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Review article

The efficacy and potential mechanism of the acupuncture treatment for allergic rhinitis: A systematic review and meta-analysis of data from animal models

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ABSTRACT

Objective: This study aimed to evaluate the efficacy of acupuncture in treating allergic rhinitis (AR) in animal models of the disease, and to explore the underlying mechanism of acupuncture in AR.
Methods: Related literature was retrieved from multiple databases, including China National Knowledge Infrastructure (CNKI), Wan Fang databases, SinoMed databases, VIP database, PubMed, EMBASE, the Cochrane Library, up to September 2023. The inclusion criteria were focused on animal experiments that investigated the effect of acupuncture therapy on animal models of AR. Studies combining acupuncture with other Chinese medicine therapies were excluded. Data were extracted independently by two reviewers using standardized forms. A total of 75 studies were finally included. The risk of bias in individual studies was evaluated using the Systematic Review Centre for Laboratory animal Experimentation (SYRCLE) tool, and the quality of reporting was evaluated according to Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines. Meta-analyses and plotting were conducted using STATA 17.0 and RevMan 5.4. When heterogeneity was present, a random effects model was applied. Subgroup, meta-regression and sensitivity analyses were also performed.
Results: The SYRCLE scores ranged from 3 to 7, and the ARRIVE scores ranged from 6.5 to 11 points. Meta-analysis results demonstrated that acupuncture could significantly down-regulate EOS counts in both blood and nasal mucosa, and reduce the serum levels of IL-5, compared to the AR model group. The results of the qualitative analysis showed that acupuncture could reduce the behavior scores of AR, down-regulate serum levels of IL-4, IgE and sIgE, as well as up-regulate IFN-γ levels. Subgroup analysis results suggested that the different interventions might contribute to the observed heterogeneity.
Conclusion: Our results demonstrate that acupuncture effectively alleviates the nasal allergic symptoms in animal models, inhibits immune and inflammatory signaling transduction, and reduces the release of inflammatory mediators. This study highlights the potential of acupuncture as a promising therapeutic option for AR, however, further studies are required to fully understand its mechanisms of action.

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1. Introduction

Allergic rhinitis (AR) is a chronic inflammatory disease of the nasal mucosa triggered by an immunoglobulin E (IgE) mediated response in allergen-sensitized subjects [1]. Epidemiological data have demonstrated that the global prevalence of AR is as high as 10 %–25 % [2]. It is estimated that an annual health expenditure of $2–5 billion is spent each year to treat patients with AR in the United States [3]. The concept of "one airway, one disease", proposed by Grossman to elucidate the pathophysiology of asthma and AR, has been emphasized in many epidemiological studies [4]. According to epidemiological findings, up to 40 % of AR patients were concomitant with asthma and up to 80 % of asthma patients have AR [5]. Early diagnosis and appropriate treatment are crucial to prevent the progression of AR.

Currently, the clinical treatments for AR primarily include allergen avoidance, pharmacotherapy, environmental control, surgical treatment, immunotherapy, and patient education [6]. Among these, surgical treatment lacks sufficient evidence while having low patient acceptance, and pharmacotherapy is the mainstream treatment of AR [7]. Although pharmacotherapy can be effective, it also presents numerous problems and potential side effects. For instance, intranasal corticosteroid can cause local nasal issues (epistaxis, nasal irritation), headaches, and even nasal septal perforation [4]. Additionally, Allergen-specific immunotherapy, globally recognized as a superior treatment for AR, is the only treatment targeting the immunological cause of the disease, yet it faces challenges related to safety, adherence, cost, and cost-effectiveness [8,9]. Due to the lack of satisfactory therapies for AR, new approaches are needed to enhance the treatment outcomes.

Acupuncture, a characteristic treatment in Chinese medicine (CM), stimulates the specific acupuncture points to treat diseases by inserting fine filiform needles, or by using moxibustion [10]. Numerous clinical studies have indicated the efficacy of acupuncture against AR, with minimal adverse reactions [11]. Animal experiments are widely used in preclinical medical research for exploring novel therapeutic approaches, which have become indispensable tools to study mechanisms and treatments of diseases and play a key role in scientific and medical research [12]. Since the early 2000s, an increasing number of pre-clinical studies on the effects of acupuncture in AR animal models have been published, demonstrating the anti-inflammatory and anti-allergic effects of acupuncture [13–15]. Indeed, acupuncture has been proved to regulate the immune system, decrease the inflammatory cytokine levels, and improve the local pathological conditions in animal models [16–18].

Animal experimentation is essential for research aimed at improving human health and healthcare [19]. Meta-analyses of animal studies are proven valuable, often providing new and important information from previously published animal experiments. They can help resolve discrepancies between pre-clinical studies and clinical trials outcomes, and inform the design of clinical trials [19–21].

Pre-clinical systematic review can systematically evaluate the efficacy, identify areas for further animal experiments, suggest improvements in animal handling, and provide a foundation for future clinical research. However, systematic reviews are not yet widespread in laboratory animal science, and no systematic evaluation or meta-analysis of acupuncture's effectiveness in AR animal models currently exist. Thus, we performed a systematic review and meta-analysis on the data gathered from animal models to assess the efficacy of acupuncture in AR, and discuss the underlying mechanism. This will contribute to a further understanding and in-depth studies on the therapeutic potential of this complementary therapy.

2. Methods

2.1. Material and methods

This systematic review and meta-analysis were conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [22], the PRISMA 2020 checklist is provided in Supplementary Table S1. We registered the protocol in INPLASY (INPLASY202380110).

2.2. Search strategy

Seven electronic databases, including China National Knowledge Infrastructure (CNKI), Database for Chinese Technical Periodicals (VIP), Wan Fang database, SinoMed databases, PubMed, Embase and Cochrane Library, were utilized to retrieve relevant publications in English or Chinese, covering the period from inception to September 2023. A detailed search strategy for PubMed is provided in Table 1. References of selected articles and previous systematic reviews were also manually screened to identify additionally relevant studies.

Table 1
Search strategy in PubMed.

#1	"Acupuncture"[Mesh] or "Acupuncture Therapy"[Mesh] or "Acupuncture, Ear"[Mesh] or "Acupuncture Points"[Mesh] or "Moxibustion"[Mesh]
#2	"Rhinitis, Allergic"[Mesh] or Allergic Rhinitides or Rhinitides, Allergic or Allergic Rhinitis
#3	"Mice"[Mesh] OR "Rats"[Mesh] OR "Rabbits"[Mesh]
#4	mechanism[Title/Abstract] OR animal study[Title/Abstract] OR preclinical study[Title/Abstract]
#5	#3 OR #4
#6	#1 AND #2 AND #5

2.3. Eligibility criteria

Study subjects: Allergic rhinitis animal models were sensitized using ovalbumin (OVA).

Types of intervention: All types of acupuncture or acupuncture-related therapies, including the use of needling, acupuncture points, or moxibustion.

Types of control: Allergic rhinitis model group (AR model group)

Outcome measures.

(1) Animal behavioral indicator: Behavior score.
(2) Macro dissection: Spleen weight.
(3) Micro-pathohistology: (A) Histopathological changes in the nasal mucosa and eosinophil (EOS) levels observed through morphological method. (B) Diff-Quick staining method: The total number and classification of cells in nasal lavage fluid observed under microscope.
(4) Changes in immune indexes: (A) Enzyme-linked immunosorbent assay (ELISA): Levels of Interleukin-4 (IL-4), Interleukin-5 (IL-5), Interleukin-13 (IL-13), Interferon - γ (IFN-γ), thymic stromal lymphopoietin (TSLP) and IgE in nasal lavage fluid and peripheral blood; (B) Immunohistochemistry: Detection of TSLP level in nasal mucosa.

2.4. Exclusion criteria

(1) Combined use of other Chinese medicine therapies, such as Chinese herbal medicine, Tuina, and cupping.
(2) Case report/case series, reviews, meta-analysis, conference abstract, and clinical trials.
(3) Repeated publications.

Acupuncture combined with other Chinese medicine therapies was excluded to ensure that the therapeutic effects could be attributed solely to acupuncture treatment.

2.5. Study selection

All reviewers have received training to assure consistency among them. Search results were imported into EndNoteX9, and duplicate citations were removed. If the full text was not available or there were missing data in the article, we contacted the first or corresponding authors. Two reviewers (LYX and LK) independently screened and selected the studies according to the predefined inclusion and exclusion criteria. In case of any disagreements, discussions were held or a third reviewer was consulted to resolve the discrepancies.

2.6. Data extraction

Two reviewers (LYX and LJ) independently extracted data from the eligible studies, which were then rechecked after the initial extraction. To ensure reproducibility and consistency, the reviewers used standardized data extraction template. Inter-reviewer disagreements were resolved by consensus or by consulting a third reviewer (XJ). The following information was extracted: country, animal characteristics (species and sex), intervention treatment, acupoints, acupuncture session, control group and outcome measurement (Table 2). When results were only displayed in chart, data values were extracted using GetData Graph Digitizer software. If necessary, we attempted to contact the first or corresponding authors of the studies to obtain the original data. When standard error (SE) of means was reported instead of standard deviation (SD), SD was calculated by multiplying the SE by the square root of the sample size ($SD = SE \times \sqrt{n}$).

2.7. Quality assessment

2.7.1. Risk of bias assessment

The risk of bias for each included experiment was independently assessed by 2 reviewers (LYX and ZXH) using the Systematic Review Centre for Laboratory animal Experimentation (SYRCLE) risk of bias tool [23]. The risk of bias for each domain was graded as low, high, or unclear. Each item was scored 1 if the risk of bias was rated as low. Due to the characteristics of acupuncture, we assumed that blinding the acupuncturists was nearly impossible.

2.7.2. Quality of reporting evidence

The reporting quality of included studies was assessed by two independent reviewers (ZXH and XLL) using the Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines [24]. Each item was scored 1, 0.5, or 0, if the respective criterion was fully met, partially met, or not met, respectively.

Higher scores indicate greater quality of the article. Any disagreement was resolved via consensus with a third reviewer (XJ).

Table 2
The Characteristics of the included studies.

Study	Country	Animals (Species, Sex)	Intervention treatment (n)	Acupoints	Acupuncture Treatment Course	Control Group (n)	Outcome Measurement
Jung, D. 2012 [30]	Republic of Korea	BALB/c mice, female	Disposable intradermal needles (7); Moxibustion (7)	The juncture of the medial canthus and nostril	7 days	AR model group(7); Levocetirizine group(7)	EOS, Substance P (SP), STAT6, NFkB, iNOS
Tu 2020 [31]	China	SD rats, male	Prescription NO.1 acupoint application (10); Prescription NO.2 acupoint application (10)	Dazhui (DU14), Fengmen (BL12), Feishu (BL13), Pishu (BL20)	28 days	Blank group(10); AR model group(10)	The score of behavioral symptoms, NGF, IL-4、IL-5、IL-13、IgE and IFN-γ, The pathological structure of nasal mucosa and mast cells, The ultrastructure of nasal mucosa, TB staining
Yang 2016 [32]	China	SD rats, half female and half male	Acupoint injection (11)	Yingxiang (LI20)	Once every other day, 7 times	AR model group(11); Sham group(Acupoint injection of physiological saline group:11; Non acupoint injection group:11)	Behavioral indexes, Histamine, histopathological changes in the nasal mucosa
Yang 2018 [33]	China	SD rats, male	CIAA for 1 week (C1) group(7 or 8); CIAA for 2 weeks (C2) group(7 or 8)	Yingxiang (LI20), Zusanli (ST36)	14 consecutive days	Blank group; AR model group(7 or 8); Sham group(7 or 8); Western medicine group(7 or 8)	Animal Behavior, Mast Cells, SP, sIgE, IL-4, IFN-γ,TLR1、TLR2 and TLR4
Han 2019 [34]	Republic of Korea	BALB/c mice, female	Acupoint injection: Dexamethasone(Dex)2 μg/kg(5); Dexamethasone(Dex)20 μg/kg(5); Dexamethasone(Dex)200 μg/kg(5)	Zusanli (ST36)	10 consecutive days	Blank group(5); AR model group(5); Sham group(5)	Rubbing score, Spleen weight, Serum biomarkers, Inflammatory cytokines and chemokines levels in nasal mucosaltissue, Caspase-1/RIP-2
Zhang 2011 [35]	China	SD rats, half female and half male	Moxibustion (10)	Xinhui (Du22)	2 weeks	Blank group(10); AR model group(10); Western medicine group(10)	IgE
Chen 2006 [36]	China	BALB/c mice, female	Acupoint application (12)	Dazhui (GV14)	4 weeks	Blank group(12); AR model group(12); Sham group(12); Western medicine group(12)	Behavioral indexes, histopathological changes in the nasal mucosa, the degranulating mast cells, EOS, sIgE, the proliferation response of specific lymphocytes, Thl/Th2, BALF lymphocyte cytokine
Chen 2012 [37]	China	SD rats, half female and half male	Acupoint application with ordinary powder (10); Acupoint application with submicron powder (10)	Dazhui (GV14), Feishu (BL13), Shenshu (BL23)	10 days	Blank group(10); AR model group(10); Western medicine group(10)	Behavioral indexes, histopathological changes in the nasal mucosa, EOS, IL-4, TGF-β1, IFN-γ, IL-17
Chen 2016 [38]	China	Wistar rats, male	Acupoint catgut embedding (10)	Yingxiang (LI20), Fengchi (GB20)	After acupoint catgut embedding, there is no need for any treatment in the rat acupoints	Blank group(10); AR model group(10); Western medicine group(10)	Nasal symptom score, Ig E, IL-4, histopathological changes in the nasal mucosa
Chen 2017 [39]	China	Wistar rats, male	Heat-sensitive moxibustion (10); Moxibustion (10)	Feishu (BL13), Shenshu (BL23), Fengchi (GB20), Yingxiang (LI20)	14 days	Blank group(10); AR model group(10); Western medicine group(10)	Nasal symptom score, Ig E, IL-4, histopathological changes in the nasal mucosa
Chen 2015 [40]	China	SD rats, half female and half male	Acupoint catgut embedding (20)	Yingxiang (LI20)	Once every 14 days for a total of 3 times	Blank group(20); AR model group(20)	Animal behavior score, histopathological changes in the nasal mucosa, SP, CGRP, VIP
Chen Q 2016 [41]	China	SD rats, half female and half male	Acupoint catgut embedding (12)	Yingxiang (LI20)	14 days	Blank group(12); AR model group(12)	IL-4, IL-10, INF-γ, s Ig E
Chen 2019 [42]	China	Wistar rats, male	Acupoint application (10)	Feishu (BL13), Pishu (BL20), Shenshu (BL23)	On the 24th, 26th, 28th, 30th, 32nd, 34th, and	Blank group(10); AR model group(10); Western medicine group(10)	Behavioral indexes, IgE, TGF-β1, EOS

