet

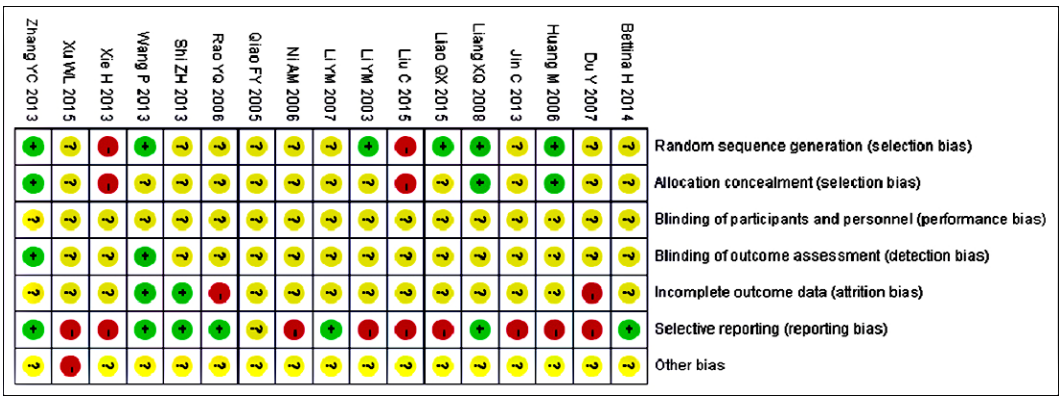

Figure 4. Risk of bias graph: acupuncture VS. antihistamine

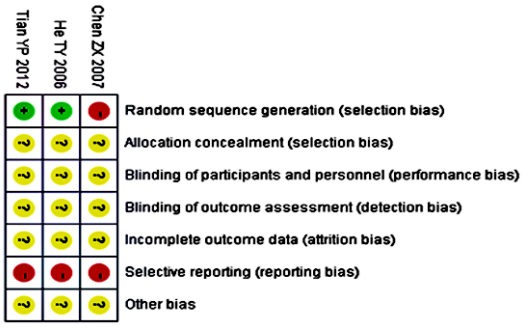

Figure 5. Risk of bias graph: acupuncture VS. *Bi Yan Kang* Tablet

4.2.2 Allocation concealment

Only 3 articles used the same correct method (sealed envelope) of allocation concealment. It's highly unlikely to complete allocation concealment in 2 articles with the wrong method of random sequence generation (considered high risk). There were no specified allocation concealment methods in the rest articles.

4.2.3 Blinding

There were little descriptions regarding blinding in the included studies. It's possible that some articles did use blinding but no description or did not use blinding at all (all considered unspecified). Only 2 articles mentioned that the review and statistical analysis were

conducted by professionals where were not involved in the study.

4.2.4 Incomplete outcome data

As for dropout cases, only 1 article reported, conducted follow-up and intention to treat (ITT) analysis; and 1 article explained the reason of drop out and excluded its correlation with efficacy.

4.2.5 Selective reporting

All included studies share the same issue of having more subjective scores than objective indicators. Some articles only used effective rate as the outcome measurement, reporting bias is therefore highly possible.

4.2.6 Other bias

One article did not mention the differences in baseline data, it is considered as high risk due to highly possible bias.

4.3 Effects of interventions

4.3.1 Acupuncture versus antihistamine medicines

(1) Comparison of total effective rate

Of 17 included studies that compared the efficacy between acupuncture and antihistamines, 14 studies reported the analysis on total effective rate; however, specific total effective rate was absent in 1 article[40], and we failed to get in touch with the author, there was no way to perform combining effect and we only performed analysis on the rest 13 articles. The heterogeneity test on these 13 articles showed $P \leqslant 0.1$ and $I^2 \geqslant 50\%$, indicating a statistical heterogeneity in included studies. Then we re-evaluated clinical methodology in included studies and did not find the source of heterogeneity. Consequently, we used random effect model for combining effect, RR = 1.24 > 1, 95%CI[1.15, 1.33], $P < 0.00001$, indicating that acupuncture achieved a better total effective rate than that of antihistamines (Figure 6).

