Acupuncture for the treatment of allergic rhinitis: A systematic review and meta-analysis

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ABSTRACT

Background: *Because acupuncture may modulate the immune system, it has been proposed as a useful treatment for patients with allergic rhinitis (AR). Here, we assessed the evidence for the clinical efficacy of acupuncture for the management of AR patients by performing a systematic review and meta-analysis of the published literatures.*

Methods: *By searching PubMed, EMBASE, the Cochrane clinical trials database, and the China National Knowledge Infrastructure from 1980 through July 11, 2013, we collected and analyzed the randomized controlled trials (RCTs) of acupuncture for the treatment of AR patients to assess its efficacy and safety.*

Results: *Thirteen full papers that met our inclusion criteria were included, and a total of 2365 participants, including 1126 as treatment group and 1239 as control group, were enrolled. Compared with control group, acupuncture treatment group exerted a significant reduction in nasal symptom scores (weighted mean difference [WMD]: −4.42, 95% confidence interval [CI]: −8.42 to −0.43, $p = 0.03$), medication scores (WMD: 1.39, 95% CI: −2.18 to −0.61, $p = .0005$), and serum IgE (WMD: −75.00, 95% CI: −91.17 to −58.83, $p < 0.00001$). Data relating to Rhinitis Quality of Life Questionnaire (RQLQ) and 36-Item Short-Form (SF-36) component score in included studies were analyzed, which ultimately point to the efficacy of acupuncture treatment in improving quality of life in AR patients. No fatal events were reported in any of the included studies, and no serious systemic reaction, which needed treatment in the hospital, was related to the acupuncture treatment.*

Conclusion: *Our meta-analysis suggests that that acupuncture could be a safe and valid treatment option for AR patients.*

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Allergic rhinitis (AR) is a prevalent nasal hypersensitivity reaction to common allergens, including house dust mite, animal dander, and pollens from grasses, trees, and weeds, which is characterized by pruritus, sneezing, rhinorrhea, and nasal congestion. AR is now estimated to affect some 1.4 billion people globally and continues to be on the rise.[1] Although AR is not a life-threatening illness, it underlies many complications (*e.g.*, asthma) and affects quality of life[2] and work productivity.[3] Drugs currently used for the management of AR include antihistamines, corticosteroids, antileukotrienes, anticholinergics, and mast cell stabilizers.[4] Due to ineffective medication or significant side effects, some AR patients try to seek alternative therapies for symptom relief. An interesting survey showed that AR is the allergic condition commonly treated with complementary and alternative medicine, and acupuncture treatment seems to be used most frequently.[5]

Acupuncture developed from the traditional Chinese medicine techniques by stimulating acupoints that are located at lines of meridians that correspond to the flow of energy through the body.[6] The antiinflammatory actions of acupuncture treatment are thought to be mediated via the reflexive central inhibition of the innate immune system.[7] The rationale for using acupuncture to treat AR patients includes a modulation of cytokines and postulated antiinflammation action. Evidence for the efficacy and safety of acupuncture treatment for AR patients is still limited. Previous meta-analyses that evaluated the effectiveness of acupuncture for AR patients have not presented consistent conclusions.[8,9] Whether acupuncture has any apparent effect on AR patients remains unclear.

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MATERIALS AND METHODS

Search Strategy

We searched PubMed, EMBASE, the Cochrane clinical trials database, and the China National Knowledge Infrastructure from 1980 through July 11, 2013. The search strategies used the next major keywords: AR, acupuncture, and hay fever. Chinese and English restriction was imposed. The authors independently examined the output generated from the search (title and abstract). All potentially relevant articles were obtained.

The specific inclusion criteria were as follows: (1) randomized controlled trial (RCT); (2) patients with diagnosed AR; (3) administration of acupuncture compared with sham acupuncture, or another comparator treatment group or no treatment group; (4) one of the next clinical outcomes had to be reported: nasal symptom scores, relief medication scores, Rhinitis Quality of Life Questionnaire (RQLQ) score, 36-Item Short-Form (SF-36) Health Survey, total IgE, and safety; and (5) trials that tested other forms of acupuncture (no needle insertion), such as laser acupuncture, transcutaneous electrical nerve stimulation, and moxibustion, were excluded. Acupuncture was defined as the insertion of needles into the skin and underlying tissues at the acupoints to achieve "de qi" (an irradiating feeling considered to indicate effective needling). Sham acupuncture was defined as acupuncture with or without penetration at the acupoints or nonacupoints.