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Table 2 (*continued*)

Study	Country	Animals (Species, Sex)	Intervention treatment (n)	Acupoints	Acupuncture Treatment Course	Control Group (n)	Outcome Measurement
					36th days from the beginning of the study		
Chen,XL 2019 [43]	China	SD rats, male	Acupoint application: 1 h ginger modulation (10); 1 h honey modulation (10); 4 h honey modulation (10)	Dazhui (GV14), Fengmen(BL12), Feishu (BL13), Pishu (BL20)	28 days	Blank group(10); AR model group(10)	Behavioral indexes, NGF, IL-4, IL-5, IL-13, IgE, IFN-γ, IgE mRNA, IgE, EOS, histopathological changes in the nasal mucosa
Song 2011 [44]	China	SD rats, half female and half male	Acupuncture(10)	Yingxiang (LI20), Shangxing(GV23)	28 days	Blank group(10); AR model group(10); Western medicine group(10)	Behavioral indexes, IL-4
Chen,Y 2012 [45]	China	SD rats, half female and half male	Acupuncture(12)	Feishu (BL13), Shenshu (BL23), Dazhui (GV14)	10 days	Blank group(12); AR model group(12); Western medicine group(12)	IL-4, IFN-γ, EOS, histopathological changes in the nasal mucosa
Chen 2003 [46]	China	Wistar rats, half female and half male	Pricking Acupoint Blood (24)	Yingxiang (LI20), Hegu (LI4), Quchi (LI11) , Zusanli (ST36)	10 days	Blank group(24); AR model group(24); Western medicine group(24); Acupoint application(24)	Total score of rhinitis superposition, IL-4, IgE
Chen,YH 2003 [47]	China	Wistar rats, half female and half male	Pricking blood(24); Acupoint application(24)	Yingxiang (LI20), Hegu (LI4), Zusanli (ST36)	10 days	Blank group(24); AR model group(24); Western medicine group(24)	Total score of rhinitis superposition, Substance P (SP)
Ding 2015 [48]	China	SD rats, male	Acupuncture(20)	Lieque (LU7)	6 days	Blank group(20); AR model group(20)	Behavioral indexes, histopathological changes in the nasal mucosa
Zhao 2010 [49]	China	Wistar rats, male	Acupuncture(10)	Yingxiang (LI20), Hegu (LI4), Feishu (BL13), Zusanli (ST36)	10 days	Blank group(10); AR model group(10); Western medicine group(10)	IL-4, IFN-γ
Geng 2013 [50]	China	Hartley guinea pigs, half female and half male	Acupunture Therapy by Dispersing the Stagnated Liver-Oi(8)	Yingxiang (LI20), Feishu (BL13), Ganshu (BL18), Taichong (LR3)	15 days	Blank group(8); AR model group(8); Western medicine group(8); Conventional acupuncture group(8)	Behavioral indexes, IL-5, ECP, SP, EOS, histopathological changes in the nasal mucosa
Gong 2021 [51]	China	SPF New Zealand rabbits, half female and half male	Intranasal acupuncture(8)	Neiyingxiang (EX-HN9)	Once every other day, 7 times	Blank group(8); AR model group(8); Sham acupuncture group(8)	Behavioral indexes, IgE, IL-4,IFN-γ, SP、VIP、NPY
Guo 2018 [52]	China	Wistar rats, half female and half male	Acupuncture(10)	Dazhui (GV14), Feishu (BL13), Shenshu (BL23)	14 days	Blank group(10); AR model group(10); Western medicine group(10)	Nasal symptom score, histopathological changes in the nasal mucosa, EOS, IL-4、IL-12, GATA-3 mRNA
Hou 2014 [53]	China	SD rats, half female and half male	Acupoint injection (12); Acupoint injection + Acupoint catgut embedding (12)	Yintang (EX-HN3), Yingxiang (LI20), Feishu (BL13), Pishu (BL20), Shenshu (BL23)	Once every 7 days, 2 times	Blank group (12); AR model group(12)	Behavioral indexes, OVAsIgE, IFN-γ, IL-4, histopathological changes in the nasal mucosa
Hu 2019 [54]	China	Wistar rats, male	Acupoint application: Raw mustard seed (10); Fried mustard seed (10)	Feishu (BL13), Pishu (BL20), Shenshu (BL23)	Once every other day, 7 times	Blank group(10); AR model group(10); Western medicine group(10)	Behavioral indexes, IgE, IL 4, IFN-γ
Hu 2023 [55]	China	SD rats, half female and half male	Acupuncture(10)	Yingxiang (LI20), Hegu (LI4)	10 days	Blank group(10); AR model group(10)	Behavioral indexes, histopathological changes in the nasal mucosa, EOS, Ig E, IFN-γ, IL-2, IL-12, IL-4, IL-5, IL-6, T-bet, GATA-3
Hu,R 2023 [56]	China	SD rats, male	Moxibustion (10)	Yingxiang (LI20), Zusanli (ST36)	7 days was a course of treatment, and 2 courses of intervention	Blank group(10); AR model group(10)	Behavioral indexes, EOS, sIgE, IL-4, IFN-γ, SP, GFAP, OX-42

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Table 2 (*continued*)

Study	Country	Animals (Species, Sex)	Intervention treatment (n)	Acupoints	Acupuncture Treatment Course	Control Group (n)	Outcome Measurement
Hu,R; Liu,Y 2023 [57]	China	SD rats, half female and half male	Moxibustion (10)	Zusanli (ST36)	14 days	Blank group(10); AR model group(10); Sham group(10)	Behavioral indexes, histopathological changes in the nasal mucosa, EOS, sIgA, $CD4^+$, $CD8^+$
Huang 2020 [58]	China	SD rats, female	Acupoint catgut embedding (15)	Baihui (GV20), Feishu (BL13), Pishu (BL20)	3 weeks	Blank group(15); AR model group(15)	Behavioral indexes, histopathological changes in the nasal mucosa and lung tissue and hippocampus, OX-42, IgE, IL-4, NKB, TLR-2
Huang,Y 2020 [59]	China	SD rats, female	Acupoint catgut embedding (8)	Yingxiang (LI20)	Once a week, 2 times	Blank group(8); AR model group(8); Western medicine group(8); Sham group(8)	Behavioral indexes, sIgE, IL-2, IL-4, IL-5, IL-6, IL-10, IL-12, histopathological changes in the nasal mucosa, CD80、CD86
Chen,J 2008 [60]	China	BALB/c mice, female	Acupoint catgut embedding (12)	Dazhui (GV14)	4 weeks	Blank group(12); AR model group(12); Western medicine group(12); Phosphate buffer (PBS) group(12)	EOS, sIgE
Jin 2020 [61]	China	Wistar rats, male	Acupoint application: Raw mustard seed (10); Fried mustard seed (10)	Feishu (BL13), Pishu (BL20), Shenshu (BL23)	Once every other day, 7 times	Blank group(10); AR model group(10); Western medicine group(10)	Behavioral indexes, IL-1β, IL-6, TNF-α, IFN-γ, mast cells
Jin 2018 [62]	China	Wistar rats, male	Acupoint application(10)	Feishu (BL13), Pishu (BL20), Shenshu (BL23)	Once every other day, 7 times	Blank group(10); AR model group(10); Western medicine group(10)	EOS, histopathological changes in the nasal mucosa, TLR4, NF-κB mRNA, NF-κB
Zhang,Q 2022 [63]	China	SD rats, half female and half male	Acupoint injection(8); Acupoint injection + Moxibustion(8); Acupoint injection + Acupoint catgut embedding (8); Acupoint injection + Acupuncture (8)	Yingxiang (LI20), Zusanli (ST36), Feishu (BL13), Zusanli (ST36)	14 days	Blank group(8); AR model group(8)	Nasal symptom score, histopathological changes in the nasal mucosa,IFN-γ、IL-4
Li 2022 [64]	China	SD rats, male	Acupoint catgut embedding(9)	Yingxiang (LI20)	14 days	Blank group(9); AR model group(9); Western medicine group(9)	histopathological changes in the nasal mucosa, MC, SP, β-tryptase
Li 2015 [65]	China	SD rats, male	Acupoint catgut embedding(15)	Yingxiang (LI20)	14 days	Blank group(15); AR model group(15)	Behavioral indexes, EOS, ICAM - 1
Li 2014 [66]	China	SD rats, male	Acupoint catgut embedding(15)	Yingxiang (LI20)	14 days	Blank group(15); AR model group(15)	Behavioral indexes, histopathological changes in the nasal mucosa, SP, CGRP, NKA
Liu 2019 [67]	China	New Zealand large-eared rabbits, male	Acupuncture at Wai yingxiang (6); Intranasal acupuncture (6)	Yingxiang (LI20); Neiyingxiang (EX-HN9)	Once every other day, 7 times	Blank group(6); AR model group(6); Sham group(6)	Behavioral indexes, routine blood test, IgE, histopathological changes in the nasal mucosa, TRPV1, SP
Liu 2013 [68]	China	SD rats, half female and half male	Acupoint catgut embedding(14)	Baihui (GV20), Feishu (BL13), Pishu (BL20)	4 weeks	Blank group(14); AR model group(14); Sham group(14); Western medicine group(14)	The symptom scores, histopathological changes in the nasal mucosa, IgE, IFN-Y, IL-4, TGF-B1, IL-17, SP
Liu,QF 2013 [69]	China	SD rats, half female and half male	Acupoint application(8)	Dazhui (GV14), Feishu (BL13), Pishu (BL20), Shenshu (BL23)	14 days	Blank group(8); AR model group(8); Western medicine group(8); Integrated Chinese and Western medicine group(8)	The number of nasal rubbing, sneezing, histopathological changes in the nasal mucosa, IgE, leukotrienes D4, histamine, the mast cell degranulation rate
Liu 2011 [70]	China	Clean grade mice, half female and half male	Medicinal vesiculation(10)	Dazhui (GV14), Feishu (BL13)	7 days	Blank group(10); AR model group(10); Western medicine group(10)	Symptom observation, Allergy incubation period, EOS, MC, Ig E, IL-4
Lu 2013 [71]	China	SD rats, half female and half male	Acupuncture(10)	Zusanli (ST36), Feishu (BL13), Shenshu (BL23)	7 days	Blank group(10); AR model group(10); Western medicine group(10)	IL-5, IL-5 mRNA

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Table 2 (*continued*)

