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Review Article

Intranasal acupuncture therapy for allergic rhinitis: A systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Background: Allergic rhinitis (AR) is a prevalent allergic condition affecting the nasal mucosa. Intranasal acupuncture therapy (IAT), an innovative therapy that involves the precise insertion of acupuncture needles into specific nasal acupoints, has demonstrated potential effects in managing AR. The aim of this study was to evaluate the effectiveness and safety of IAT in the management of AR.

Methods: Nine databases were systematically searched for randomized controlled trials (RCTs) from their inception to September 2024. We included participants who were diagnosed with AR and who received IAT alone or as add-on treatment to conventional treatment. The Cochrane risk of bias 2.0 tool and the GRADE approach were used to assess the quality of the studies. A meta-analysis was performed via RevMan 5.4.1 software.

Results: Twenty-one RCTs with 1889 participants were included. The certainty of evidence was generally low or moderate. Compared with sham acupuncture, the IAT significantly reduced the total nasal symptom score (MD −2.65, 95% CI −4.01 to −1.29, 1 RCT, 30 participants, moderate evidence). Compared to an antihistamine, IAT was associated with a lower total nasal non-symptom score (MD −0.44, 95% CI −0.64 to −0.25, 5 RCTs, 295 participants, moderate evidence) and a better quality of life measured by the rhinoconjunctivitis quality of life questionnaire (MD −13.72, 95% CI −18.01 to −9.43, 4 RCTs, 255 participants, moderate evidence). No serious adverse events were reported.

Conclusion: The IAT may be beneficial for improving AR-related symptoms and quality of life. However, the safety of the IAT remains unclear due to inadequate reporting. Further high-quality, rigorously designed, and well-reported trials are needed.

Protocol registration: PROSPERO, CRD42024526357.

1. Introduction

Allergic rhinitis (AR) is a prevalent chronic inflammatory condition of the nasal mucosa characterized by symptoms such as sneezing, itching, nasal congestion, and runny nose.[1] The pathogenesis of AR involves an immunoglobulin E (IgE)-mediated response to airborne allergens, leading to the activation of mast cell and basophils that release histamine and other inflammatory mediators.[2] The prevalence of AR has increased significantly over the past few decades, affecting approximately 5–50% of the global population.[3] Given its high prevalence, AR imposes a considerable healthcare and economic burden.[4] In addition, the AR burden is further exacerbated by its association with multiple comorbid conditions, such as asthma, sinusitis, otitis media, and conjunctivitis.[5-7]

According to the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines (2016 version), antihistamines, intranasal corticosteroids (INCS), and leukotriene receptor antagonists (LTRA) are recommended

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as the first-line therapies for AR.[8] However, these treatments, which can only effectively manage nasal symptoms in the short-term, are often associated with side effects when used long-term and cannot alleviate AR complications such as insomnia and fatigue.[9] This situation leads to low patient compliance and a poor quality of life.[10] Consequently, there is growing interest in alternative and complementary therapies for AR management.[11]

Acupuncture is widely used for treating AR and is recommended in several clinical guidelines for its satisfying efficacy and safety.[12-14] Intranasal acupuncture therapy (IAT), an innovative type of acupuncture, involves directly stimulating points within the nasal cavity and has been shown to provide potential benefits for patients diagnosed with AR.[15] The commonly used acupoints in IAT are the Neiyingxiang (EX-HN9) and Biqiu acupoints. The Neiyingxiang (EX-HN9) is located at the junction of the inferior turbinate root and the lateral wall of the nasal cavity, which has abundant nerve endings.[15] While the Biqiu acupoint is an anatomical area that contains branches of the anterior ethmoidal and sphenopalatine nerves, making it a target point for AR.[16]

The underlying mechanism by which IAT treats AR involves the regulation of both immune as well as neural pathways to alter the inflammatory cascade associated with allergic reactions. Several studies have explored the immunological mechanisms of IAT for AR. For instance, Liu et al. [17] found that IAT can alleviate AR symptoms by reducing eosinophil chemotaxis in the nasal mucosa and decreasing serum IgE levels. Additionally, IAT may exert its treatment effects by downregulating TRPV1 activity, leading to a reduction in substance P (SP) secretion from C-type sensory nerve fibers. Gong et al. [18] demonstrated that IAT may modulate the excitability of nerves in the nasal mucosa and thereby balance the Th1/Th2 immune response and diminish neurogenic inflammation.

Although several clinical trials have been conducted to explore the effects of IAT for AR, more robust evidence from critical evaluations is still required. The aim of this study is to systematically evaluate the effectiveness and safety of IAT to improve AR clinical practices.

2. Methods

2.1. Protocol and registration

This systematic review was conducted in accordance with the Cochrane Handbook [19] and reported following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA 2020) statement.[20] The PRISMA 2020 checklist was reported in Supplement 1. The protocol of the review was registered at PROSPERO (CRD42024526357) on March 31, 2024 (Available from: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=526357).

2.2. Inclusion and exclusion criteria

2.2.1. Type of studies

All types of randomized controlled trials (RCTs) were included, with no restriction on the publication status or language.

2.2.2. Types of participants

Participants diagnosed with AR—seasonal or perennial—by any relevant clinical guidelines were included. No limitation was placed on age or sex or race or severity of the condition.

2.2.3. Type of interventions

IAT procedures used alone or in combination with conventional pharmacotherapies were included. There were no restrictions on acupoints, acupuncture frequency, or acupuncture manipulation. Eligible comparison treatments were placebo treatments (sham acupuncture), no treatment, and conventional pharmacotherapies (such as antihistamines, INCS, or LTRA).

2.2.4. Type of outcomes

The primary outcome measure was AR-related symptoms, including nasal symptoms and non-nasal symptoms, where symptoms could be measured by the well-designed scales.