Quality Assessment

The methodological quality of each RCT was assessed according to the Cochrane Collaboration's tool for assessing risk of bias.[10]

Data Analysis

Outcome data, extracted from the included studies, were entered into RevMan software, version 5.1.0 (The Cochrane Collaboration, Oxford, UK) for statistical analysis. Differences were expressed as

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weighted mean difference (WMD) with 95% confidence intervals (CIs) for continuous outcomes. Statistical heterogeneity across trials was assessed with the χ^2 statistic ($p < .1$) and the I^2 statistic.[11] Heterogeneity across studies was tested by using the I^2 statistic, which is a quantitative measure of inconsistency across studies. As a guide, I^2 values of 25%, 50%, and 75% correspond to low, medium, and high levels of heterogeneity, respectively.[12] For the χ^2 statistic, the heterogeneity test was considered statistically significant if the *p*-value was under 0.1. When a significant heterogeneity was found, a random-effects model was used to calculate the pooled results and 95% CI. Otherwise, a fixed-effects model was applied. Publication bias was assessed by visually inspecting funnel plots.[13]

RESULTS

Characteristics of the Studies

Our searches identified 174 abstracts of potential relevance, of which 68 were selected for in-depth appraisal of full text papers. Thirteen full papers satisfied our inclusion criteria.[14–26] As shown in Fig. 1, the search strategy with flow diagram is presented per PRISMA guidelines.[27]The studies were published between 1996 and 2013. Ten trials were published in English language, three were published in Chinese. The methods, participants, interventions, and outcomes of the included studies are listed in the Table 1. In total, there were 2365 participants: 1126 as treatment group and 1239 as control group. Ten of the included RCTs adopted a parallel group design, two had a cross-over RCT design, and one was a parallel and cross-over trial. Five trials tested seasonal AR, six trials tested perennial AR, and two trials did not specify the type of AR. Twelve RCTs provided acupuncture on a regular basis, at least once weekly. The number of treatment sessions varied from 1 to 30. One RCT performed acupuncture only once.[17] A wide range of outcome measures was used, with the most common nasal symptom scores, relief medication scores, RQLQ, and total IgE.

Quality Assessment and Publication Bias

All the included trials mentioned randomization, but only eight of them adequately described methods of random sequence generation.[14,15,18,19,21,23,25,26] Allocation concealment and blinded fashion was clearly stated in nine studies,[14–19,21,25,26] and blinding of study subjects was almost universally maintained by use of sham acupuncture. Four studies did not conduct allocation concealment and blinded fashion.[20,22–24] Most of the outcome measurements about efficacy in this study were subjective and likely to be influenced by the lack of blinding. Hence, we considered that there are some risks in detection bias. The numbers and reasons for withdrawal or dropout were reported in details in eight trials.[14,16,18–20,23,25,26] Quality assessment was shown in Fig. 2. Furthermore, there was no evidence of significant publication bias by inspection of the funnel plots.

Nasal Symptom Scores

Nasal symptom reporting remains the most appropriate end point for the study of AR. Five of the included studies reported nasal symptom scores, recorded in patient diaries, as a primary outcome measure.[16,17,19,21,26] Acupuncture group produced significantly greater diminution of nasal symptoms than did control group (WMD: −4.42,