Study	Country	Animals (Species, Sex)	Intervention treatment (n)	Acupoints	Acupuncture Treatment Course	Control Group (n)	Outcome Measurement
Yang 2015 [72]	China	Wistar rats, male	Acupoint injection(10)	Quchi (LI11)	7 days	AR model group(10); Physiological saline group(10); Acupoint injection group(10)	Behavioral indexes, EOS, histopathological changes in the nasal mucosa
Pu 2018 [73]	China	SD rats, male	Press needle(10)	Dazhui (GV14), Feishu (BL13)	14 days	Blank group(10); AR model group(10); Western medicine group(10)	Nasal symptom score, histopathological changes in the nasal mucosa, IgE, IL-4, IL-2
Tai 2008 [74]	China	SD rats, both male and female	Acupuncture(10)	Xiaguan (ST7)	7 days	Blank group(10); AR model group(10)	Behavioral indexes, histopathological changes in the nasal mucosa
Xie 2007 [75]	China	SD rats, female	Acupoint application(10)	Dazhui (GV14)	4 weeks	Blank group(10); AR model group(10); Western medicine group(10)	IL-4, IFN-γ
Wang 2005 [76]	China	SD rats, half female and half male	Electroacupuncture: Low frequency (8); High frequency (8)	Feishu (BL13)	10 days	AR model group(8); Western medicine group(8); Sham group (8)	Behavioral indexes, histopathological changes in the nasal mucosa, EOS, IgE, IL-4, CD3, CD4, CD8, CD4/CD8, TNF
Wang 2012 [77]	China	Hartley guinea pigs, half female and half male	Acupunture Therapy by Dispersing the Stagnated Liver-Oi(8)	Yingxiang (LI20), Feishu (BL13)), Ganshu (BL18), Taichong (LR3)	15 days	Blank group(8); AR model group(8); Western medicine group(8); Conventional acupuncture group(8)	Behavioral indexes, IFN-γ, IL-4, IgE
Wu 2013 [78]	China	SD rats, half female and half male	Acupuncture(12)	Dazhui (GV14), Feishu (BL13), Shenshu (BL23)	10 days	AR model group(12); Western medicine group(12)	EOS, histopathological changes in the nasal mucosa
Zheng 2021 [79]	China	SD rats, male	Acupoint catgut embedding(10)	Baihui (GV20), Feishu (BL13), Pishu (BL20)	4 weeks	AR model group(10); Western medicine group(10)	Behavioral indexes, **IgE**, Eotaxin, **IFN-γ, IL-4, IL-5**, IL-17, p-JNK, histopathological changes in the nasal mucosa
Wang 2021 [80]	China	SD rats, male	Moxibustion(30)	Feishu (BL13)	28 days	Blank group(10); AR model group(10); Western medicine group(10)	Behavioral indexes, histopathological changes in the nasal mucosa, IgE, IL-4, IL-5, IL-13, IL-12, IFN-γ, $CD3^+$, $CD4^+$, Th1, Th2
Wang,Y 2019 [81]	China	SD rats, half female and half male	Acupoint injection(8)	Yintang (EX-HN3), Yingxiang (LI20)	7 days	Blank group(8); AR model group(8); Sham group(8)	The symptom scores, IL-17, Foxp3、RORγt
Xiang 2014 [82]	China	SD rats, half female and half male	Acupoint application(10)	Dazhui (GV14), Feishu (BL13), Pishu (BL20), Neiguan (PC6)	30 days	Blank group(10); AR model group(10); Western medicine group(10)	General situation, IgE, IL-2, ECP, ICAM-l
Xu 2010 [83]	China	Dutch guinea pigs, half female and half male	Acupoint injection(10)	Yingxiang (LI20)	7 days	Blank group(10); AR model group(10); Sham group(point injecting water group:10; non-point injecting astragalus group:10)	The symptom scores, histopathological changes in the nasal mucosa, LTB4, IgE
Zhang,L 2017 [84]	China	SD rats, half female and half male	Acupoint application(10)	Dazhui (GV14), Feishu (BL13), Pishu (BL20), Shenshu (BL23)	14 days	Blank group(10); AR model group(10); Western medicine group(10)	Behavioral indexes, EOS, IgE, IL-4, LTC4
Xue 2015 [85]	China	BALB/c mice, male	Acupuncture + model(6); Acupuncture (6)	Yingxiang (LI20)	7 days	Blank group(6); AR model group(6); Western medicine group(6)	The symptom scores, histopathological changes in the nasal mucosa, sIgE, IL-1β, IL-10
Yang 2009 [86]	China	Wistar rats, male	Acupoint injection(10)	Quchi (LI11)	7 days	Blank group(10); AR model group(10); Muscle injection group(10); Physiological saline group(10)	The symptom scores, histamine

(*continued on next page*)

Table 2 (*continued*)

Study	Country	Animals (Species, Sex)	Intervention treatment (n)	Acupoints	Acupuncture Treatment Course	Control Group (n)	Outcome Measurement
Yang,SS 2018 [87]	China	SD rats, male	Acupoint catgut embedding: 1 week(10); 2 weeks (10)	Yingxiang (LI20)	7 days, 14 days	Blank group(10); AR model group(10); Western medicine group(10); Sham group(10)	Behavioral indexes, histopathological changes in the nasal mucosa, sIgE, IL-4, IFN-r, SP, NF-kBp65, TLR2, TLR4, Mast cell degranulation rate, TNF-α, IL-6, GFAP, OX-42
Yang 2017 [88]	China	SD rats, male	Acupoint catgut embedding: 1 week(8); 2 weeks(8); 3 weeks(8)	Yingxiang (LI20), Quchi (LI11), Zusanli (ST36)	14 days	Blank group(8); AR model group(8); Western medicine group(8)	Behavioral indexes, histopathological changes in the nasal mucosa, Mast cell degranulation rate, SP、NF-κBp65, TLR2、TLR4
Zhang 2020 [89]	China	SD rats, female	Acupoint catgut embedding(8)	Yingxiang (LI20)	Once a week for 2 consecutive weeks	Blank group(8); AR model group(8); Western medicine group(8); Sham group(8)	Behavioral indexes, sIgE, histopathological changes in the nasal mucosa, Endoplasmic reticulum morphology, Epithelial cell junction, Claudin-1, Occludin
Zhang,MN 2020 [90]	China	SD rats, female	Acupoint catgut embedding(6)	Yingxiang (LI20)	Day 29 and day 36	Blank group(6); AR model group(6)	Behavioral indexes, histopathological changes in the nasal mucosa, Endoplasmic reticulum morphology, Epithelial cell junction, Claudin-1, Occludin
Zhang,NY 2011 [91]	China	SD rats, half female and half male	Acupuncture (10)	Dazhui (GV14), Feishu (BL13),Shenshu (BL23)	10 days	Blank group(10); AR model group(10); Western medicine group(10)	Behavioral indexes, EOS, leukotrienes , IL-4, Toll-like receptor, NF-κB
Zhang 2017 [92]	China	SD rats, half female and half male	Acupoint injection(8)	Yintang (EX-HN3), Yingxiang (LI20)	7 days	Blank group(8); AR model group(8)	EOS, Eotaxin, Eotaxin mRNA
Liang 2018 [93]	China	SD rats, half female and half male	Acupoint injection(8)	Yintang (EX-HN3), Yingxiang (LI20)	Once every 3 days, 4 times	Blank group(8); AR model group(8); Sham group(8)	Behavioral indexes, H1R, H4R, H4R mRNA
Zhao 2008 [94]	China	SD rats, half female and half male	Acupoint injection(10)	Yintang (EX-HN3), Feishu (BL13), Zusanli (ST36)	5 times for a course	AR model group(10); Intramuscular injection group (10); Physiological saline group (10)	Symptom scores, EOS, CD4, CD8, CD4/CD8, curative effect, histopathological changes in the nasal mucosa
Zheng 2009 [95]	China	SD rats, half female and half male	Acupoint application(10)	Dazhui (GV14), Feishu (BL13), Shenshu (BL23)	14 days	Blank group(10); AR model group(10); Western medicine group(10)	Behavioral indexes, IgE, IFN-γ, IL-4, histopathological changes in the nasal mucosa, EOS
Zheng,XL 2018 [96]	China	Wistar rats, half female and half male	Acupuncture (10)	Fengchi (GB20), Yintang (EX-HN3), Yingxiang (LI20)	10 days	Blank group(10); AR model group(10); Western medicine group(10)	Behavioral indexes, IgE, IL-1β, TNF-α
Zhou 2023 [97]	China	SD rats, male	Acupoint injection(8)	Yintang (EX-HN3), Yingxiang (LI20)	Once every 4 days, 4 times	Blank group(8); AR model group(8); Sham group(8)	The symptom scores, histopathological changes in the nasal mucosa, IgE, IL-4, IFN-γ, TLR4, MyD88, AP-1
Chen 2018 [98]	China	SD rats, half female and half male	Acupoint catgut embedding(12)	Yintang (EX-HN3)	14 days	Blank group(12); AR model group(12)	IL-4, IL-10, INF-Y, sIgE
Huang 2013 [99]	China	SD rats, half female and half male	Acupuncture(10)	Zusanli (ST36), Feishu (BL13), Shenshu (BL23)	14 days	Blank group(10); AR model group(10); Western medicine group(10)	IL-5, histamine
Chen 1999 [100]	China	Hartley guinea pigs, half female and half male	Pricking Acupoint Blood (8)	Yintang (EX-HN3), Quchi (LI11), Zusanli (ST36), Hegu (LI4)	10 days	Blank group(8); AR model group(8); Western medicine group(8)	Behavioral indexes, histopathological changes in the nasal mucosa

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Table 2 (*continued*)

Study	Country	Animals (Species, Sex)	Intervention treatment (n)	Acupoints	Acupuncture Treatment Course	Control Group (n)	Outcome Measurement
Liu 2020 [101]	China	SD rats, male	Acupoint catgut embedding(10)	Yingxiang (LI20)	28 days	Blank group(10); AR model group(10)	The symptom scores, lung tissues histomorphology, OPN
Liu,M 2016 [102]	China	SD rats, half female and half male	Acupoint catgut embedding(14)	Baihui (GV20), Feishu (BL13), Pishu (BL20)	Once every 2 weeks, 2 times	Blank group(14); AR model group(14); Western medicine group(14); Sham group(14)	The symptom scores, IL-17, TGF-β1
Zhang,Y 2017 [103]	China	SD rats, half female and half male	Acupoint injection(8)	Yintang (EX-HN3), Yingxiang (LI20)	After the success of the model, there were four treatments on days 1, 5, 9, and 13	Blank group(8); AR model group(8); Sham group(8)	Behavioral indexes, Foxp3 mRNA, Foxp3, RORγt, IL-17
Zhou 2019 [104]	China	SD rats, half female and half male	Acupuncture(10)	Xiaguan (ST7)	7 days	Blank group(10); AR model group(10); Western medicine group(10)	The symptom scores, IL-6, TNF-α

Note: Individual study ID was established by the first author's name and year of publication.

Abbreviations: AR, allergic rhinitis; EOS, Eosinophils; SP, Substance P; STAT6, Signal Transduction and Transcription Activating Factor 6; NFkB, Nuclear factor activated B cells κ- Light chain enhancement; iNOS, inducible nitric oxide synthase; NGF, nerve growth factor; IL-4, Interleukin-4; IL-5, Interleukin-5; IL-13, Interleukin-13; Ig, Immunoglobulin; IFN-γ, interferon-gamma; CIAA, Catgut Implantation at Acupoint; SIgE, Specific Immunoglobulin E; TLR, Toll-like receptor; Th, T helper cell; BAL, Bronchoalveolar lavage; TGF-β1, transforming growth factor-β1; HE staining, hematoxylin-eosin staining; CGRP, calcitonin-gene-related peptide; VIP, Vasoactive Intestinal Peptide; ECP, eosinophil cationic protein; NPY, neuropeptide Y; GATA-3, GATA binding protein 3; OVA, Ovalbumin; T-bet, T-box transcription factor; GFAP, glial fibrillary acidic protein; CD, cluster of differentiation; NKB, Neurokinin B; TNF, tumor necrosis factor; MC, mast cell; ICAM - 1, intercellular cell adhesion molecule-1; NKA, Neurokinin A; Foxp3, forkheadbox Protein 3; LTB4, Leukotriene B4; LTC4, Leukotriene C4; H1R, histamine 1 receptor; H4R, histamine 4 receptor; MyD88, myeloiddifferentiationfactor88; AP-1, activator protein-1; OPN, osteopontin; MC, must cell.

2.8. Statistical analysis

Meta-analysis was conducted when three or more studies reported data on the same outcome. All statistical analyses were performed using Review Manager (RevMan) Version 5.4 and Stata software version 17.0. For continuous variables, the input data were expressed as means and SD, and the effect measures were expressed as standardized mean difference (SMD) [25]. Heterogeneity among the included studies was assessed using I^2 test. If the data had low heterogeneity ($P \geq 0.05$ and $I^2 \leq 50$ %), the effect size was analyzed with a fixed effect model; if the data had significant heterogeneity ($P < 0.05$ or $I^2 > 50$ %), the effect size was analyzed with a random effect model. Sensitivity analysis was conducted to estimate the stability and reliability of the results by removing each individual study from the analysis one at a time. Meta-regression and subgroup analyses were used to further analyze the causes of heterogeneity, focusing on the following groups as possible: intervening measure, risk of bias assessment, and animal species. In addition, Egger's tests were used to investigate the possibility of publication bias if the number of included studies for the same outcome was more than ten. Results are reported as p values with 95 % confidence intervals (CI). Forest plots and funnel plots were used to display the results of the meta-analyses.