(1) Total nasal symptom score (TNSS): The TNSS [21] is a commonly used clinical measurement tool in studies that evaluates the efficacy of treatments for AR. It is used to assess the severity of nasal symptoms, including nasal congestion, sneezing, rhinorrhea, and itching. Each symptom is typically rated using a four-point scale ("zero" to "three", where "zero" indicates no symptoms, "one" indicates mild symptoms, "two" indicates moderate symptoms, and "three" indicates severe symptoms), and the scores are summed to provide a total score that reflects the overall nasal symptom burden.
(2) Total non-nasal symptom score (TNNSS): The TNNSS [22] is a clinical measurement tool used to evaluate the severity of non-nasal symptoms associated with AR, including postnasal drip, nasal or ocular itching, nasal or facial pain, tearing, and headache (each occurrence counts as one point; absence counts as zero). The cumulative score represents the TNNSS rating.

The secondary outcome measures were:

(1) Total effective rate: the total effective rate was calculated based on the percentage improvements using the equation provided in the "Principles and Recommendations for the Diagnosis and Treatment of Allergic Rhinitis (2004 version)".[23] According to the guideline, "effective" was determined by assessing the scores of symptoms and signs, with a greater than 25% improvement being classified as effective. The detailed scoring criteria and calculation equation are displayed in the Supplement 2.
(2) Adverse effects (AE) related to IAT: Our study primarily focused on AE related to IAT, primarily nasal bleeding and pain. We assessed the incidence of AE in both treatment and control groups using the equation: number of participants experienced AE/ number of randomized individuals.
(3) The rhinoconjunctivitis quality of life questionnaire (RQLQ)[24]: The RQLQ is a widely used tool designed to assess the quality of life (QoL) among AR patients. It is a self-reported questionnaire that each item is rated on a scale from 0 to 6. The total score is a sum of each item scores, and lower scores reflect better quality of life.
(4) Endoscopic score of nasal signs: the endoscopic score of nasal signs was defined according to the guidelines in the "Principles and Recommendations for the Diagnosis and Treatment of Allergic Rhinitis".[23] This system assesses scores assigned based on the severity of the swelling in the inferior turbinate under the nasal endoscopy ("zero" for no swelling, "one" for mild swelling, "two" for moderate swelling, and "three" for severe swelling).
(5) Serum immunoglobulin E (IgE).

2.3. Search strategy

Nine electronic databases were searched from their inception to September 13, 2024, including five Chinese databases (the Chinese National Knowledge Infrastructure [CNKI], the China Science and Technology Journal Database [VIP], SinoMed, the Yiigle Database, and the Wanfang Database) and four international databases (PubMed, Embase, the Cochrane Library, and the Web of Science Core Collection). A manual search of the reference lists of eligible studies was performed to identify potential studies. The search strategies are reported in the Supplement 3.

2.4. Study selection and data extraction

The retrieved records were imported into NoteExpress v3.5 to exclude the duplicates. Titles, abstracts, and the full texts were screened

by two independent reviewers according to the eligibility criteria. Any disagreement was resolved by the third author.

Data extraction from all eligible articles was conducted independently by two authors. Any disagreements were resolved through discussion and consultation with a third author (XYC). The extracted data included: (1) basic characteristics of the study (first author, year of publication, study design, country, setting, sample size, and funding), characteristics of participants (age, sex, race/ethnicity, clinical diagnosis, diagnostic criteria, comorbidities, severity and duration of AR, and traditional Chinese medicine (TCM) syndrome differentiation), comparison, and interventions (detailed description of the intervention, frequency, and duration); (2) primary and secondary outcomes, follow-up time, and measurement tools; (3) methodological characteristics of the studies (randomization, allocation, blinding, participants enrolled/analyzed, discrepancies between protocol, and declarations of interests).

2.5. Risk of bias assessment

The risk of bias of the included RCTs were assessed using the Cochrane Collaboration's "Risk of Bias (RoB) 2.0" tool [19] by two authors. A third author was consulted to resolve any disagreements. The RoB 2.0 comprises five different domains: (1) bias rising from the randomization process; (2) bias due to deviations from intended interventions; (3) bias due to missing outcome data; (4) bias in the measurement of outcome; and (5) bias in the selection of the reported result. Each domain was judged as "Low RoB", "Some Concerns" or "High RoB".

2.6. Data analysis and synthesis

The Cochrane RevMan 5.4.1 software was applied to perform the meta-analysis. For dichotomous outcomes, risk ratios (RR) with relevant 95% confidence intervals (CI) were presented. Data for continuous outcomes were calculated as the mean difference (MD) with a relevant 95% CI. A random-effects model was utilized to pool the data due to the significant clinical heterogeneity. A $P < 0.05$ was considered statistically significant. I-square (I^2) was used to test the heterogeneity according to the Cochrane Handbook for Systematic Reviews of Interventions.[19] The following criteria were used: 0 to 40% might not represent important heterogeneity; 30 to 60% might represent moderate heterogeneity, 50 to 90% might represent substantial heterogeneity, and 75 to 100% might represent considerable heterogeneity.

To determine whether the findings differed among studies, a subgroup analysis was conducted for each outcome if substantial heterogeneity existed and if sufficient data were available as follows: (1) Bloodletting therapy: benefits from treatment could vary in this group compared to without bloodletting; (2) Seasonal AR: benefits from treatment could vary in this group compared to those diagnosed with perennial AR.

Sensitivity analyses were conducted to determine whether the findings were robust to arbitrary decisions made regarding eligibility and analysis. These analyses considered whether the review conclusions differed if (1) eligibility was restricted to studies without high or unclear risk of selection bias; (2) the summary effect measure had been the odds ratio (OR) rather than the RR; or (3) alternative imputation strategies had been implemented. A funnel plot was used to explore the publication bias if more than ten studies were included in the meta-analysis.