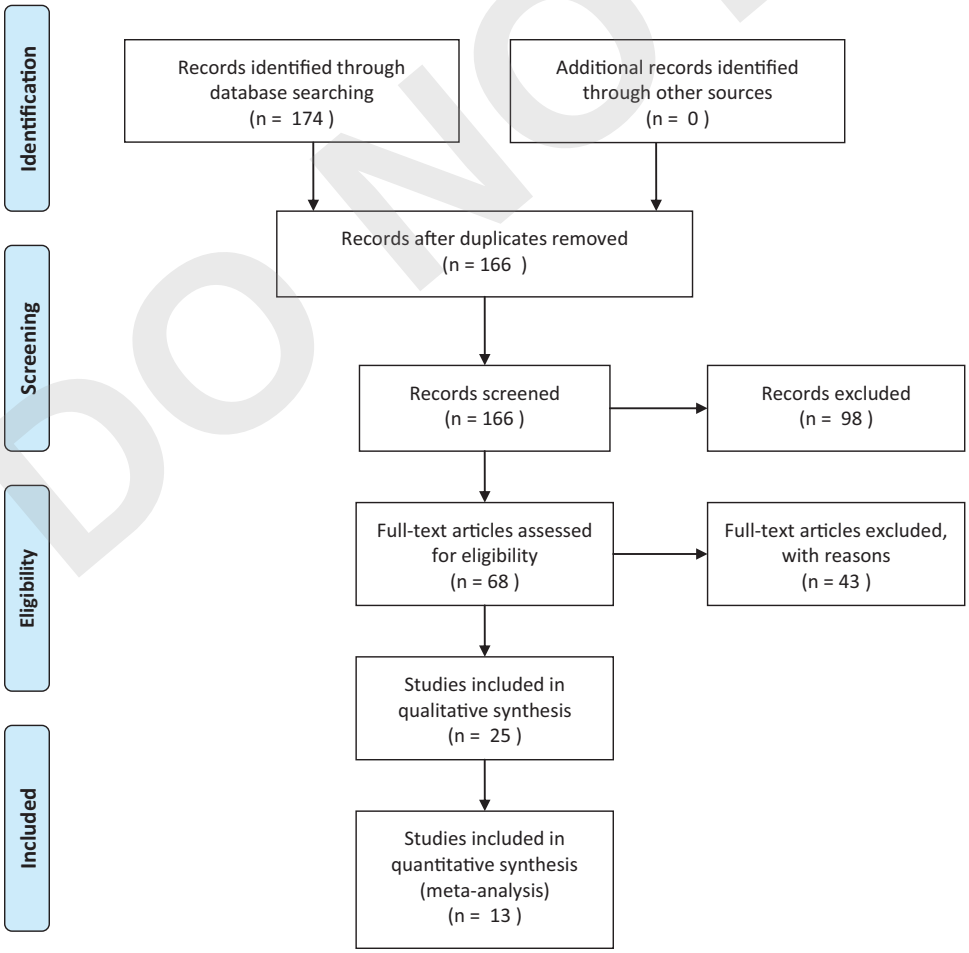

Figure 1. *Literature search strategy. PRISMA flowchart detailing literature search and review.*

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Table 1. **Characteristics of included studies**

Study ID, Origin	Study Design	Disease Diagnosis	Group (N)	Age, y Mean (SD)	Intervention	Treatment Regimen	Total Duration	Outcome Measure
Williamson *et al.*,[14] UK	Parallel	SAR	A (51)	31.9 (NR)	MA	3 or 4 times weekly	10 weeks	SS, medication use, and adverse effects
			S (51)	29.9 (NR)	Sham MA	3 or 4 times weekly	10 weeks	
Wolkenstein and Horak,[15] Germany	Parallel	SAR	A (12)	NR	MA	Once weekly	9 weeks	Nasal secretion and SS
			S (12)	NR	Sham MA	Once weekly	9 weeks	
Xue *et al.*,[16] Australia	Cross-over	SAR	A (17)	44.2 (15.69)	MA	3 times weekly	4 weeks	TNSS and TNNSS; RMS; and adverse effects
			S (13)	44.5 (10.88)	Sham MA	3 times weekly	4weeks	
Petti *et al.*,[17] Italy	Parallel	PAR	A (30)	NR	MA plus EA	Only once	No	TNSS and cytokines (IL-2, IL-6, and IL-10)
			S (30)	NR	Sham MA	Only once	No	
			N (30)	NR	No treatment	No	No	
Magnusson *et al.*,[18] Sweden	Parallel	SAR	A (18)	35.3 (9.5)	MA	12 sessions	3 months	VAS, skin test, IgE, and adverse effects
			S (14)	31.4 (8.7)	Sham MA	12 sessions	3 months	
Ng *et al.*,[19] China	Parallel	PAR	A (35)	11.72 (3.18)	MA	2 sessions weekly	8 weeks	TNSS, RMS, VAS, blood and nasal eosinophil counts, IgE, and side effects
			S (37)	11.00 (3.82)	Sham MA	2 sessions weekly	8 weeks	
Rao *et al.*,[20] China	Parallel	PAR/SAR	A (47)	44.28 (NR)	MA	6 times weekly	4 weeks	Score of symptoms and signs, IgE, IL-4, IFN, and side effects.
			N (49)	43.39 (NR)	Auricular acupressure	6 times weekly	4 weeks	
			N (46)	40.35 (NR)	Medication	6 times weekly	4 weeks	
Xue *et al.*,[21] Australia	Parallel	PAR	A (42)	42.5 (14.2)	MA	Twice weekly	8 weeks	TNSS, RMS, and adverse events
			S (38)	44.2 (11.0)	Sham MA	Twice weekly	8 weeks	
Li *et al.*,[22] China	Parallel	PAR	A (50)	39 (NR)	EA	30 sessions	34 days	Total effective rates and VIP and SP
			N (50)	40 (NR)	Medication	3 times daily	34 days	
Brinkhaus *et al.*,[23] Germany	Cross-over	PAR/ SAR	A (487)	39.0 (11.5)	MA	15 sessions	3 months	RQLQ, SF-36, and adverse effects
			N (494)	39.4 (12.3)	No acupuncture	No	3 months	
Zheng *et al.*,[24] China	Parallel	PAR	A (30)	NR	MA	Once daily	20 days	Total effect rate and side effects
			N (30)	NR	Medication	Twice daily	20 days	
Brinkhaus *et al.*,[25] Germany	Parallel and Cross-over	SAR	A (212)	33.4 (7.5)	MA	12 sessions	8 weeks	RQLQ, RMS, VAS, SF-36, adverse events
			S (102)	33.0 (8.2)	Sham MA	12 sessions	8 weeks	
			N (108)	32.2 (8.1)	Medication	No	8 weeks	
Choi *et al.*,[26] Korea and China	Parallel	PAR	A (95)	38.9 (11.33)	MA	3 times weekly	4 weeks	TNSS, TNNSS, RQLQ, and adverse events
			S (93)	37.0 (12.23)	Sham MA	3 times weekly	4 weeks	
			N (42)	38.0 (12.40)	No acupuncture	No	No	