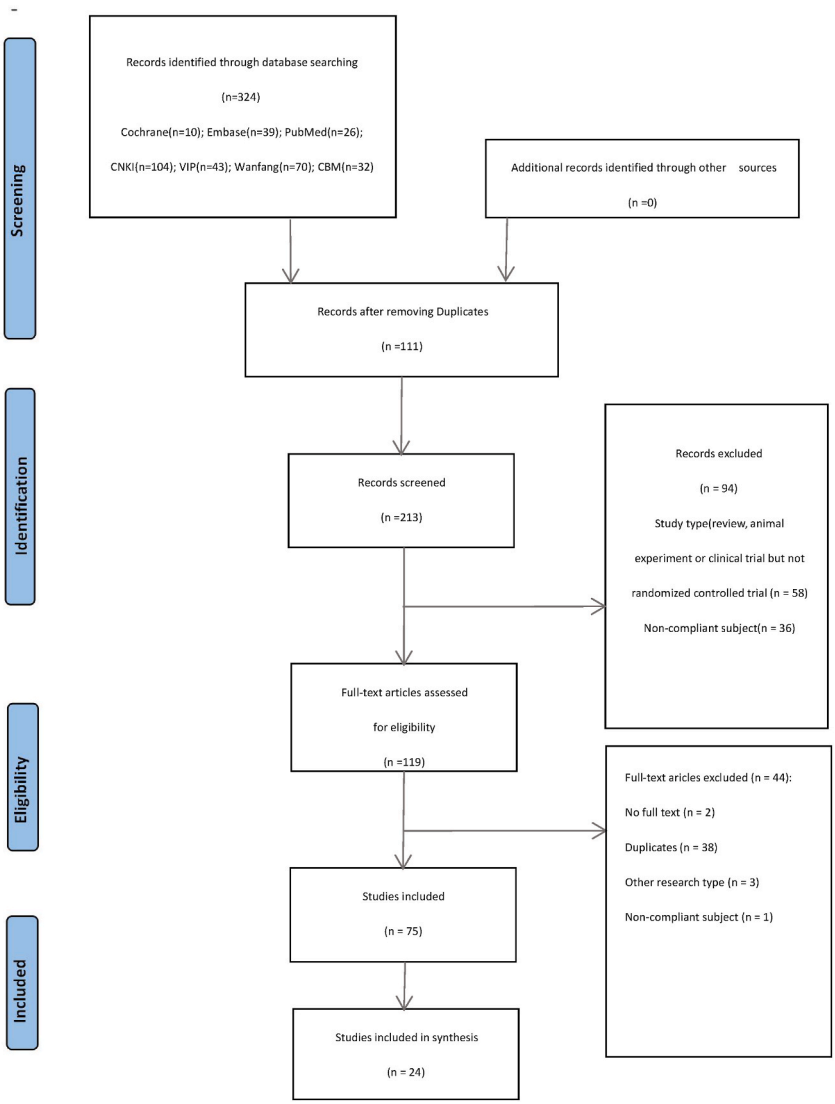
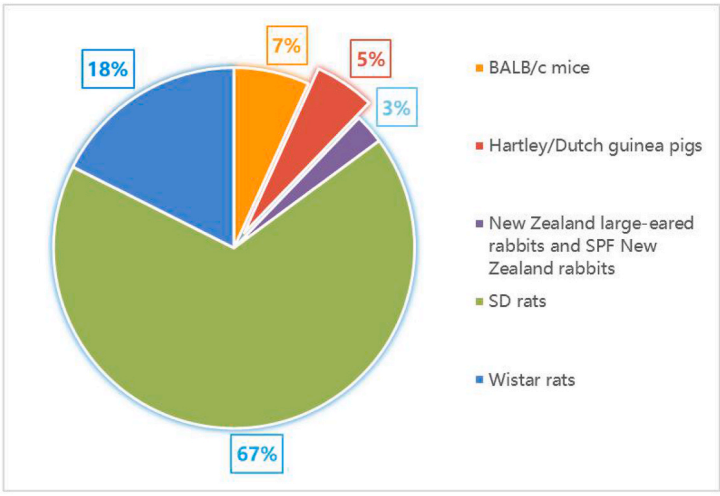
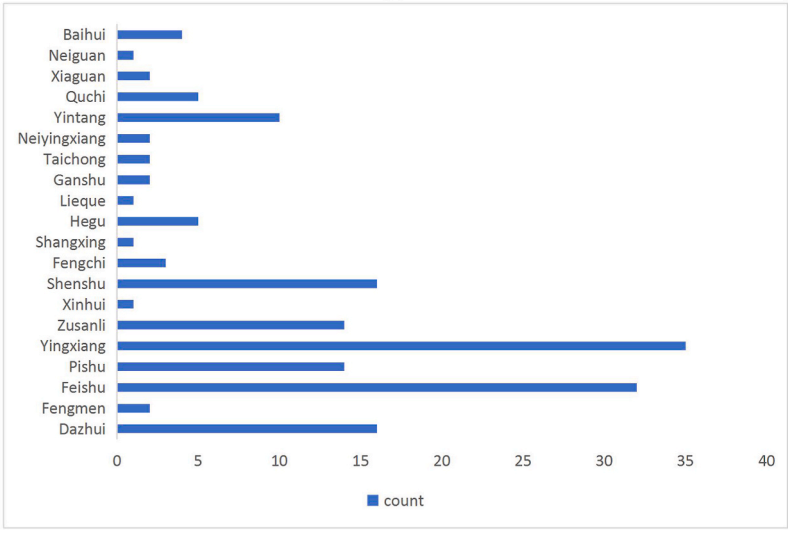


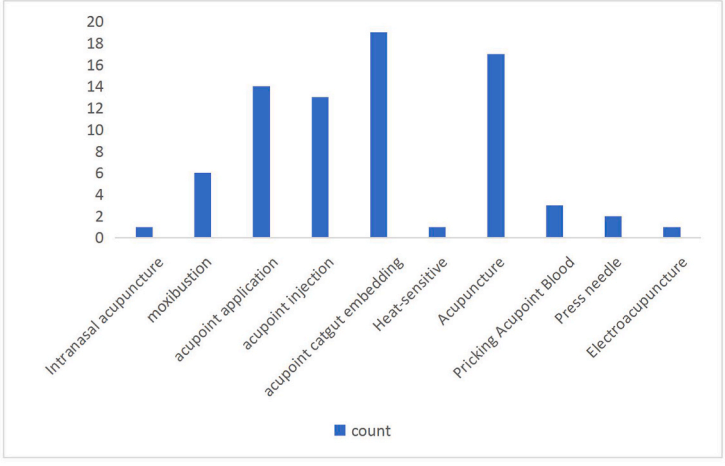
Fig. 1. Flow diagram of the study.



(A)



(B)



(C)

Fig. 2. The characteristics of included studies.
Notes: (A)The animal species of included studies, (B)The selection of points in included studies, (C)The types of acupuncture used in included studies, (D)The duration of treatment in included articles.

3. Results

3.1. Search results and study selection

Fig. 1 presents a detailed flowchart outlining the identification, screening, exclusion, and inclusion of articles. The electronic search across all databases resulted in a total of 324 potentially relevant records. After the removal of duplicates, 213 articles remained. After screening the title and abstract based on inclusion criteria, 94 irrelevant articles were excluded. The remaining 119 studies underwent full-text review, of which 44 were excluded. A list of excluded studies is provided in Supplementary Table S2.

3.2. Study characteristics

A total of 75 studies were included [30–104]. Most studies used Sprague Dawley rats (SD rats). Moreover, Wistar rats, BALB/c mice, Dutch guinea pigs, Hartley guinea pigs and New Zealand large-eared rabbits were also adopted. Among the 75 animal studies, nine used female animals, twenty-six used males, and forty studies used both female and male animals. All AR animal models were developed with OVA as the specific antigen. 58 studies mentioned the methods to verify the successful establishment of the model.

Acupoint application was employed in 14 studies, acupoint catgut embedding in 19 studies, acupoint injection in 13 studies, moxibustion in 6 studies, and pricking blood therapy in 3 studies. Additionally, intradermal needling, electroacupuncture, intranasal needle, heat-sensitive moxibustion and press-needle were also used. The characteristics of the studies are provided in Table 2 and Fig. 2.

3.3. Quality assessment

The risk of bias in the included studies was assessed using the SYRCLE tool, with the results illustrated in Table 3 and Fig. 3. 36 studies adequately described the method of randomized sequence generation, while 38 studies mentioned randomization but did not describe the specific method. All studies reported the similarity of each group at baseline. However, none of the studies reported the methods of allocation concealment and random housing of animals, resulting in an "unclear risk" of bias. Additionally, clear information on whether the caregivers and researchers were blinded, or whether animals were randomly selected for outcome assessment, was not provided. None of the studies blinded the caregivers or investigators to the intervention, with only 3 studies blinding the outcome evaluators. 13 studies provided no explanation for incomplete outcome data. Ideally, we would have compared the results listed in each study protocol with those reported in the papers, but since this was impossible, we compared the results reported in the included studies with those listed in the methods section [26]. In 5 studies, the outcomes reported in the methods section were not fully consistent with the final reported results. The risk of bias scores ranged from 3 to 7, with means ± SD of 4.37 ± 0.85.

Reporting quality were evaluated according to the ARRIVE 2.0 checklist. The quality was poor for item 5 (Blinding), item 14 (Ethical statement), item 16 (Animal care and monitoring), item 18 (Generalizability/translation), item 19 (Protocol registration) and item 20 (Data access). The details are presented in Table 4 and Fig. 4. Regarding the study design, most studies did not fully describe the randomization or whether blinding was used. In terms of sample size, inclusion and exclusion criteria, outcome measures, and other parts, most studies either partly reported or did not report these details, which would decrease the reliability of experiments. The quality scores ranged between 6.5 and 11, with a mean ± SD of 8.78 ± 0.97.

3.4. Results of meta-analysis

3.4.1. Behavioral scores

Regarding the behavioral scores, 37 studies were included. Due to significant heterogeneity ($I^2 = 86\ \% > 50\ \%$, $P < 0.01$) and the inability to identify its source, we only performed a qualitative analysis. In the included studies, the behavioral scores of the acupuncture group were significantly lower than those of the AR model group, including moxibustion [35,39,56,57,80], acupoint catgut embedding [38,40,59,68,79,87,89,101,102], needle puncture at acupoints [44,48,50–52,55,73,96,104], acupoint injection [32,53,63,81,83,86,93,94,97,103], and acupoint application [31,42,54,61]. Although other studies have not compared the acupuncture group with the AR model group [46,47], they have indicated that acupuncture therapy exhibits better efficacy compared to the pre-treatment. In summary, behavioral scores have been used as a simple and objective index of therapeutic effect, and animals in the acupuncture group showed a significant improvement in AR symptoms.

3.4.2. The serum levels of IL-5

Regarding the levels of IL-5, 7 trials were included in the meta-analysis. A random effect model was adopted due to statistically significant heterogeneity ($I^2 = 79\ \% > 50\ \%$, $P < 0.01$). The result showed that acupuncture significantly reduced serum levels of IL-5 in comparison with the AR models group [SMD = -4.25, 95 % CI = (−5.67, −2.83), $P < 0.01$] (Fig. 5). We undertook a series of sensitivity analyses to examine the robustness of the results. Analysis for serum levels of IL-5 showed that the heterogeneity disappeared when one study (Wang 2021) was removed ($I^2 = 0.0\ \% < 50\ \%$, $P = 0.84 > 0.05$), with no changes in results despite the reductions in heterogeneity. Therefore, we reasoned that this study might have contributed to the heterogeneity (Fig. 6).

3.4.3. EOS count

Regarding the EOS count, 19 trials were included in the meta-analysis. Because of the significant heterogeneity ($I^2 = 89\ \% > 50\ \%$,

Table 3
Risk of Bias assessment based on the SYRCLE Tool.