2.7. GRADE assessment

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework [25] was used to assess the certainty of each outcome. Estimates of effect were rated as high, moderate, low, or very low certainty evidence based on the RoB, inconsistency, indirectness, imprecision, and publication bias. The initial rating was conducted by individual authors (XHL, XYC, QYW, and XRP) and verified by at least one third author (XYJ). Any disagreements were resolved by discussion.

3. Results

3.1. Description of studies

Twenty-one RCTs [15,16,26-44] with 1889 participants were included in this systematic review. The selection process is presented in Fig. 1. Our search yielded 827 citations, of which 142 citations were removed for duplication. After screening the titles and abstracts, a total of 641 reports were excluded. The full texts of 44 studies were examined in detail, and 23 studies were excluded under the full-text screen. The details are reported in the Supplement 4.

3.2. Characteristics of included studies

The characteristics of the 21 RCTs are summarized in Table 1. All of the studies used parallel randomized group designs and were single-center studies. Four trials applied [26,27,31,39] a three-arm design, and three trials used a four-arm design.[16,33,35] The other fourteen trials used a two-arm design with paralleled groups. Among the included studies, twenty RCTs were published in Chinese and one [15] in English. All of the studies were conducted on the outpatients in China. The participant ages varied from 16 to 60 years old. The sample sizes of the included RCTs ranged from 30 to 180 participants. Participants of 18 trials were diagnosed with "Allergic Rhinitis" according to the different version of "Guidelines for the Diagnosis and Treatment of Allergic Rhinitis" published by the Chinese Society of Otolaryngology Head and Neck Surgery, Rhinology Group.[23,45-47] Two trials [32,42] diagnosed based on the "Clinical practice guideline: Allergic rhinitis" published by the American Academy of Otolaryngology-Head and Neck Surgery Foundation.[48] While the other one was diagnosed based on the "Allergic Rhinitis and its impact on Asthma (ARIA)" guidelines.[8] Additionally, two of the included RCTs reported TCM diagnostic patterns that encompassed lung and spleen qi deficiency syndrome [39] and lung qi deficiency and cold syndrome.[16]

The details of IAT therapy of the included studies are displayed in the Supplement 5. Two specific intranasal acupoints, Neiyingxiang (EX-HN9) and Biqiu, are utilized in IAT. Out of the included RCTs, 14 trials employed both aforementioned acupoints for treatment. Six trials chose only the Neiyingxiang (EX-HN9),[29,30,34,38-40] while one trial [43] used the Biqiu acupoint alone. Four trials combined bloodletting therapy with IAT.[26,28,37,41] The treatment duration ranged from two weeks to one month.

3.3. Quality assessment

The overall risk of bias of the 21 trials and a summary of RoB 2.0 results are displayed in Fig. 2. Twenty of the included trials were judged as some concern. One trial [29] was judged as high risk of bias for missing outcome data. The majority of trials were assessed as having some concerns regarding to the risk of bias primarily due to insufficient reporting in the analysis intentions, and this hindered a proper evaluation of the selection of the reported result domain. Additionally, subjective outcomes were assessed as some concerns in the measurement of the outcome domain due to the absence of blinding. The risk of bias evaluation of each outcome in the included studies is presented in the Supplement 6.

Additionally, the certainty of evidence assessed ranged from very low to high. The primary reasons for downgrading included risk of bias, inconsistency, and imprecision, as detailed in Supplement 7.

3.4. Effects of interventions

3.4.1. Primary outcomes

3.4.1.1. Total nasal symptom score (TNSS). There were 12 trials that reported the TNSS outcome.[16,31,32,34-37,39-43] As shown in Fig. 3, compared to sham acupuncture, IAT significantly associated with reduced

Table 1
Characteristics of the included RCTs.