We conducted further sensitivity analysis to address the heterogeneity in 13 included studies. After removing the high-risk (low-quality) studies on risk of bias assessment, we re-performed the meta-analysis on 4 included studies. The heterogeneity test showed $P > 0.1$ and $I^2 < 50\%$, indicating that there was no statistical heterogeneity in these 4 studies. Consequently, we used the fixed effect model for combining effect, RR = 1.18 > 1, 95%CI[1.09, 1.28], $P < 0.0001$, still indicating that acupuncture achieved a better total effective rate than that of antihistamines for AR (Figure 7).

We analyzed the 4 studies using the random effect model and obtained the consistent outcome with the fixed effect model, RR = 1.18 > 1, 95%CI[1.09, 1.28], $P < 0.0001$. After removing the article that had the most cases[35], we analyzed the rest 3 studies and obtained the similar results, RR = 1.25 > 1, 95%CI[1.10, 1.42], $P = 0.0006$. There were no significant changes in combining effect size after above tests, suggesting a reliable outcome with low sensitivity.

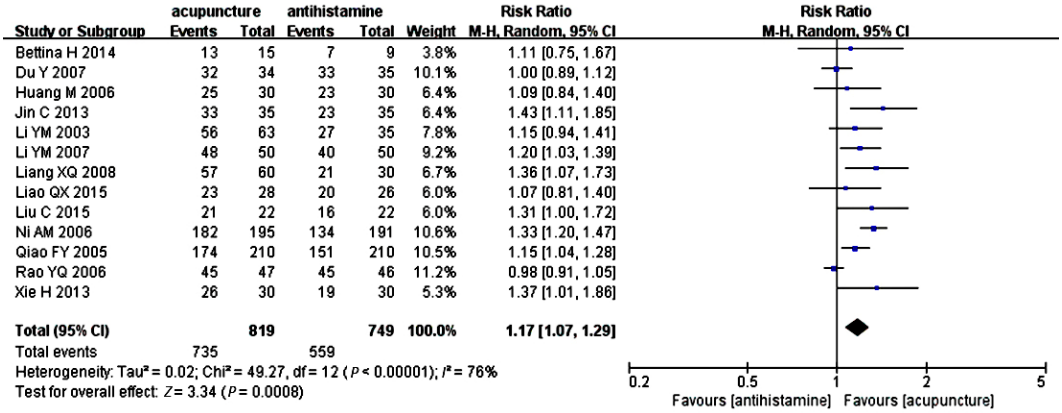

Figure 6. Acupuncture versus antihistamine medicines: comparison of total effective rate

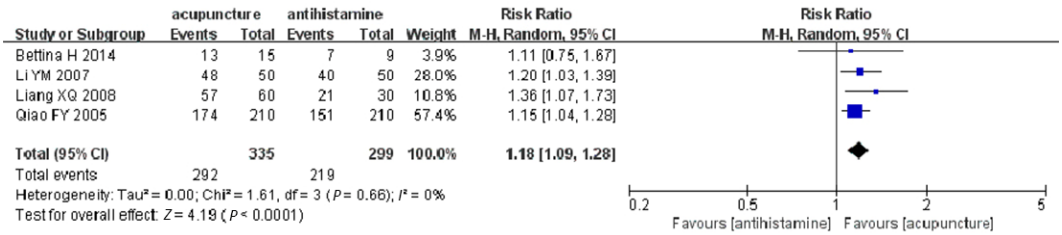

Figure 7. Acupuncture versus antihistamine medicines: comparison of total effective rate (4 studies)

The funnel plot was performed to analyze the publication bias (Figure 8). The skewed distribution suggested a potential publication bias.

(2) Comparison of TNSS

Of 17 included studies that compared the efficacy between acupuncture and antihistamines, 8 reported TNSS analysis. The heterogeneity test on these 13 articles showed $P \leqslant 0.1$ and $I^2 \geqslant 50\%$, indicating a statistical heterogeneity in included studies. So we re-evaluated clinical methodology in the included studies. Since 1 article[31] contained 2 acupuncture groups that had different acupuncture points, we combined the two groups using statistical methods. After removing this study[31], the heterogeneity test on the rest 7 studies showed $P > 0.1$ and $I^2 < 50\%$, indicating that there was no heterogeneity in the included studies. Consequently, we used fixed effect model for combining effect, MD = –0.93 < 0, 95%CI [–1.22, –0.63], $P < 0.00001$, indicating that acupuncture achieved better TNSS than antihistamines for AR patients (Figure 9).