Study	1	2	3	4	5	6	7	8	9	10	Scores
Jung, D. 2012	?	L	?	?	?	?	?	L	L	L	4
Tu 2020	?	L	?	?	?	?	?	?	L	L	3
Yang 2016	L	L	?	?	?	?	?	L	L	L	5
Yang 2018	?	L	?	?	?	?	?	?	L	L	3
Han 2019	?	L	?	?	?	?	?	L	L	L	4
Zhang 2011	?	L	?	?	?	?	?	L	L	L	4
Chen 2006	?	L	?	?	?	?	?	L	L	L	4
Chen 2012	L	L	?	?	?	L	?	L	L	L	6
Chen 2016	?	L	?	?	?	?	?	L	L	L	4
Chen 2017	L	L	?	?	?	?	?	L	L	L	5
Chen 2015	L	L	?	?	?	?	?	L	L	L	5
Chen Q 2016	L	L	?	?	?	?	?	L	L	L	5
Chen 2019	L	L	?	?	?	?	?	L	L	L	5
Chen,XL 2019	?	L	?	?	?	?	?	L	L	L	4
Song 2011	?	L	?	?	?	?	?	L	L	L	4
Chen,Y 2012	L	L	?	?	?	?	?	L	L	L	5
Chen 2003	?	L	?	?	?	?	?	L	L	L	4
Chen,YH 2003	?	L	?	?	?	?	?	L	L	L	4
Ding 2015	L	L	?	?	?	?	?	L	L	L	5
Zhao 2010	?	L	?	?	?	?	?	L	L	L	4
Geng 2013	L	L	?	?	?	?	?	L	L	L	5
Gong 2021	L	L	?	?	?	?	?	L	L	L	5
Guo 2018	?	L	?	?	?	?	?	?	L	L	3
Hou 2014	?	L	?	?	?	?	?	L	L	L	4
Hu 2019	L	L	?	?	?	?	?	L	L	L	5
Hu 2023	L	L	?	?	?	?	?	L	L	L	5
Hu,R 2023	L	L	?	?	?	?	?	?	L	L	4
Hu,R; Liu,Y 2023	L	L	?	?	?	?	?	L	L	L	5
Huang 2020	L	L	?	?	?	?	?	L	L	L	5
Huang,Y 2020	?	L	?	?	?	?	?	H	L	L	3
Chen,J 2008	?	L	?	?	?	?	?	L	L	L	4
Jin 2020	L	L	?	?	?	?	?	?	L	L	4
Jin 2018	L	L	?	?	?	L	?	L	L	L	6
Zhang,Q 2022	?	L	?	?	?	?	?	L	L	L	4
Li 2022	L	L	?	?	?	?	?	?	L	L	4
Li 2015	L	L	?	?	?	?	?	L	L	L	5
Li 2014	L	L	?	?	?	?	?	L	L	L	5
Liu 2019	L	L	?	?	?	?	?	?	?	L	3
Liu 2013	L	L	?	?	?	L	L	L	L	L	7
Liu,QF 2013	L	L	?	?	?	?	?	L	L	L	5
Liu 2011	?	L	?	?	?	?	?	L	H	L	3
Lu 2013	?	L	?	?	?	?	?	L	L	L	4
Yang 2015	?	L	?	?	?	?	?	L	L	L	4
Pu 2018	L	L	?	?	?	L	?	L	L	L	6
Tai 2008	?	L	?	?	?	?	?	?	L	L	3
Xie 2007	H	L	?	?	?	?	?	L	L	L	4
Wang 2005	?	L	?	?	?	?	?	L	L	L	4
Wang 2012	L	L	?	?	?	?	?	L	L	L	5
Wu 2013	L	L	?	?	?	?	?	L	L	L	5
Zheng 2021	?	L	?	?	?	?	?	L	L	L	4
Wang 2021	L	L	?	?	?	L	?	L	L	L	6
Wang,Y 2019	?	L	?	?	?	?	?	L	L	L	4
Xiang 2014	?	L	?	?	?	?	?	L	H	L	3
Xu 2010	L	L	?	?	?	?	?	L	L	L	5
Zhang,L 2017	?	L	?	?	?	?	?	L	L	L	4
Xue 2015	?	L	?	?	?	?	L	?	L	L	4
Yang 2009	?	L	?	?	?	?	?	L	L	L	4
Yang,SS 2018	L	L	?	?	?	?	?	?	L	L	4
Yang 2017	L	L	?	?	?	?	?	L	L	L	5
Zhang 2020	L	L	?	?	?	?	?	H	L	L	4
Zhang,MN 2020	L	L	?	?	?	?	?	L	L	L	5
Zhang,NY 2011	?	L	?	?	?	?	?	L	L	L	4
Zhang 2017	?	L	?	?	?	?	?	L	L	L	4
Liang 2018	?	L	?	?	?	?	?	L	L	L	4
Zhao 2008	L	L	?	?	?	?	L	L	L	L	6
Zheng 2009	?	L	?	?	?	?	?	L	L	L	4
Zheng,XL 2018	L	L	?	?	?	?	?	L	L	L	5
Zhou 2023	?	L	?	?	?	L	?	L	L	L	5

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Table 3 (*continued*)

Study	1	2	3	4	5	6	7	8	9	10	Scores
Chen 2018	L	L	?	?	?	?	?	L	L	L	5
Huang 2013	?	L	?	?	?	?	?	L	L	L	4
Chen 1999	?	L	?	?	?	?	?	?	L	L	3
Liu 2020	?	L	?	?	?	?	?	L	L	L	4
Liu,M 2016	L	L	?	?	?	L	?	L	?	L	5
Zhang,Y 2017	?	L	?	?	?	?	?	L	L	L	4
Zhou 2019	?	L	?	?	?	?	?	L	?	L	3

Notes: L, low-risk bias; H, high risk bias; ?, unclear.

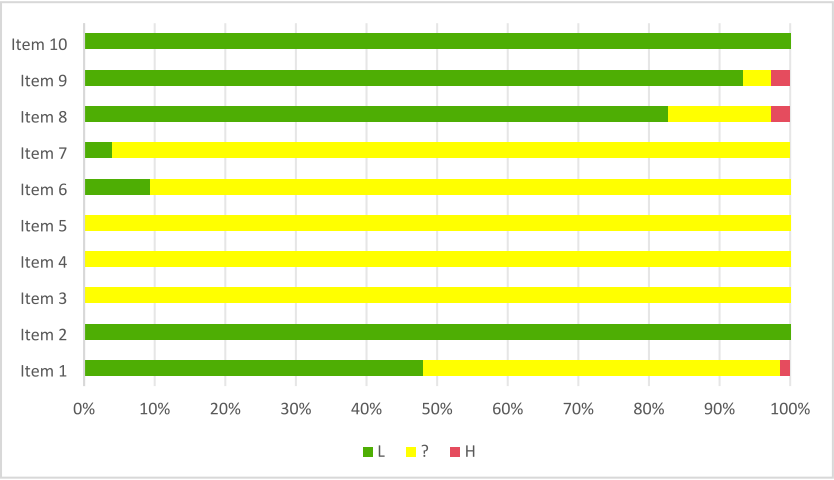

Fig. 3. SYRCLE percentage distribution diagram (%).

$P < 0.01$), a random effect model was used for data consolidation analysis. The results suggested that the experiment group significantly reduced the EOS count compared to the control group [SMD = -4.24, 95%CI = (−5.28, −3.19), $P < 0.01$] (Fig. 7). Acupuncture therapy could reduce both blood EOS [SMD = -2.22, 95%CI = (−4.01, −0.42), $P < 0.05$] and nasal mucosal EOS counts [SMD = -4.63, 95%CI = (−5.89, −3.38), $P < 0.01$], with statistically significant differences. Meta-regression was performed to identify the sources of heterogeneity, which indicated that different interventions were likely to be the sources of heterogeneity in the nasal mucosal EOS count subgroup ($P = 0.026 < 0.05$). Therefore, we further conducted a subgroup analysis based on the different types of interventions. The subgroup of acupoint injection showed significantly lower heterogeneity ($I^2 = 0$ %, $P > 0.05$), while heterogeneity remained high in the other subgroups. The results of the subgroup analysis are presented in Fig. 8.

3.4.4. Other immunological indicators

In the included studies, various acupuncture therapies were employed as the experimental groups. Due to statistically significant heterogeneity and the inability to determine its source ($I^2 > 50$ %, $P < 0.05$), only qualitative analyses were performed.

Regarding the serum levels of IL-4, 29 studies showed that acupuncture treatment groups significantly reduced IL-4 levels, including acupoint application [31,36,37,43,54,70,75,84,95], acupoint catgut embedding [33,38,41,58,59,79,87,98], moxibustion [39,56,80], needle puncture at acupoints [44,45,51,52,55,73,76], and acupoint injection [53,97]. However, Wang 2012 [77] has shown that there was no significant difference between the needle puncture group and the AR model group. Collectively, acupuncture may potentially reduce IL-4 and IL-5 levels, thereby ameliorating the inflammatory response.

In terms of the serum levels of IFN-γ, 18 studies demonstrated that the levels of IFN-γ were significantly up-regulated in the acupuncture groups compared to AR model groups, including acupoint application [31,36,37,43,54,61,75], needle puncture at acupoints [45,51,55], acupoint injection [53,97], moxibustion [56,80], and acupoint catgut embedding [41,79,87,98]. However, Wang 2012 [77] has shown that there was no significant difference between the needle puncture group and the AR model group. Overall, the results indicated that acupuncture could up-regulate IFN-γ levels, which may contribute to maintaining the dynamic balance between Th1 and Th2.

Regarding the serum levels of IgE, 25 studies demonstrated that acupuncture decreased IgE levels compared to the AR model groups, including moxibustion [35,39,80], acupoint catgut embedding [38,58,68,79], acupoint application [31,42,43,54,69,70,82,84,95], needle puncture at acupoints [51,55,67,73,76,96], and acupoint injection [53,83,97]. However, Wang 2012 [77] has shown that there was no significant difference between the needle puncture group and the AR model group. Overall, acupuncture could significantly decrease IgE levels, thereby alleviating the inflammatory reaction.

In addition, acupuncture treatment decreased the serum sIgE levels compared to the AR model groups, including acupoint

Table 4
Reporting quality assessment based on ARRIVE 2.0 guidelines.

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Scores
Jung, D. 2012	P	P	P	P	N	P	P	P	P	Y	Y	P	Y	P	N	N	P	P	N	N	Y	10
Tu 2020	P	N	P	P	N	P	P	P	P	P	Y	P	Y	P	P	N	P	N	N	Y	P	9.5
Yang 2016	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	N	N	N	P	9
Yang 2018	P	P	P	N	N	P	P	P	P	P	P	P	Y	P	N	N	Y	N	N	Y	Y	9.5
Han 2019	P	P	P	P	N	P	P	Y	P	P	Y	P	Y	Y	P	N	P	P	N	N	P	10.5
Zhang 2011	P	P	P	P	N	P	P	P	P	P	P	P	Y	N	Y	N	P	P	N	N	N	8.5
Chen 2006	P	P	P	P	N	P	P	P	P	P	P	P	Y	N	Y	P	Y	P	N	N	N	9.5
Chen 2012	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	P	Y	N	N	N	N	9.5
Chen 2016	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	P	N	N	N	9
Chen 2017	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	P	N	N	P	9.5
Chen 2015	P	P	P	P	N	P	P	P	P	P	P	P	Y	N	Y	P	Y	N	N	N	P	9.5
Chen Q 2016	P	P	P	P	N	N	P	P	P	P	P	P	Y	N	Y	N	P	N	N	N	P	8
Chen 2019	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	N	N	N	P	9
Chen,XL 2019	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	P	P	N	N	N	P	9.5
Song 2011	P	P	P	P	N	P	P	P	P	P	P	P	Y	N	N	N	P	N	N	N	N	7
Chen,Y 2012	P	P	P	P	N	P	P	P	P	P	Y	Y	Y	N	P	N	P	N	N	N	N	8.5
Chen 2003	P	P	P	P	N	P	N	P	P	P	Y	N	Y	N	N	N	P	N	N	N	P	7
Chen,YH 2003	P	P	P	P	N	P	N	P	P	P	P	P	Y	N	N	N	P	N	N	N	P	7
Ding 2015	P	P	P	P	N	P	P	P	P	P	P	P	Y	N	N	P	P	N	N	N	P	8
Zhao 2010	P	P	P	P	N	P	P	P	P	P	Y	N	Y	N	P	N	P	N	N	N	P	8
Geng 2013	P	P	P	P	N	Y	P	P	P	P	P	P	Y	N	P	P	Y	N	N	N	N	9
Gong 2021	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	P	P	N	N	N	P	9.5
Guo 2018	P	N	P	P	N	P	P	P	P	P	Y	P	Y	N	P	N	Y	N	N	N	P	8.5
Hou 2014	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	P	P	P	N	N	N	N	8.5
Hu 2019	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	P	N	P	N	N	N	N	8
Hu 2023	P	P	P	P	N	P	P	P	P	P	P	P	Y	Y	P	N	P	P	N	N	P	9.5
Hu,R 2023	P	P	P	P	N	P	P	P	P	P	Y	P	Y	Y	Y	N	P	N	N	N	P	10
Hu,R; Liu,Y 2023	P	P	P	P	N	P	P	P	P	P	Y	P	Y	Y	P	N	P	N	N	N	P	9.5
Huang 2020	P	P	P	P	N	P	Y	P	P	P	Y	P	N	N	Y	P	Y	N	N	N	P	9.5
Huang,Y 2020	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	Y	N	N	N	P	9.5
Chen,J 2008	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	N	N	N	P	9
Jin 2020	P	P	P	P	N	P	P	P	P	P	Y	P	Y	P	Y	N	P	N	N	N	P	9.5
Jin 2018	P	P	P	P	N	P	P	P	P	P	Y	P	Y	Y	P	N	P	N	N	N	P	9.5
Zhang,Q 2022	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	N	N	N	P	9
Li 2022	P	P	N	P	N	P	P	P	P	P	Y	P	Y	Y	Y	P	P	N	N	N	P	10
Li 2015	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	P	N	P	N	N	N	P	8.5
Li 2014	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	N	N	N	P	9
Liu 2019	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	P	P	N	N	N	N	9
Liu 2013	P	P	P	P	P	P	P	P	P	P	Y	P	Y	N	Y	P	Y	N	N	N	N	10
Liu,QF 2013	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	P	P	N	N	N	N	9
Liu 2011	P	P	P	P	N	P	N	P	P	P	P	P	Y	N	Y	N	P	N	N	N	N	7.5
Lu 2013	P	P	P	P	N	P	P	P	P	P	P	P	Y	N	Y	N	P	N	N	N	N	8
Yang 2015	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	P	P	P	N	N	N	N	8.5
Pu 2018	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	P	Y	N	N	N	N	9.5
Tai 2008	P	P	P	P	N	P	P	P	P	P	P	P	Y	N	N	N	P	N	N	N	N	7
Xie 2007	P	P	P	N	N	P	P	P	P	P	N	N	Y	N	Y	P	P	N	N	N	N	7
Wang 2005	P	P	P	P	N	P	N	P	P	P	P	P	Y	N	P	N	Y	N	N	N	N	7.5
Wang 2012	P	P	P	P	N	Y	P	P	P	P	P	N	Y	N	P	P	P	N	N	N	N	8
Wu 2013	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	P	P	P	N	N	N	N	8.5