Study ID	Sample size (M/F) Clinical Diagnosis (Severity of AR)	Mean age /Mean disease duration (yrs)	Comparison	Duration of interventions (follow-up)	Outcomes	Effect estimate of each outcome [95% CI]
Deng (2013)[26]	A: 19 (10/9); B: 19 (10/9); C:19 (11/8) AR (NR)	A: 30.5; B: 30.8; C: 31.3 A: 6.1; B: 6.1; C: 6.1	(A) IAT[#] (B) A + C (C) Fluticasone propionate nasal spray	2w (NR)	1) Total effective rate Endoscopic score of nasal signs	A *vs.* C: RR 1.27 [0.80, 2.03]; B *vs.* C: RR 1.55 [1.02, 2.34] A *vs.* C: MD 0.34 [−0.15, 0.83]; B *vs.* C: MD −0.10 [−0.74, 0.54]
Dong (2024)[27]	A: 45 (16/29); B: 45 (21/24); C: 45 (20/25) Persistent AR (moderate to severe)	A: 34.9; B: 34.0; C: 37.0 A: 5.3; B: 5.8; C: 4.8	(A) IAT (B) IAT + traditional acupuncture (C) Budesonide nasal spray	2w (NR)	Total effective rate	A *vs.* C: RR 1.06 [0.84, 1.34]
Fei (2023)[28]	A: 30 (18/12); B: 30 (16/14) AR (NR)	A: 32.5; B: 34.3 A: 6.3; B: 7.5	(A) IAT[#] + B (B) Fluticasone propionate nasal spray	4w (NR)	Total effective rate IgE	RR 1.26 [1.02, 1.55] MD −49.96 [−59.92, −40.00]
Gong (2018)[29]	A: 24 (8/16); B: 20 (7/13) Persistent AR (moderate to severe)	A: 39.6; B: 29.8 A: 1.8;B: 2.0	(A) IAT (B) Loratadine tablets + Budesonide nasal spray	2w (NR)	Total effective rate RQLQ IgE	RR 0.97 [0.87, 1.08] MD 3.85 [−3.90, 11.60] MD 21.79 [−0.53, 44.11]
Gong (2020)[30]	A: 81 (36/45); B: 80 (33/47) Persistent AR (moderate to severe)	A: 38.0; B: 38.3 A: 6.2; B: 6.2	(A) IAT (B) Loratadine tablets + Budesonide nasal spray	2w (NR)	Total effective rate RQLQ	RR 0.97 [0.87, 1.08] MD 2.00 [1.43, 2.57]
Li (2019)[31]	A: 37 (20/17); B: 37 (19/18); C: 38 (19/19) AR (NR)	A: 36.7; B: 36.4; C: 38.4 A: 0.8; B: 0.9; C: 0.9	(A) IAT (B) IAT + C (C) Loratadine tablets	2w (30d, 2m, 3m 4m, 5m, 6m)	TNSS TNNSS Total effective rate RQLQ	A *vs.* C: MD −0.19 [−0.64, 0.26] B *vs.* C: MD −0.82 [−1.27, −0.37] A *vs.* C: MD −0.40 [−0.87, 0.08] B *vs.* C: MD −0.96 [−1.51,−0.41] A *vs.* C: RR 1.20 [0.88, 1.62] B *vs.* C: RR 1.45 [1.12, 1.89] A *vs.* C: MD −17.5 [−24.08, −10.92] B *vs.* C: MD −31.93 [−39.48, −24.39]
Li (2021)[32]	A: 30 (16/14); B: 30 (15/15) AR (NR)	A: 38.6; B: 37.9 A: 0.9; B: 1.0	(A) IAT (B) Loratadine tablets	2w (NR)	TNSS TNNSS Total effective rate RQLQ	MD −0.65 [−1.21, −0.09] MD −0.60 [−1.11, −0.09] RR 1.24 [0.94, 1.63] MD −15.23 [−20.34, −10.12]
Li (2022)[33]	A: 35 (17/18); B: 35 (18/17); C: 35 (19/16); D: 35 (17/18) AR (NR)	A: 30.7; B: 30.3; C: 29.9; D: 31.0 A: 4.5; B: 4.7; C: 4.7; D: 4.9	(A) IAT + C (B) IAT (C) Intradermal needling (D) Mometasone furoate nasal spray	2w (30d, 90d, 180d)	Total effective rate	B *vs.* D: RR 1.12 [0.86, 1.46]
Li (2023)[34]	A: 49 (26/23); B: 49 (29/20) AR (moderate to severe)	A: 31.8; B: 32.4 A: 7.9; B: 8.0	(A) IAT + B (B) Loratadine tablets + Budesonide nasal spray	2w (NR)	TNSS TNNSS Total effective rate Endoscopic score of nasal signs RQLQ	MD −0.20 [−0.37, −0.03] MD −0.21 [−0.42, 0.00] RR 1.22 [1.02, 1.46] MD −0.51 [−0.91, −0.10] MD −4.39 [−7.44, −1.34]
Li (2024)[35]	A: 45 (18/27); B: 45 (24/21); C: 45 (20/25); D: 45 (26/19) AR (moderate to severe)	A: 36.6; B: 34.8; C: 35.2; D: 33.9 A: 5.2; B: 5.3; C: 5.0; D: 4.0	(A) IAT (B) IAT + C (C) oral herbal medicine (D) Mometasone furoate aqueous nasal spray	2w (NR)	TNSS TNNSS Total effective rate IgE	A *vs.* D: MD −0.13 [−0.63, 0.37] A *vs.* D: MD −0.15 [−0.58, 0.28] A *vs.* D: RR 1.06 [0.83, 1.36] A *vs.* D: MD −44.62 [−55.58, −33.66]
LiY (2024)[36]	A: 30 (15/15); B: 30 (16/14) AR (NR)	A: 37.9; B: 38.6 A: 11.0; B: 11.6	(A) IAT (B) Loratadine tablets	14d (NR)	TNSS TNNSS RQLQ	MD −0.65 [−1.21, −0.09] MD −0.60 [−1.11, −0.09] MD −15.23 [−20.34, −10.12]

(*continued on next page*)

Table 1 (*continued*)