We analyzed the 7 studies using the random effect model and obtained the consistent outcome with the fixed effect model, MD = –0.89 < 0, 95%CI[–1.31, –0.47], $P < 0.0001$. There were no significant changes in combining effect size after above tests, suggesting a reliable outcome with low sensitivity.

(3) Comparison of IgE

Of 17 included studies that compared the efficacy between acupuncture and antihistamines, 5 reported IgE determination. Since 1 article[25] did not mention specific numeric and 1 article[30] used mg/dL as the IgE unit, which was different from IU/mL in other studies, only 3 studies were included for analysis. The heterogeneity test on these 3 studies showed $P > 0.1$ and $I^2 < 50\%$, indicating that there was no statistical heterogeneity. Consequently, we used the fixed effect model for combining effect, MD = 1.46 > 0, 95%CI [–10.84, 13.75], $P = 0.82$, suggesting that acupuncture achieved similar effect as antihistamines on IgE (Figure 10).

We analyzed the 3 studies using the random effect model and obtained the consistent outcome with the fixed effect model, MD = 1.05 < 0, 95%CI[–18.86, 20.96], $P = 0.92$. There were no significant changes in combining effect size after above tests, suggesting a reliable outcome with low sensitivity.

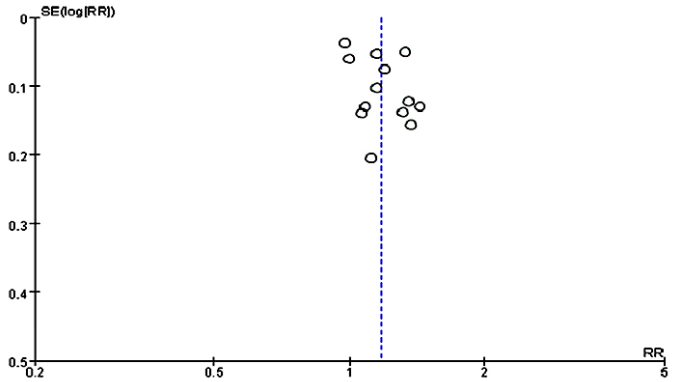

Figure 8. The funnel plot of reporting bias (Note: Acupuncture versus antihistamine medicines: comparison of total effective rate)