(*continued on next page*)

Table 4 (*continued*)

Study	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	Scores
Zheng 2021	P	P	P	P	N	P	P	P	P	P	Y	P	Y	Y	Y	N	P	N	N	N	P	10
Wang 2021	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	P	Y	N	N	N	P	10
Wang,Y 2019	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	N	N	N	P	9
Xiang 2014	P	P	P	P	N	P	P	P	P	P	P	P	Y	N	N	N	P	N	N	N	N	7
Xu 2010	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	P	P	P	N	N	N	N	8.5
Zhang,L 2017	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	P	N	P	N	N	N	P	8.5
Xue 2015	P	P	N	P	Y	P	P	P	P	P	Y	P	Y	N	N	N	P	N	N	N	P	8.5
Yang 2009	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	P	P	P	P	N	N	N	9
Yang,SS 2018	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	P	Y	N	N	N	P	10
Yang 2017	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	P	N	P	P	N	N	P	9
Zhang 2020	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	N	N	N	N	8.5
Zhang,MN 2020	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	P	N	P	N	N	N	P	8.5
Zhang,NY 2011	P	P	P	P	N	P	P	P	P	N	Y	P	Y	N	Y	N	P	N	N	N	N	8
Zhang 2017	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	N	N	N	P	9
Liang 2018	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	N	N	N	P	9
Zhao 2008	P	Y	P	P	Y	P	P	P	P	P	Y	P	Y	N	Y	P	P	P	N	N	N	11
Zheng 2009	P	P	P	P	N	P	N	P	P	P	Y	P	Y	N	P	N	P	N	N	N	N	7.5
Zheng,XL 2018	P	P	P	P	N	P	P	P	P	P	Y	P	Y	P	Y	N	P	N	N	N	P	9.5
Zhou 2023	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	P	N	N	N	P	9
Chen 2018	P	P	P	P	N	N	P	P	P	P	P	P	Y	N	Y	P	P	N	N	N	N	8
Huang 2013	P	P	P	P	N	N	P	P	P	P	N	P	Y	N	Y	N	P	N	N	N	N	7
Chen 1999	P	P	N	P	N	P	N	P	P	P	P	P	Y	N	N	N	P	N	N	N	P	6.5
Liu 2020	P	P	P	P	N	P	P	P	P	P	Y	P	Y	Y	Y	N	P	N	N	N	P	10
Liu,M 2016	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	P	P	N	N	N	P	9.5
Zhang,Y 2017	P	P	P	P	N	P	P	P	P	P	Y	P	Y	N	Y	N	Y	N	N	N	N	9
Zhou 2019	P	P	P	P	N	N	P	P	P	P	Y	P	Y	N	P	N	P	N	N	N	N	7.5

Notes: P, partly yes; Y, yes; N, non-conformance.

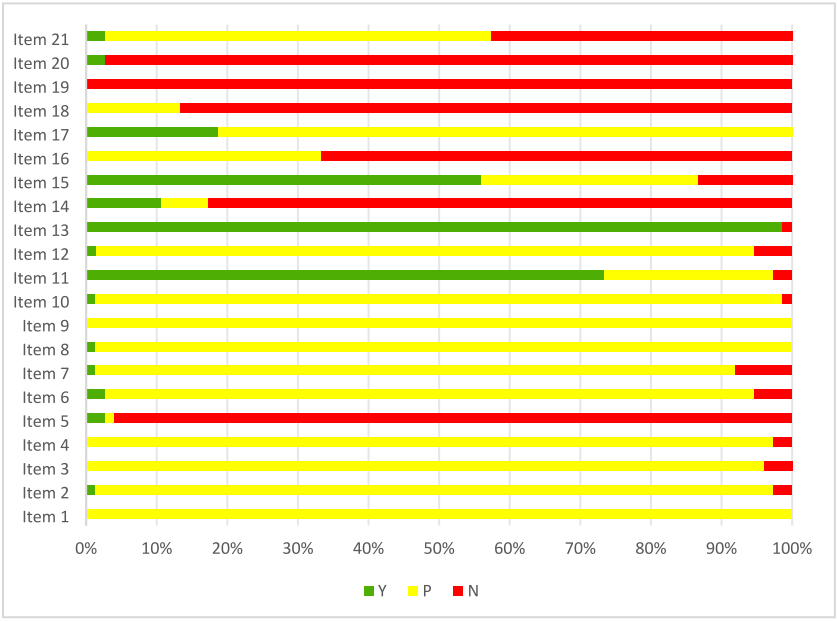

Fig. 4. ARRIVE 2.0 percentage distribution diagram (%).

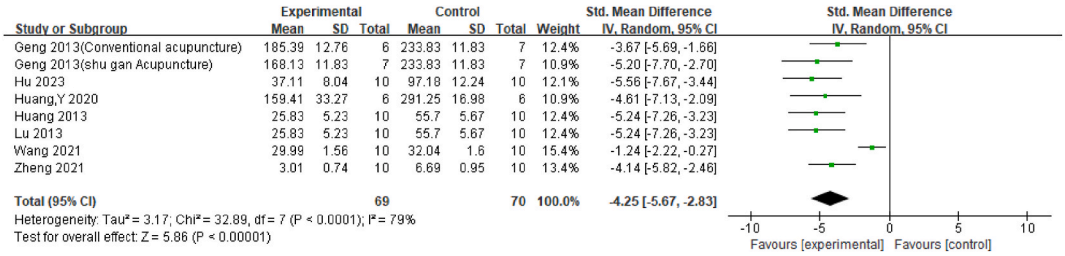

Fig. 5. Random-effect forest plot of serum levels of IL-5 comparing acupuncture vs AR models.

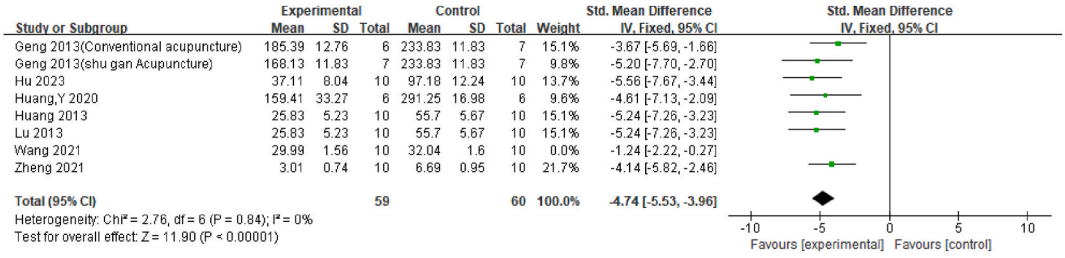

Fig. 6. Random-effect forest plot of serum levels of IL-5 when removed one study (Wang 2021).

application [36,60], acupoint catgut embedding [33,41,59,87,89,98], acupoint injection [53], and moxibustion [56].

3.4.5. Publication bias

We performed Egger's test and created funnel plot to assess possible publication bias. The funnel plot was clearly non-symmetrical, and the Egger's test indicated significant publication bias in nasal mucosal EOS counts (P-value was less than 0.01). The publication bias of these results should not be ignored, as non-significant findings might not be published, potentially influencing the results. Funnel plot is presented in Fig. 9.

3.4.6. An overview of the proposed mechanism of acupuncture in animal models of AR

All included studies provided detailed information about possible mechanisms of acupuncture treatment in animal models of AR.

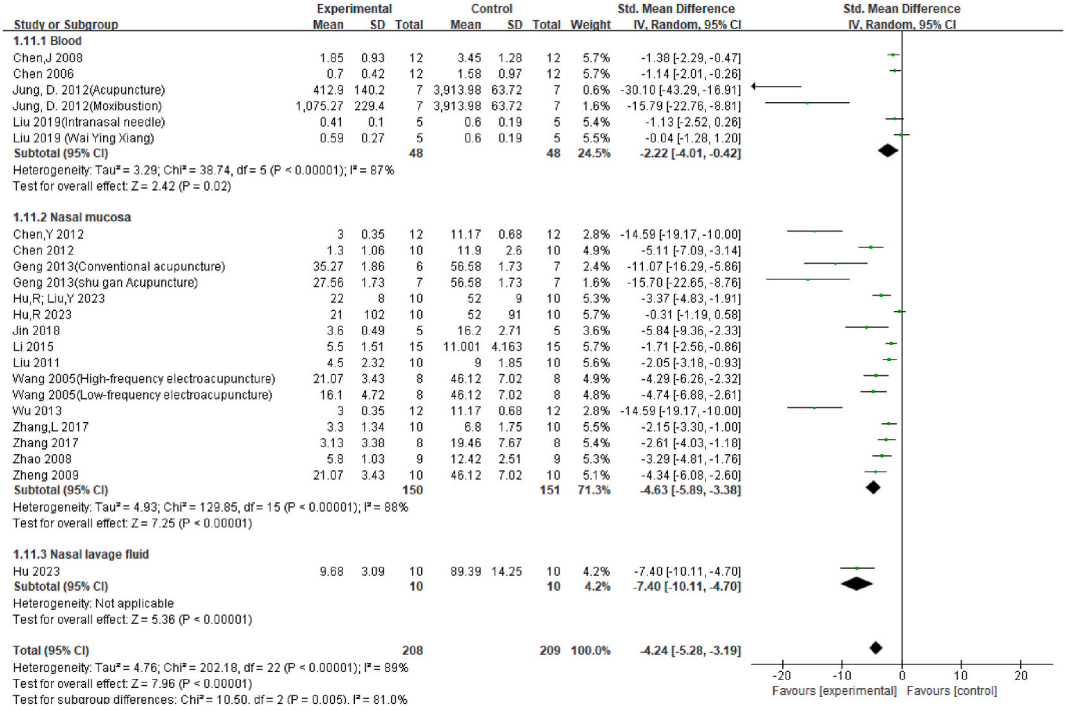

Fig. 7. Random-effect forest plot of EOS comparing acupuncture vs AR models.

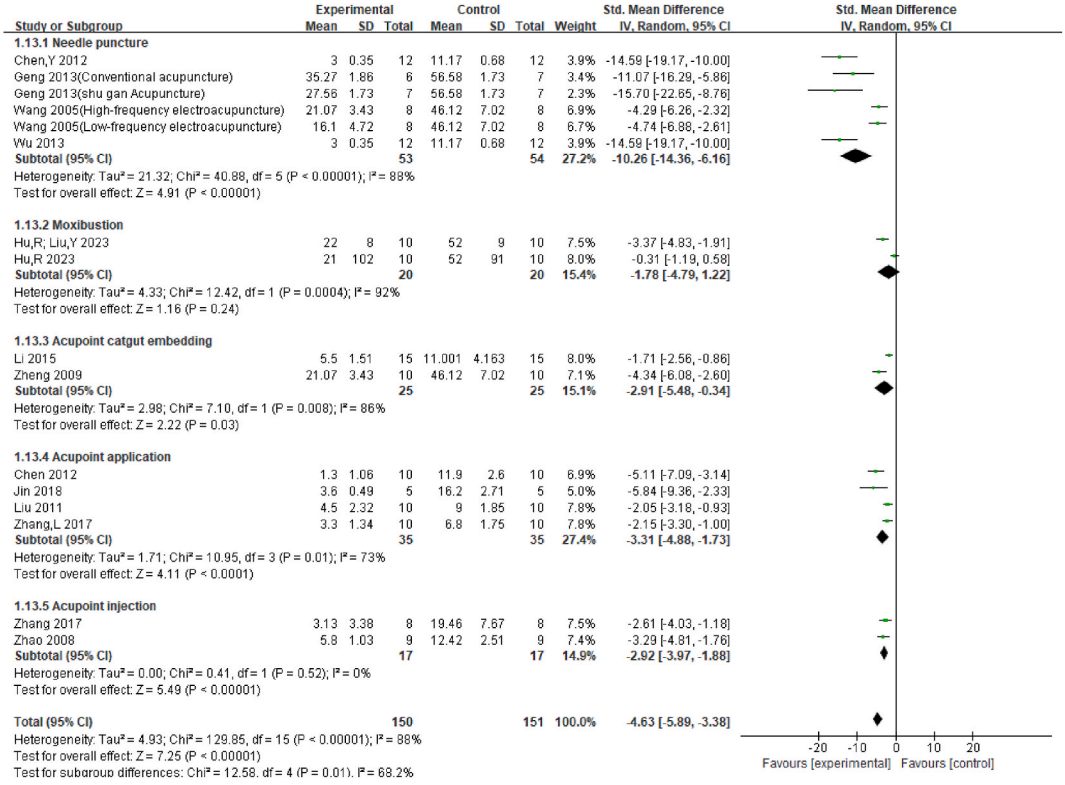

Fig. 8. Forest map for subgroups analysis on the nasal mucosal EOS count.