Study ID	Sample size (M/F) Clinical Diagnosis (Severity of AR)	Mean age /Mean disease duration (yrs)	Comparison	Duration of interventions (follow-up)	Outcomes	Effect estimate of each outcome [95% CI]
Liu (2023)[15]	A: 75 (35/40); B: 38 (20/18) Persistent AR (moderate to severe)	A: 41.0; B: 8.5 A: 41.0; B: 8.5	(A) IAT (B) Loratadine tablets + Budesonide nasal spray	2w (6w)	RQLQ	MD 1.56 [−0.25, 3.37]
Shi (2019)[37]	A: 30 B: 30 AR (NR)	NR	(A) IAT[#] (B) Fluticasone propionate nasal spray	4w (4w)	TNSS Endoscopic score of nasal signs Total effective rate IgE	MD −0.03 [−0.35, 0.30] MD −0.04 [−0.40, 0.32] RR 0.97 [0.86, 1.08] MD −11.88 [−29.45, 5.69]
Sun (2022)[38]	A: 39 (21/18); B: 38 (19/19) AR (NR)	A: 30.3; B: 29.5 A: 3[*]; B: 4[*]	(A) IAT + B (B) Montelukast sodium chewable tablets	1m (NR)	Total effective rate RQLQ Endoscopic score of nasal signs	RR 1.17 [0.97, 1.41] MD −4.00 [−10.52, 2.52] MD 0.00 [−0.33, 0.33]
Tao (2022)[39]	A: 30 (13/17); B: 30 (14/16); C: 30 (16/14) AR (NR)	A: 34.5; B: 34.4; C: 33.9 A: 5.7; B: 6.0; C: 6.8	(A) IAT (B) Traditional acupuncture (C) Loratadine tablets	2w (NR)	TNSS TNNSS Total effective rate RQLQ IgE	A *vs.* C: MD −1.87 [−2.42, −1.32] A *vs.* C: MD −0.40 [−0.67, −0.13] A *vs.* C: RR 1.24 [0.94, 1.63] A *vs.* C: MD −9.16 [−11.74, −6.58] A *vs.* C: MD −49.57 [−71.42, −27.72]
Wang (2023)[16]	A: 30 (15/15); B: 30 (13/17); C: 30 (16/14); D: 30 (12/18) AR (NR)	A: 35.1; B: 34.0; C: 34.9; D: 34.1 A: 4.2; B: 4.3; C: 4.1; D: 4.6	(A) IAT + C (B) IAT + D (C) Budesonide nasal spray (D) C + Yu-ping-feng granules	2w (NR)	TNSS TNNSS Total effective rate RQLQ	A *vs.* C: MD −2.17 [−3.55, −0.79] A *vs.* C: MD −0.74 [−0.93, −0.55] A *vs.* C: RR 1.14 [0.87, 1.49] A *vs.* C: MD −12.27 [−14.58, −9.96]
Wang (2021)[40]	A: 20 B: 10 AR (NR)	NR	(A) IAT (B) Shame acupuncture	2w (1m, 3m)	TNSS RQLQ	MD −2.65 [−4.01, −1.29] MD −5.50 [−20.89, 9.88]
Wu (2019)[41]	A: 30 (17/13); B: 30 (14/16) AR (NR)	A: 33.2; B: 34.0 NR	(A) IAT[#] (B) Fluticasone propionate nasal Spray	4w (NR)	TNSS Total effective rate Endoscopic score of nasal signs IgE	MD 0.04 [−0.31, 0.39] RR 0.96 [0.76, 1.22] MD −0.30 [−0.69, 0.09] MD −95.36 [−199.65, 8.93]
Xiao (2023)[42]	A: 20 (4/16); B: 20 (6/14) AR (NR)	A: 24; B:25 A: 3[*]; B: 4.5[*]	(A) IAT (B) Loratadine tablets	2w (NR)	TNSS TNNSS Total effective rate	MD 3.50 [1.47, 5.53] MD 0.00 [−1.06, 1.06] RR 1.21 [0.86, 1.71]
Xia (2024)[43]	A: 55 (23/32); B: 52 (20/32) Persistent AR (NR)	A: 40.3; B: 39.7 A: 6.5; B: 5.5	(A) IAT (B) Fluticasone propionate nasal spray	3w (NR)	TNSS Total effective rate RQLQ Endoscopic score of nasal signs	MD −1.06 [−1.89, −0.23] RR 1.10 [0.95, 1.28] MD −6.11 [−7.50, −4.72] MD −0.05 [−0.24, 0.14]
Yuan (2018)[44]	A: 30 (11/19); B: 30 (10/20) AR (NR)	A: 34.1; B: 33.8 A: 4.7; B: 4.8	(A) IAT[#] (B) Budesonide nasal spray	20d (NR)	Total effective rate	RR 1.22 [0.98, 1.52]

AE, adverse event; AR, allergic rhinitis; F, female; IAT, intranasal acupuncture therapy; IgE, immunoglobulin E; NR, not reported; M, male; MD, mean difference; RQLQ, rhinoconjunctivitis quality of life questionnaire; RR, risk ratios; TNSS, total nasal symptom score; TNNSS, total non-nasal symptom score.

Notes:

[*] Median

[#] IAT combined with bloodletting therapy; yrs, year(s); m, month(s); w, week(s);