SD = standard deviation; SAR = seasonal allergic rhinitis; A = acupuncture; S = sham acupuncture; N = no acupuncture; MA = manual acupuncture; EA = electroacupuncture; SS = symptom score; TNSS = total nasal symptom scores; TNNSS = total nonnasal symptom score; RQLQ = Rhinitis Quality of Life Questionnaire; RMS = relief medication scores; PAR = perennial allergic rhinitis; NR = not reported; VAS = visual analog scale; VIP = vasoactive intestinal peptide; SP = substance P; IFN = interferon; IL = interleukin.

95% CI: −8.42 to −0.43, $p = .03$) (Fig. 3). There was evidence of significant heterogeneity between studies ($p < .001$), but no unifying reasons were found to explain the difference of effect in the studies included. The robustness of these findings was analyzed in sensitivity analysis, which was performed by sequentially excluding individual studies. However, significant heterogeneity between studies was still evident, and the test for overall effect remained significant.

Relief Medication Scores

Medication scores reflecting concurrent use of antiallergic medication were reported in four studies.[16,19,21,25] In Xue *et al.*'s study,[16] no subject recorded using any relief medication during the real acupuncture treatment phase, so no statistical analysis was performed. Data in other three trials were available and analyzed.[19,21,25] There was a high degree of heterogeneity between the studies when combined in the meta-analysis ($p = .006$, $I^2 = 80\%$), which was associated with a nonsignificant trend in favor of the acupuncture group, WMD: −0.89 (95% CI, −2.03 to 0.25, $p = .12$) (Fig. 4). Sensitivity analysis was performed by excluding the data of Ng *et al.* included in the meta-analysis.[19] The revised WMD was 1.39 (95% CI, −2.18 to −0.61, $p < .001$) (Fig. 5), which showed that the results became significant. Meanwhile, heterogeneity disappeared ($p = .40$, $I^2 = 0\%$).

RQLQ Score

Three of the included studies reported the QLQ.[23,25,26] There was a high degree of heterogeneity between the studies when combined in the meta-analysis ($p < .00001$, $I^2 = 96\%$), which was associated with a nonsignificant trend in favor of the acupuncture group, WMD: −0.23 (95% CI, −0.89 to 0.43, $p = .50$). Sensitivity analysis was performed by excluding the data of Brinkhaus *et al.* that included in the above meta-analysis.[23] The revised WMD was −0.50 (95% CI, −0.71 to −0.29, $p < .001$), which meant the results became significant. At the same time, heterogeneity disappeared ($p = .51$, $I^2 = 0\%$).