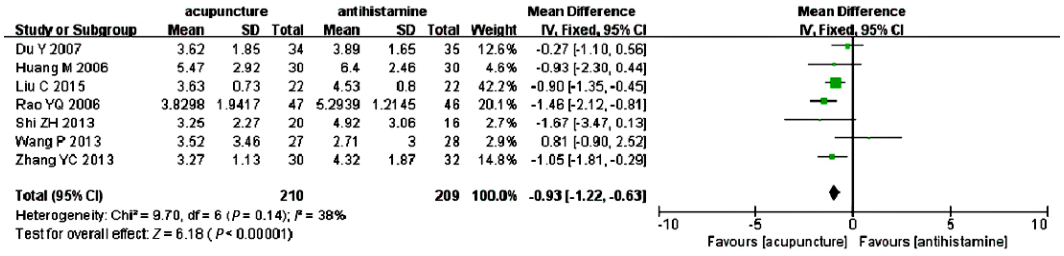

Figure 9. Acupuncture versus antihistamine medicines: comparison of TNSS

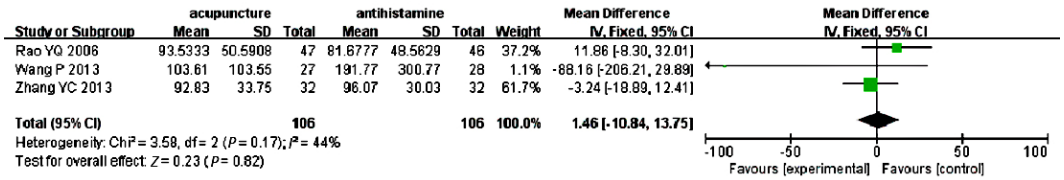

Figure 10. Acupuncture versus antihistamine medicines: comparison of IgE

4.3.2 Acupuncture needling versus *Bi Yan Kang* Tablet

The total effective rate was analyzed in all 3 studies that compared the efficacy between acupuncture and *Bi Yan Kang* Tablet. The heterogeneity test on 3 articles showed $P>0.1$ and $I^2<50\%$, indicating there was no statistical heterogeneity. Consequently, we used the fixed effect model for combining effect, RR＝1.50＞1, 95%CI[1.30, 1.73], $P<0.00001$, indicating that acupuncture achieved a better total effective rate than *Bi Yan Kang* Tablet for AR (Figure 11).

We analyzed the 3 studies using the random effect model and obtained the consistent outcome with the fixed effect model, RR＝1.46＞1, 95%CI[1.28, 1.66], $P<0.00001$. There were no significant changes in combining effect size after above tests, suggesting a reliable outcome with low sensitivity.

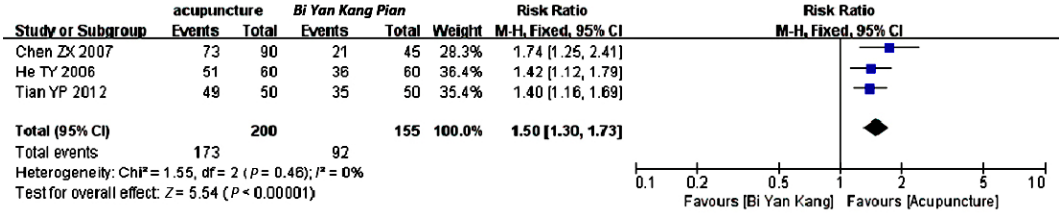

Figure 11. Acupuncture versus *Bi Yan Kang* Tablet: comparison of total effective rate

5 Discussion

5.1 Summary of main results

A total of 20 eligible studies were included according to the search strategy and inclusion criteria. All these studies used acupuncture (including EA) alone for AR and antihistamine or *Bi Yan Kang* Tablet as the control medicine. Seventeen studies compared the efficacy between acupuncture and antihistamine and 3 compared the efficacy between acupuncture and *Bi Yan Kang* Tablet. The combining effect analysis was conducted using data extraction. The results have shown that simple acupuncture achieved a better total effective rate for AR than antihistamine and *Bi Yan Kang* Tablet; acupuncture is better than antihistamine in improving the TNSS; however, whether it is better than *Bi Yan Kang* Tablet needs more evidences; and acupuncture and antihistamine had no significant differences in improving the IgE, and further research is needed in this regard.

5.2 Quality of the evidence

The assessment of overall risk of bias showed a low risk in fewer studies and a high risk in most studies, suggesting an absence of high level of evidence. The included RCTs lack randomization and blinding methods, leading to risk of bias and low level of evidence in conclusions.

5.3 Potential biases in the review process

There are several limitations in this review: (a) the diagnostic criteria are too general, not unified, outdated or not internationally recognized; (b) the inclusion criteria did not mention the AR classifications, for example, more clinical evidences are needed to determine the efficacy differences of acupuncture for intermittent and persistent AR; (c) the inclusion criteria did not require overall evaluation on outcome measurement: potential efficacy-related or objective indicators were absent in most studies, and clinical efficacy was used as the only outcome in many studies; (d) a large number of studies, for example, academic dissertations, might be missed in literature search.

5.4 Conclusion

In 2015, AAO-HNSF updated the *Clinical Practice Guidelines for Allergic Rhinitis*[7] and supplemented acupuncture treatment as a therapy with low level of evidence. We need more high-quality clinical trials to support acupuncture intervention, especially through convincing studies that compared the efficacy between acupuncture and established conventional treatment. Due to the variety of acupuncture methods for AR, it's appropriate to study these individual therapies one by one. As a result, this systematic review focuses on simple acupuncture therapy. Currently, Chinese herbal medicine is not recognized to be effective for AR, its efficacy needs further proof. This study used Chinese patent medicine *Bi Yan Kang* Tablet as a control medicine; however, there is little information in this regard and more work needs to be done in the future.

Conflict of Interest

The authors declared that there was no potential conflict of interest in this article.

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