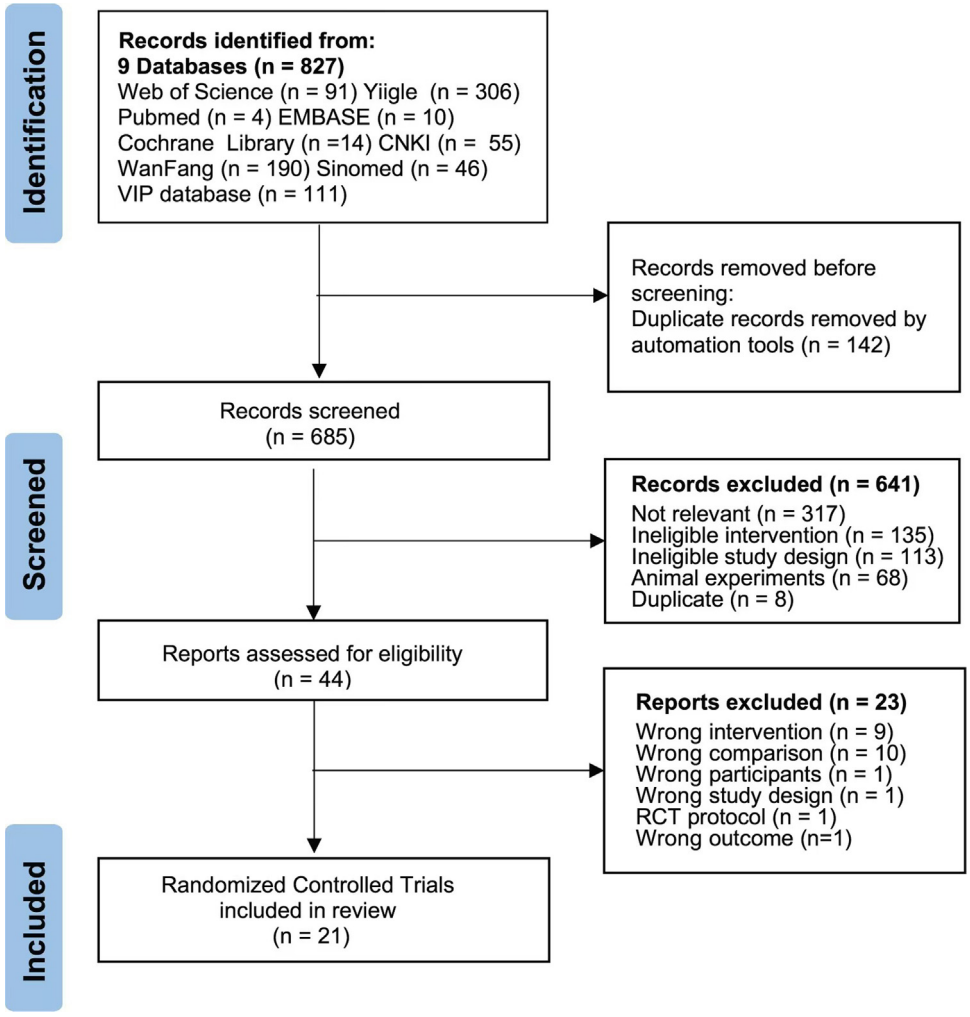

Fig. 1. PRISMA flow diagram.
Abbreviations: EMBASE, Excerpta Medica dataBASE; CNKI, China National Knowledge Infrastructure; RCT, randomized controlled trial; VIP, China National Knowledge Infrastructure.

TNSS (MD −2.65, 95% CI −4.01 to −1.29, 1 RCT, 30 participants, moderate evidence).[15] Compared to an antihistamine, IAT showed no statistically significant difference in the TNSS (MD −0.38, 95% CI −1.25 to 0.49, 5 RCTs, 295 participants, moderate evidence). The difference between IAT (without or with bloodletting therapy) and INCS was not statistically significant either (MD −0.53, 95% CI −1.44 to 0.37, 2 RCTs, 197 participants, low evidence; MD 0, 95% CI −0.24 to 0.24, 2 RCTs, 120 participants, low evidence). The meta-analysis demonstrated a significant improvement in the TNSS in the IAT plus an antihistamine group compared to an antihistamine used alone (MD −0.82, 95% CI −1.27 to −0.37, 1 RCT, 75 participants, low evidence). Compared to INCS, IAT plus INCS showed significant improvement on the TNSS (MD −2.17, 95% CI −3.55 to −0.79, 1 RCT, 60 participants, low evidence). The effects of IAT plus INCS plus an antihistamine on TNSS improvement were better than INCS plus an antihistamine (MD −0.20, 95% CI −0.37 to −0.03, 1 RCT, 98 participants, low evidence).

3.4.1.2. Total non-nasal symptom score (TNNSS). There were eight trials that reported the TNNSS outcome.[16,31,32,34-36,39,42] Compared to an antihistamine, IAT was associated with a lower TNNSS (MD −0.44, 95% CI −0.64 to −0.25, 5 RCTs, 295 participants, moderate evidence) (Fig. 3). There was no significant difference between IAT without bloodletting therapy and INCS in the TNNSS (MD −0.15, 95% CI −0.58 to 0.28, 1 RCT, 90 participants, low evidence). Compared to an antihistamine used alone, IAT plus an antihistamine significantly reduced the TNNSS (MD −0.96, 95% CI −1.51 to −0.41, 1 RCT, 75 participants, low evidence). Compared to INCS, IAT plus INCS also showed a significant effect on improving the TNNSS (MD −0.74, 95% CI −0.93 to −0.55, 1 RCT, 60 participants, low evidence). Compared to INCS plus an antihistamine, IAT plus INCS plus an antihistamine indicated a trend towards statistical significance in reducing the TNNSS (MD −0.21, 95% CI −0.42 to 0.00, 1 RCT, 98 participants, low evidence).

3.4.2. Secondary outcomes

3.4.2.1. Total effective rate. Eighteen RCTs reported total effective rate outcomes (Supplement 8).[16,26-34,36-39,41-44] Compared to an antihistamine, IAT showed a significant increase in the total effective rate (RR 1.21, 95% CI 1.04 to 1.39, 4 RCTs, 235 participants, moderate evidence). No significant statistical difference was observed between IAT with bloodletting therapy and INCS (RR 0.98, 95% CI 0.88 to 1.08, 3 RCTs, 158 participants, low evidence). Notably, the implementation without bloodletting therapy into IAT was related to an increased total effective rate (RR 1.11, 95% CI 1.01 to 1.22, 5 RCTs, 417 participants, high evidence). Compared to INCS plus an antihistamine, IAT did not show a significant effect on the total effect rate (RR 1.03, 95% CI 0.93 to 1.14, 2 RCTs, 202 participants, low evidence).

One study demonstrated that IAT combined with an antihistamine was more effective than an antihistamine used alone (RR 1.45, 95% CI

(A) Overall risk of bias

(B) Summary of risk of bias

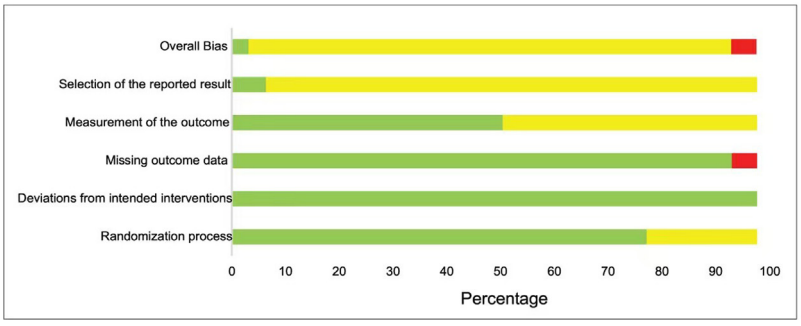

Fig. 2. Risk of bias of the 21 trials using the RoB2 tool.
Abbreviations: ESNS, endoscopic score of nasal signs; IAT, intranasal acupuncture therapy; IgE, immunoglobulin E; INCS, intranasal corticosteroids; LTRA, leukotriene receptor antagonists; NA, not available; RQLQ, rhinoconjunctivitis quality of life questionnaire; TNSS, total nasal symptom score; TNNSS, total non-nasal symptom score.