Physical Component Score of SF-36

Physical component score of SF-36 evaluated the quality of life which related to one's physical health. The meta-analysis of two RCTs

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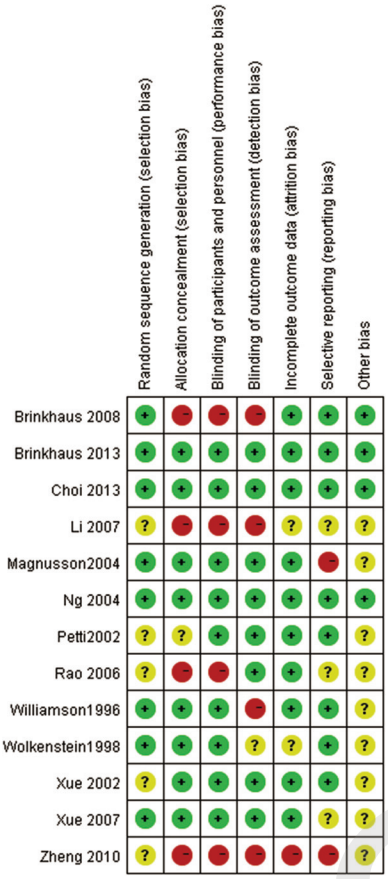

Figure 2. Risk of bias summary. Judgments about each risk of bias item for each included study.

revealed that the acupuncture group was superior to the control group in improving physical health (n = 1403; WMD: 3.17, 95% CI, 1.45–4.89, p = .0003; medium level of heterogeneity: p = .10, I^2 = 63%).[23,25]

Mental Component Score of SF-36

Two studies' data in mental health of SF-36 were included.[23,25] The WMD was 2.64 (95%CI, 0.38–4.90, p = .02), indicating a significant trend in favor of the acupuncture group, although medium level of heterogeneity was observed (p = .09, I^2 = 65%).

Total IgE

Three studies measured changes in serum total IgE.[18–20] The WMD was −75.00 (95% CI, −91.17 to −58.83, p < .00001), indicating a significant decrease of total IgE in the acupuncture group. There was no evidence of heterogeneity between studies (p = .38, I^2 = 0%).

Adverse Events

Ten RCTs evaluated adverse events of acupuncture,[14,16,18–21,23–26] and three studies did not.[15,17,22] Two of them reported no adverse effects during their study period,[16,24] and eight studies reported mild adverse effects, such as needling pain, papules, pruritus, subcutaneous bleeding, dizziness, numbness, and headache.[14,18–21,23,25,26] Only two trials reported that the adverse effects of both real and sham acupuncture made study participants drop out because of pain, headache, or drowsiness.[18,20] The authors reported that the occurrence was not significantly different compared with sham acupuncture. No fatal events were reported in any of the included studies. No serious systemic reaction, which needed treatment in the hospital, was related to the acupuncture treatment.

DISCUSSION

Nowadays, many AR patients prefer to choosing acupuncture treatment due to the fact that it is more appealing, less invasive,

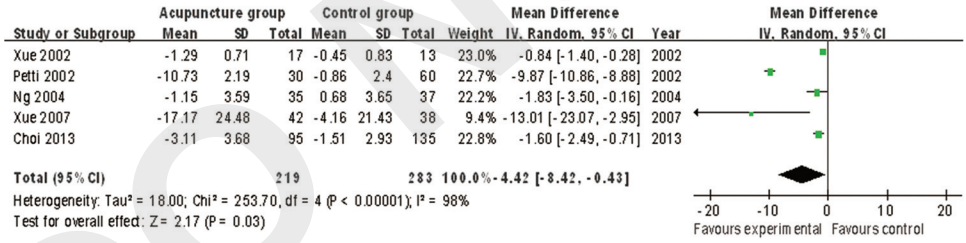

Figure 3. Meta-analysis of the RCTs comparing nasal symptom scores between acupuncture group and control group.

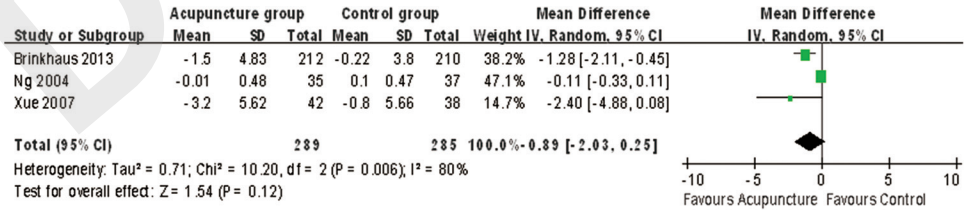

Figure 4. Meta-analysis of the RCTs comparing relief medication scores between acupuncture group and control group (before sensitivity analysis).