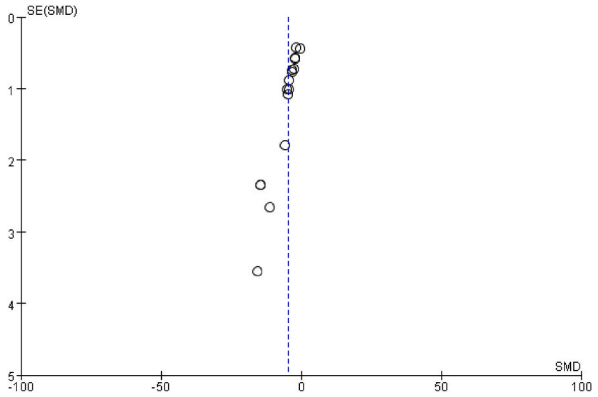

Fig. 9. Funnel plot of publication bias on nasal mucosal EOS.

Table 5 outlines all the proposed mechanisms.

4. Discussion

4.1. Summary of findings

We included 75 animal experiments to evaluate the efficacy of acupuncture treatment for AR and to understand the underlying mechanisms. The results of meta-analysis indicated that acupuncture could significantly down-regulate EOS counts in both blood and nasal mucosa, and reduce the serum levels of IL-5, compared to AR model groups. The result of the qualitative analysis showed that acupuncture could improve the behavioral scores of AR, down-regulate serum levels of IL-4, IgE and sIgE, as well as up-regulate IFN-γ levels. Accordingly, we conclude that acupuncture therapy has significant anti-inflammatory and anti-allergic effects in AR models, and suggest that acupuncture may be an effective treatment for AR. We summarized the scientific evidence of acupuncture's effects on AR, which will guide future research in this developing area. However, the results and conclusions of this study should be interpreted with caution due to the unsatisfactory quality evaluation results. Internal and external validity are detailed and analyzed as follows.

4.2. Methodological and reporting interpretations

The risk of bias is reflected in the SYRCLE scores, with 44 studies (59 %) receiving a score of less than five out of a possible ten, indicating that the quality of the included trials was generally not high. We are cautious about interpreting the study results given the methodological limitations of the studies. Some obvious methodological issues include: (1) Sequence generation: Only 36 of the included studies reported the specific method of sequence generation. The generation of sequences in random assignment not only helps avoid allocation bias but also facilitates drawing inferential conclusions. (2) Random Housing and Outcome Assessment: Explaining the random housing of animals or selecting animals randomly for outcome assessment can enhance the quality of animal experiments and ensure the reliability of results. However, these studies only illustrated the random grouping of animals but did not indicate the process of randomly housing within the animal room. Only 7 studies mentioned the randomness of selecting animals for outcome assessment. (3) Blinding: Considering the characteristics of acupuncture, it is difficult to blind investigators, but attempts should be made to blind the outcome assessors to minimize bias [27]. Failure to blind outcome assessors in animal experiments may lead to inflated false-positive results [28]. However, only 3 studies mentioned the blinding of assessors. Publication bias is a prevalent issue in preclinical research, necessitating increased methodological rigor and transparency in reporting. The SYRCLE tool is encouraged for use by researchers to review their own articles before publication to ensure transparency and complete reporting.

The ARRIVE guideline was used for reporting quality assessment of animal studies, revealing many limitations. (1) Study Design and Methods: Some experimental designs and methods, including randomization and blinding methods, were not adequately described or fully reported. (2) Ethical Statements and Protocol Registration: Many studies lacked ethical statement or protocol registration, affecting the transparency and reliability of the studies. (3) Animal Welfare: Most studies did not sufficiently describe the welfare of the animals, including housing, feeding conditions, and rearing environment. Additionally, there was a lack of reporting on measures taken to deal with adverse reactions. (4) Outcome Specification: Primary and secondary outcomes were not clearly specified or emphasized in numerous studies. (5) Animal Model Specificity: The specificity and basis of the animal species or models used were not described in numerous studies, and there was a lack of relevant description explaining their correlations with human biology. (6) Descriptive Detail: Many studies lacked sufficient descriptive detail for the experiments and justification for performing these procedures, hindering other researchers from repeating the experiments. These numerous disadvantages may influence the authenticity and the reliability of experimental results, and may not provide accurate references. We recommend that future studies strictly adhere to the ARRIVE guideline, provide sufficient and clear information, give humanistic care to experimental animal, and strictly follow randomized principles.

Table 5
Proposed mechanisms of studies included.

Research	Proposed mechanisms	Reference
Jung, D. 2012	The antiallergic and anti-inflammatory effects of acupuncture and moxibustion are exerted through regulation of Th2 cell differentiation and NFkB activity	[30]
Tu 2020	Improved the allergic inflammation response by reducing the expression of NGF, IL-4, IL-13, IL-5 and IgE in the nasal mucosa and enhancing the expression of IFN-γ	[31]
Yang 2016	Effectively inhibited the release of histamine, an important mediator in rhinitis, and alleviated local inflammatory damage to the nasal mucosa	[32]
Yang 2018	Attenuated the development of nasal neurogenic and cytokine-mediated inflammation, eventually inhibiting AR development. [Decreased Th2 cytokine (IL-4), sIgE levels, SP expression, and expression of Toll-like receptors, TLR2 and TLR4]	[33]
Han 2019	Ameliorated nasal itching motions, inhibited the release of allergic mediators and suppressed the expression of caspase-1 and RIP-2	[34]
Zhang 2011	Stabilized mast cell membrane and reduced permeability by blocking the release of allergic mediators and direct anti histamine effects	[35]
Chen 2006	Stabilized mast cell membranes, inhibited mast cell degranulation, and weakened the production of inflammatory mediators	[36]
Chen 2012	Locally reduced the number of EOS, improved the permeability of capillaries, and controlled the exudation and infiltration of mucosal tissue; Changed cilia and intracellular state; and decreased IL-17	[37]
Chen 2016	Reduced the level of lgE by reducing the level of IL4	[38]
Chen 2017	Reduced the level of IgE by reducing the level of IL-4	[39]
Chen 2015	The local stimulation response generated by embedding thread at Yingxiang acupoint, through the "Yingxiang acupoint - H-forked nerve - sphenoid nerve ganglion - nasal mucosa" neural pathway, preemptively suppresses the incoming impulses of C-type sensory nerve fibers in the nasal cavity, inhibits the release of SP, CGRP, VIP and other sensory nerve skin in its axonal reflex, thereby reducing the neurogenic inflammatory response of allergic rhinitis nasal mucosa and alleviating AR symptoms	[40]
Chen Q 2016	Acupoint catgut embedding improved the inflammatory response involving Th2 cells in AR animal models and improved the expression levels of IL-4, IL-10, and IgE. Therefore, it may alleviate symptoms of allergic rhinitis by regulating Th1/Th2 balance	[41]
Chen 2019	Reduced IgE level in serum and reduced TGF -β1 level in the serum	[42]
Chen,XL 2019	Reduced the expression of NGF, IL-4, IL-13, IL-5, and IgE in nasal mucosa tissue and enhanced IFN-γ Expression. It may improve the allergic inflammatory response of AR rats through the NGF/IL-4 pathway	[43]
Song 2011	Suppressed the secretion function of Th2 cells, reduced IL-4 level, reduced the release of inflammatory cytokines, inhibited the infiltration of inflammatory mediators into the nasal mucosa, and thus alleviate nasal mucosal inflammation	[44]
Chen,Y 2012	Reduced IL-4 level in the serum, increased IFN-γ level, reduced the infiltration of eosinophils in nasal mucosa, and corrected the imbalance of Th1/Th2	[45]
Chen 2003	Reduced the level of IgE by reducing the level of IL-4	[46]
Chen,YH 2003	Improvement of nasal mucosal hypersensitivity may be achieved by re-adjusting the level of SP in the hypothalamic-pituitary-adrenal axis and affecting the synthesis or release of SP in the target nasal mucosa	[47]
Ding 2015	Accelerated the self-repair of nasal mucosal epithelium and inhibited the infiltration of inflammatory cells, especially EOS	[48]
Zhao 2010	Regulates IL-4 and IFN-γ levels in the serum, thereby maintaining the dynamic balance of Th1/Th2 cytokines	[49]
Geng 2013	Inhibited the release of IL-5, SP, ECP and attenuated EOS infiltration	[50]
Gong 2021	Down-regulated SP and VIP protein expression in nasal mucosa, and reduced IgE and IL-4 levels in serum; up-regulated NPY protein expression in nasal mucosa, and up-regulated IFN-γ, and adjusted the imbalance of Th1/Th2	[51]
Guo 2018	Elevated IL-12 levels in the serum, decreased IL-4 levels in the serum, and decreased GATA-3 mRNA expression in nasal mucosa	[52]
Hou 2014	Down-regulated sIgE levels, IL-4 levels, and up-regulated IFN-γ levels, corrected the immune imbalance between Th1 and Th2 cells	[53]
Hu 2019	Down-regulated IL-4 levels, up-regulated IFN-γ levels in serum to regulate Th1/Th2 balance, and in turn down-regulated IgE	[54]
Hu 2023	Reduced the level of GATA-3, decreased the secretion of IL-4, IL-5 and IL-6, increased the expression of T-bet, and restored the balance of Th1/Th2	[55]
Hu,R 2023	Decreased sIgE and IL-4 levels, increased IFN-γ levels, and regulated Th1/Th2 balance, and reduced the over-activation of SP, GFAP and OX-42	[56]
Hu,R; Liu,Y 2023	Reduced eosinophil count and down-regulated sIgA, $CD4^+$ and $CD8^+$ hyperimmune state in nasal mucosa	[57]
Huang 2020	Down-regulated IgE level, IL-4 level, NKB in nasal mucosa tissue, OX-42 in hippocampal region of brain tissue, and weakened TLR-2 expression	[58]
Huang,Y 2020	Reduced CD80 and CD86 on the surface of mature DCs, inhibited the differentiation of immature DCs into mature DCs, decreased the levels of sIgE and IL-4, IL-5, and IL-6, and increased the levels of IL-2, IL-10, and IL-12, which led to a balance between Th1/Th2	[59]
Chen,J 2008	Reduced EOS level in serum and sIgE levels	[60]
Jin 2020	Decreased IL-1β, IL-6, and TNF-α levels in serum and increased IFN-γ levels	[61]
Jin 2018	Interfered with the TLR - NF-κB pathway in the nasal mucosa, effectively reduced the sensitivity of TLR4 to foreign antigens, thereby down-regulated the expression of NF-κB and reduced the release of inflammatory cytokines	[62]
Zhang,Q 2022	Down-regulated IL-4 expression and up-regulated IFN-γ to restore the relative equilibrium state of Th1/Th2	[63]
Li 2022	Reduced the number and activity of MC by down-regulating SP, which in turn ameliorated AR nasal mucosal inflammation	[64]
Li 2015	Improved expression of EOS and ICAM-1	[65]
Li 2014	Ameliorated neurogenic inflammation involving peptidergic nerve fibers and reduced the expression of SP, CGRP, and NKA during this inflammatory response	[66]
Liu 2019	Reduced peripheral blood EOS count and TRPV1/SP expression in serum. "Intranasal acupuncture - TRPV1 - neuroendocrine - immunity" may be one of the pathway mechanisms for the treatment of AR	[67]
Liu 2013	Reduced the IgE level in serum; lowered the IL-4, IL-17 and TGF-B1 content in nasal mucosa; elevated the INF-γ content in nasal mucosa; and regulated the immunological balance of Th1/Th2 and Treg/Th17 in the nasal mucosa	[68]
Liu,QF 2013	Inhibited the expression of IgE, LTD4 and histamine, reduced the rate of mast cell degranulation, and reduced mast cell activity	[69]
Liu 2011	Reduced EOS counts in nasal mucosa tissues, inhibited MC counts and MC degranulation rate, and reduced IgE and IL-4 levels in serum	[70]