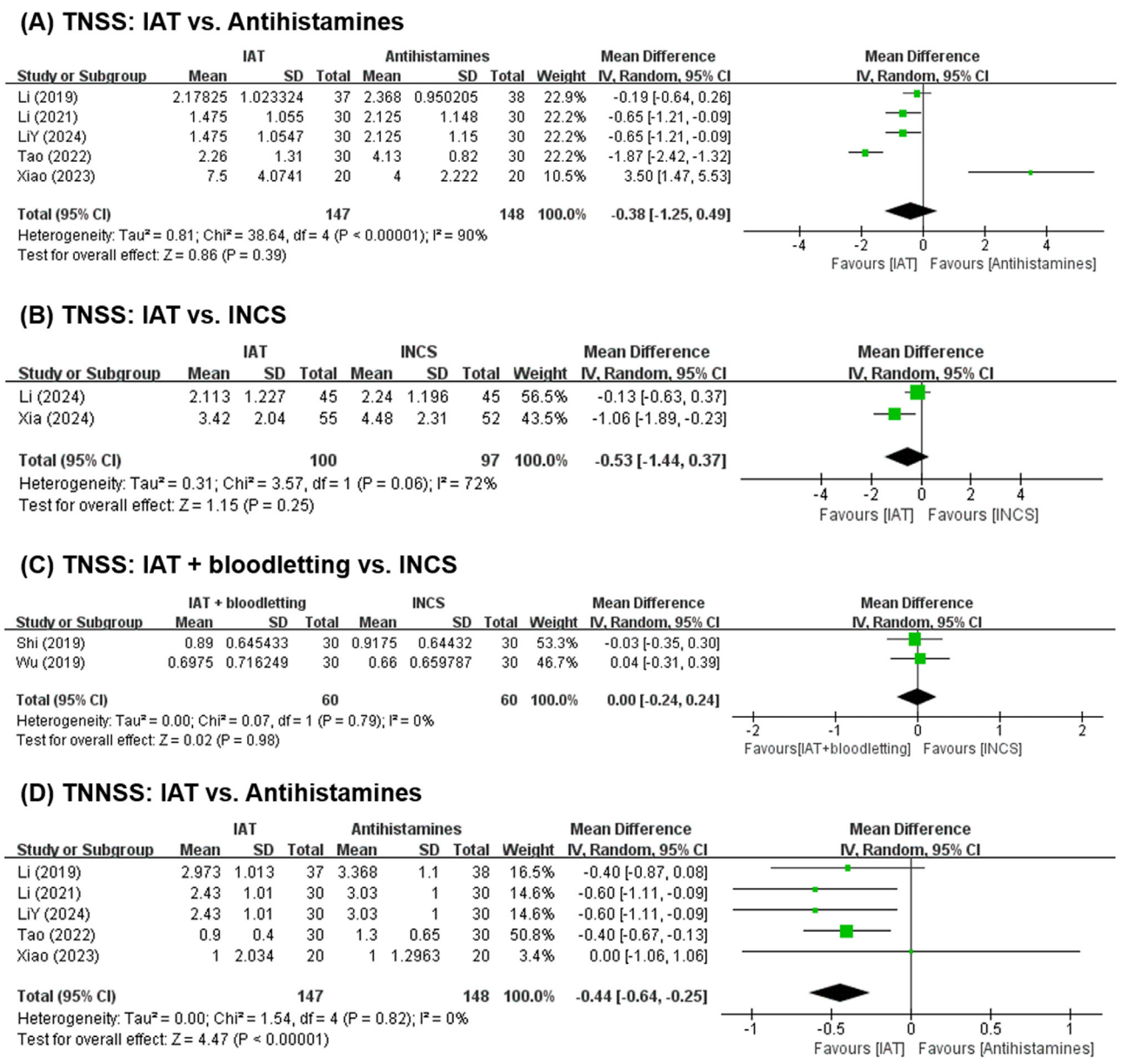

Fig. 3. Primary outcomes: AR-related symptoms measured by TNSS and TNNSS.
Abbreviations: CI, confidence interval; IAT, intranasal acupuncture therapy; INCS, intranasal corticosteroids; TNSS, total nasal symptom score; TNNSS, total non-nasal symptom score.

1.12 to 1.89, 1 RCT, 75 participants, very low evidence). IAT combined with INCS significantly improved the total effective rate compared to INCS used alone (RR 1.25, 95% CI 1.08 to 1.46, 3 RCTs, 158 participants, low evidence). In a comparison of IAT plus LTRA and LTRA used alone, no significant difference was observed on the total effective rate (RR 1.17, 95% CI 0.97 to 1.41, 1 RCT, 77 participants, low evidence). Compared to INCS plus an antihistamine, IAT combined with INCS plus an antihistamine showed an add-on effect on the total effective rate (RR 1.22, 95% CI 1.02 to 1.46, 1 RCT, 98 participants, low evidence).

3.4.2.2. Adverse events. Adverse events were reported in 15 studies,[15,16,26-30,33-36,38,39,42,43] 8 of which reported no adverse events throughout the entire trial.[16,26,28-30,34,36,38] The most common adverse event was rhinorrhagia, which, despite its occurrence, was mild and did not impede the continuation of the trials. Other mild adverse events, such as mild nausea and dryness of mouth and throat, were reported. Detailed descriptions of the adverse events are presented in Table 2. No significant statistical differences were found in the incidence of adverse events between the experimental and control groups. Moreover, no serious adverse events were reported among all of the included studies.