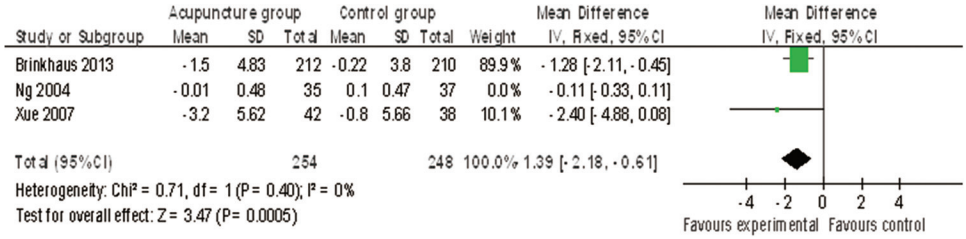

Figure 5. Meta-analysis of the RCTs comparing relief medication scores between acupuncture group and control group (after sensitivity analysis).

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and less drug like.[28,29] Nevertheless, although it is widely practiced worldwide, acupuncture treatment for AR still lacks clear evidence to make definitive recommendations for therapeutic option. One of the previous systematic reviews included seven RCTs and suggested that it was not possible to recommend acupuncture as a proven treatment for AR because of the inadequate published clinical trials.[9] The other systemic review[8] in 2009 concluded the total number of RCTs included in the analysis and the total sample size were too small to draw firm conclusions about the effectiveness of acupuncture. In the present study, we have included two latest multicenter, randomized, parallel-controlled trials[25,26] with high quality to obtain more data for novel meta-analysis and consistent conclusion.

This systematic review found 13 RCTs that satisfied our inclusion criteria. Score representing nasal symptom severity from only five studies and score quantifying concurrent medication use from only three studies were suitable for meta-analyses. Our meta-analysis showed that acupuncture group has superior effect in reduction of both rhinitis symptoms and the requirement for antiallergic medication compared with control group. The subgroup analysis can not be carried out for the limited number of RCTs. However, a few caveats should be taken into account for interpreting the findings of the present meta-analysis. The various populations (*e.g.*, sex, ethnicity and geographical background), the diverse scoring systems, and different acupuncturists and intervention protocol (*e.g.*, number of treatment sessions and treatment duration) adopted may potentially affect our results. These factors may explain the potential risk of bias and heterogeneity. Especially, we considered the high degree of heterogeneity resulted predominantly from the wide variety of scoring systems used across studies, although it is in part compensated for by use of the WMD in the meta-analyses. We consequently feel that standardized scoring systems are essential.

RQLQ, the disease-specific questionnaire designed to measure rhinitis-associated impairments of quality of life, consists of 28 items in the seven domains of sleep, nonnasal/eye symptoms, emotional function, practical problems, nasal symptoms, eye symptoms, and activities.[30] SF-36 component scales evaluate the quality of life as it relates to one's physical and mental health.[31] Data relating to RQLQ and SF-36 component score in included studies were analyzed, which ultimately point to the efficacy of acupuncture treatment in improving quality of life in AR patients.

The molecular mechanism underlying acupuncture's pharmacologic effect has not been fully understood. Recent study showed that acupuncture treatment exerted immune-modulating effects in AR patients.[32] Our meta-analysis of serum IgE levels in three included trials showed a significant decrease of IgE for the acupuncture group compared with the control group. This result showed strong and consistent evidence that acupuncture treatment leads to favorable responses in immunologic outcomes, which have been shown to be helpful in trials of proven therapeutic modalities, such as allergen-specific immunotherapy. Although these data are of interest in terms of understanding the pathophysiology of the underlying disease process and the mechanisms of action of the treatment, we acknowledge their clinical significance remains unclear.[33]

The safety of acupuncture treatment for AR patients should be further noted. In our systematic review, we found that no fatal events were reported in any of the included studies, and no serious systemic reaction, which needed treatment in the hospital, was related to the acupuncture treatment. Only a few of the included studies reported mild adverse effects, such as pain, papules, pruritus, subcutaneous bleeding, dizziness, numbness, and headache. Most adverse events were of mild severity and occurred with similar frequency among patients treated with real acupuncture and sham acupuncture. Relative to drug treatments these adverse effects may be infrequent or even negligible.[34–37]

CONCLUSION

In summary, our meta-analysis preliminarily suggests that that acupuncture could be a safe and valid treatment option for AR patients. Due to the lack of a standard acupuncture treatment protocol and a standardized scoring system, the conclusiveness of this systemic review and meta-analysis may be limited. Future large-scale, well-designed RCTs on this topic are still required to further validate our preliminary findings and focus on the long-term efficacy of acupuncture.

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