(*continued on next page*)

Table 5 (*continued*)

Research	Proposed mechanisms	Reference
Lu 2013	Decreased IL-5 level in serum and inhibited the expression of IL-5 mRNA in nasal mucosa	[71]
Yang 2015	Inhibited the aggregation and activation of eosinophils, thereby reduced the allergic inflammatory response of the nasal mucosa	[72]
Pu 2018	Decreased IgE and IL-4 levels in serum and increased IL-2 levels	[73]
Tai 2008	Decreased the number of mast cells	[74]
Xie 2007	Decreased IL-4 level in serum, and increased IFN-γ level	[75]
Wang 2005	Decreased eosinophil counts in nasal mucosal tissues, decreased IgE levels in serum, decreased CD3, CD4, CD8 levels and CD4/CD8 ratios, especially CD4 and thus decreased IL-4 levels and TNF levels in serum	[76]
Wang 2012	No evidence was provided for the effect of acupuncture on immunologic mechanisms, suggesting that there may be other pathways for the mechanism of action of acupuncture	[77]
Wu 2013	Decreased nasal mucosal eosinophil counts	[78]
Zheng 2021	Regulated the release of inflammatory mediators and cytokines, and inhibition of JNK pathway activation was a possible mechanism mediating this regulation	[79]
Wang 2021	Decreased IgE levels in serum and reduced IgE synthesis. Reversed the Th1/Th2 immune imbalance, decreased the content of Th2 - associated pro-inflammatory cytokines (IL-4, IL-5, IL-13), increased the content of Th1 - associated anti-inflammatory cytokines (IL-12, IFN-γ), and decreased the secretion of associated inflammatory cytokines in the nasal mucosa	[80]
Wang,Y 2019	Promoted the expression of Foxp3 while inhibiting the expression of RORγt and its downstream inflammatory factor IL-17, corrected the imbalance between Foxp3 and RORγt, and regulated the Th17/Treg balance by inhibiting the differentiation of Th17 cells and promoting the generation of Treg cells	[81]
Xiang 2014	Reduced IgE, ICAM-1, EOS expression in serum and regulated IL-2 levels in serum	[82]
Xu 2010	Reduced IgE concentration in serum, inflammatory mediator LTB4, and inflammatory cell infiltration	[83]
Zhang,L 2017	Reduction of EOS, IgE and IL-4 levels in serum, nasal lavage LTC4	[84]
Xue 2015	Reduced the levels of IgE, IL-1β, and IL-10 in serum	[85]
Yang 2009	Reduced histamine levels in nasal mucosa	[86]
Yang,SS 2018	SP-based mediation of TLR2 and TLR4 upstream signaling and NF-kBp65 downstream signaling transcription on the MC surface hinders MC activation degranulation	[87]
Yang 2017	Neuroimmune mechanisms via the SP/TLR2/NF-κBp65 signaling pathway to intervene in AR pathogenesis	[88]
Zhang 2020	Decreased serum sIgE and increased levels of tight junction proteins Claudin-1 and Occludin	[89]
Zhang,MN 2020	Up-regulated the expression of nasal mucosal cell tight junction proteins Claudin-1 and Occludin	[90]
Zhang,NY 2011	Inhibited the viability of eosinophils, lowered the content of LTC4 in nasal lavage, lowered the content of IL-4 in serum and the expression of TLR4 and NF-kB proteins in nasal mucosa	[91]
Zhang 2017	Down-regulated Eotaxin expression, inhibited EOS activation, and reduced localized EOS infiltration and recruitment	[92]
Liang 2018	Down-regulated the expression of H1R and H4R, reducing the biological effects of inflammatory mediator HA	[93]
Zhao 2008	Reduced eosinophil counts in nasal secretion smears and nasal mucosal sections, reduced abnormally elevated CD4 and CD8 levels, and adjusted the imbalanced CD4/CD8	[94]
Zheng 2009	Reduced eosinophils in nasal mucosal tissues, IgE, and IL-4 levels in serum	[95]
Zheng,XL 2018	Reduced IL-1β, TNF-α levels in serum	[96]
Zhou 2023	Down-regulated the expression of TLR4, MyD88, and AP-1 to correct IL-4/IFN - γ unbalance	[97]
Chen 2018	Decreased serum IL-4, IL-10 and IgE levels and increased serum INF-γ levels, thus regulating Th1/Th2 balance	[98]
Huang 2013	Reduced IL-5 and histamine levels in serum	[99]
Chen 1999	Improved inflammatory mediator cell (EC, MC) mediated response in nasal mucosa	[100]
Liu 2020	Reduced OPN positive expression absorbance values, reduced OPN protein expression	[101]
Liu,M 2016	Reduced the expression of IL-17 and TGF-β1 in the nasal mucosa	[102]
Zhang,Y 2017	Up-regulated the nasal mucosal Foxp3 mRNA content and nasal mucosal Foxp3-positive cell rate, exerted an immunosuppressive effect on Treg cells, and down-regulated nasal mucosal RORγt-positive cell rate and IL-17 content in serum, inhibited the excessive Th17-cell-mediated inflammatory response, thereby regulated the Th17/Treg balance	[103]
Zhou 2019	Suppressed the expression of IL-6 and TNF-α	[104]

Abbreviations: Th, T helper cell; NGF, nerve growth factor; IL, Interleukin; Ig, Immunoglobulin; IFN, interferon; sIgE, Specific Immunoglobulin E; SP, Substance P; TLR, Toll-like receptor; RIP, receptorinteractingprotein; EOS, Eosinophils; CGRP, calcitonin-gene-related peptide; VIP, Vasoactive Intestinal Peptide; AR, Allergic rhinitis; TGF-β1, transforming growth factor-β1; ECP, eosinophil cationic protein; NPY, neuropeptide Y; GATA-3, GATA binding protein 3; GFAP, glial fibrillary acidic protein; CD, cluster of differentiation; NKB, Neurokinin B; DC, dendritic cell; TNF, tumor necrosis factor; NF, Nuclear transcription factor; MC, must cell; ICAM, intercellular cell adhesion molecule; NKA, Neurokinin A; TRPV, transient receptor potential vanilloid; INF, interferon; LTD4, leukotrieneD4; JNK, c-Jun N-terminal kinase; Foxp3, forkheadbox Protein 3; RORγt, Retinoic acid-related orphan receptor γt; LTB, Leukotriene B; LTC, Leukotriene C; MyD88, Myeloid Differentiation Factor 88; AP-1, activator protein-1; OPN, osteopontin.

4.3. The potential mechanism

Our study found that acupuncture has the potential to suppress the signal transduction of immunity and inflammation, inhibit the release of important mediators involved in the development of rhinitis, regulate the Th1/Th2 balance, and thereby mitigate local inflammatory response and damage to the nasal mucosa.

4.3.1. Affecting inflammatory cells

(1) Suppressing the common mechanism of EOS generation, thereby exerting anti-inflammatory effects, such as inhibiting the release of IL-5 and ECP. (2) Reducing the expression of CD80 and CD86 on the surface of mature dendritic cells (DCs) and inhibiting the differentiation of immature DCs into mature DCs.

4.3.2. Suppressing inflammatory factors

(1) Inhibiting the expression of IgE, leukotriene D4 and histamine in the serum, reducing the rate of mast cell degranulation, and decreasing the content of LTC4 in the nasal lavage. (2) Stabilizing mast cell membranes, reducing their permeability, and attenuating the production of inflammatory mediators and exerting a direct antihistaminic response. (3) Interfering with the TLR-NF-κb pathway in the nasal mucosa, effectively modulating the responsiveness of TLR4 to exogenous antigens, down-regulating the expression of NF-κb, and reducing the release of inflammatory factors. (4) Down-regulating the expression of SP and VIP proteins in the nasal mucosa, reducing serum levels of IgE, IL-4, IL-5, IL-6, GATA-3, and increasing T-bet expression. (5) Up-regulating serum levels of IFN-γ and the expression of NPY proteins in the nasal mucosa, elevating Th1-related anti-inflammatory factors, and reducing the secretion of nasal mucosa-related inflammatory factors. (6) Elevating the levels of IL-2 and IL-12 while reducing IL-13, thereby decreasing Th2-associated pro-inflammatory factors.

4.3.3. Regulating the neuroimmune systems

(1) Reducing the excessive release of SP, GFAP and OX-42 in hippocampal tissues, and decreasing the expression of TNF-a and IL-6. (2) Inhibiting the expression of cytokines NGF, IL-4, IL-5, IL-13 mRNA, and promoting the expression of IFN-γ protein and mRNA. Concurrently, reducing levels of IL-4 and NGF in the nasal mucosa via the NGF/IL-4 neuroimmune pathway, and reducing the expression of CGRP and NKA during the inflammatory response. (3) Regulating neurogenic-related neuropeptides of the nasal mucosa: Local stimulation reaction of the Yingxiang acupoints can preemptively inhibit the afferent impulses of the class C sensory nerve fibers of the nasal cavity via the “trigeminal nerve - the sphenopalatine ganglion - nasal mucosa” neural pathway, inhibit the release of sensory neuropeptides, such as SP, CGRP, VIP in the axon reflex, so as to reduce the neurogenic inflammatory response of the nasal mucosa of AR.

4.4. Implications for further research

Our recommendations are as follows. First, the relatively high risk of bias may have significantly affected the outcomes. Therefore, future studies should aim to identify and implement methods to reduce bias. Secondly, animal experiments should be performed in accordance with established guidelines and tools, and the experimental procedure should be reported clearly and accurately to assist other researchers in repeating the experiments. In addition, experiments should be designed and conducted scientifically and in conformity with institutional regulations. Finally, significant differences in the selection of acupoints, treatment courses, and duration of each treatment may explain the potential source of heterogeneity. Future studies should focus on designing interventions with robust methodological designs and theoretical supports.

4.5. Limitations

This study may have the following several limitations: (1) There is potential publication bias in our results, which may limit the generalizability of our findings. (2) The overall methodological and reporting quality was weak, thereby reducing the reliability and persuasiveness of our results. (3) All pooled outcomes exhibited high heterogeneity, and we were unable to identify possible causes for some of the heterogeneity. Therefore, the interpretations of this meta-analysis should be made with caution.

5. Conclusion

In this study, the results revealed that acupuncture could effectively improve the symptoms of AR and reduce EOS count and serum levels of IL-4, IL-5, IgE, and sIgE. In parallel, IFN-γ was higher. Although there was high statistical heterogeneity across the included studies, sensitivity analyses indicated that the results were robust. Caution should be taken when extrapolating experimental data from animal species to humans [29]. However, our study provides some new evidence in support of the argument that acupuncture deserves further investigation and exploration as a complementary therapy, which can improve local inflammatory response and nasal mucosal damage caused by AR.

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Research ethics

This review did not involve animal or human participants.

Data sharing statement

Raw data were obtained directly from the PubMed, Embase, Cochrane Library, CNKI, VIP, Sino Med databases, and Wan Fang

databases.

CRediT authorship contribution statement

Yuxin Li: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Jun Xiong:** Writing – review & editing, Supervision, Resources, Funding acquisition, Conceptualization. **Zheng Zhang:** Software, Resources, Investigation. **Kai Liao:** Validation, Methodology, Investigation. **Xiaohong Zhou:** Visualization, Validation. **Jun Li:** Methodology, Investigation, Data curation. **Jie Xiang:** Writing – original draft, Methodology, Investigation. **Lingling Xu:** Writing – original draft, Methodology.

Declaration of competing interest

The authors declare that there are no conflicts of interest in this work.

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Abbreviation

AR	Allergic rhinitis
IgE	Immunoglobulin E
CM	Chinese medicine
PRISMA	preferred reporting items for systematic reviews and meta-analyses
CNKI	China National Knowledge Infrastructure
VIP	Database for Chinese Technical Periodicals
OVA	ovalbumin
SA	Sham acupuncture
EOS	Eosinophil
ELISA	Enzyme-linked immuno sorbent assay
IL-4	Interleukin-4
IL-5	Interleukin-5
IL-13	Interleukin-13
IFN-γ:	Interferon gamma
TSLP	thymic stromal lymphopoietin
sIgE	specific Immunoglobulin E
SE	standard error
SD	standard deviations
SYRCLE	Systematic Review Centre for Laboratory animal Experimentation
ARRIVE	Animal Research: Reporting of In Vivo Experiments
RevMan	Review Manager
SMD	standardized mean difference
CI	confidence intervals
SD rats	Sprague Dawley rats
DCs	dendritic cells
HPA axis	hypothalamic - pituitary - adrenal axis
INPLASY	International Platform of Registered Systematic Review and Meta-analysis Protocols

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e38413.

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