3.4.2.3. Rhinoconjunctivitis quality of life questionnaire (RQLQ). Twelve trials assessed the RQLQ as outcome indicator.[15,16,29-32,34,36,38-40,43] Compared to sham acupuncture, IAT did not show a significant effect in the RQLQ (MD −5.50, 95% CI −20.88 to 9.88, 1 RCT, 30 participants, moderate evidence). Compared to an antihistamine, IAT had a better effect on improving the RQLQ (MD −13.72, 95% CI −18.01 to −9.43, 4 RCTs, 255 participants, moderate evidence) (Supplement 9). Compared to INCS, IAT without bloodletting therapy had a significant reduction in the RQLQ after three weeks of treatment (MD −6.11, 95% CI −7.5 to −4.72, 1 RCT, 107 participants, low evidence). An antihistamine plus INCS exhibited significantly lower RQLQ scores compared

Table 2
Adverse events reported in the included trials.

Interventions *vs.* Controls	Types of AEs	No. of cases		RR, 95% CI	Study ID
		IAT	Drugs		
IAT *vs.* Antihistamines	Nausea (mild)	0/30	1/30	0.33 [0.01, 7.87]	Tao (2022)[39]
	Dryness of mouth and throat	0/20	1/20	0.33 [0.01, 7.72]	Xiao (2023)[42]
IAT *vs.* INCS	Rhinorrhagia	0/45	2/45	0.20 [0.01, 4.05]	Dong (2024)[27]
		2/35	4/35	0.50 [0.10, 2.56]	Li (2022)[33]
		1/45	2/45	0.50 [0.05, 5.32]	Li (2024)[43]
	Headaches	0/45	2/45	0.20 [0.01, 4.05]	Dong (2024)[27]
		0/45	2/45	0.20 [0.01, 4.05]	Li (2024)[43]
		0/55	2/52	0.19 [0.01, 3.85]	Xia (2024)[43]
	Nasal pain	1/45	4/45	0.25 [0.03, 2.15]	Li (2024)[35]
	Dryness of the nose	0/45	3/45	0.14 [0.01, 2.69]	Dong (2024)[27]
IAT *vs.* Antihistamines + INCS	Rhinorrhagia	1/60	0/30	1.52 [0.06, 36.34]	Liu (2023)[15]

AEs, adverse events; IAT, intranasal acupuncture therapy; INCS, intranasal corticosteroids; RR, risk ratios.

to IAT (MD 1.97, 95% CI 1.43 to 2.51, 3 RCTs, 292 participants, low evidence) (Supplement 9).

The effects of IAT plus an antihistamine on the RQLQ were better than an antihistamine used alone (MD −31.93, 95% CI −39.48 to −24.39, 1 RCT, 75 participants, low evidence). Compared to INCS used alone, IAT plus INCS showed a significant improvement in the RQLQ (MD −12.27, 95% CI −14.58 to −9.96, 1 RCT, 60 participants, low evidence). No significant differences in the RQLQ were identified between the IAT plus LTRA and LTRA groups (MD −4.00, 95% CI −10.52 to 2.52, 1 RCT, 77 participants, low evidence). Compared to INCS plus an antihistamine, IAT had an add-on effect on improving the RQLQ (MD −4.39, 95% CI −7.44 to −1.34, 1 RCT, 98 participants, low evidence).

3.4.2.4. Endoscopic score of nasal signs. Seven trials reported endoscopic score of nasal signs outcomes.[26,28,34,37,38,41,43] No statistically significant differences were observed between IAT and INCS with or without bloodletting therapy (MD −0.03, 95% CI −0.36 to 0.31, 3 RCTs, 158 participants, moderate evidence; MD −0.05, 95% CI −0.24 to 0.14, 1 RCT, 107 participants, moderate evidence) (Supplement 10), IAT plus INCS and INCS (MD −0.08, 95% CI −0.57 to 0.41, 1 RCT, 38 participants, low evidence), and IAT plus LTRA and LTRA (MD 0.00, 95% CI −0.33 to 0.33, 1 RCT, 77 participants, low evidence). The data from one study were presented as an interquartile range (IQR) with mean, and we were unable to convert to the standard deviation (SD); hence, the estimate effect could not be calculated.[28]

3.4.2.5. Serum immunoglobulin E (IgE). Six trials reported IgE outcomes.[28,29,35,37,39,41] Compared to an antihistamine, IgE was significantly lower following two weeks of IAT treatment (MD −49.57, 95% CI −71.42 to −27.72, 1 RCT, 60 participants, low evidence). The pooled analysis revealed a significant reduction in IgE for IAT without bloodletting therapy compared to INCS (MD −44.62, 95% CI −55.58 to −33.66, 1 RCT, 90 participants, low evidence). While no significant differences were observed between IAT with bloodletting therapy and INCS (MD −37.14, 95% CI −112.31 to 38.02, 2 RCTs, 120 participants, low evidence) (Supplement 11). Compared to an antihistamine plus INCS, IAT did not show a statistically significant difference (MD 21.79, 95% CI −0.53 to 44.11, 1 RCT, 44 participants, very low evidence). Compared to INCS used alone, IAT combined with INCS was more effective in reducing IgE (MD −49.96, 95% CI −59.92 to −40.00, 1 RCT, 60 participants, low evidence).

3.4.3. Sensitivity analysis

Sensitivity analyses were conducted to assess the robustness and reliability of the outcomes. After excluding the study with high risk of bias,[29] the result of the RQLQ outcome was changed in a comparison of IAT and INCS plus an antihistamine (MD 1.68, 95% CI −0.08 to 3.44, 2 RCTs, 134 participants, very low evidence). In addition, other results did not significantly alter the direction or significance of the effect during the sensitivity analysis.

Publication bias was not assessed using a funnel plot due to the limited number of studies included in the meta-analysis.

4. Discussion

4.1. Summary of evidence

Our systematic review and meta-analysis included 21 RCTs with 1889 participants that evaluated the effectiveness and safety of IAT, with or without conventional therapies for AR. Compared to sham acupuncture, moderate certainty evidence showed that IAT probably reduce the TNSS among AR patients. Compared to an antihistamine, moderate certainty evidence indicated that IAT probably reduced the TNNSS, increased the total effective rate, and improved the quality of life. Compared to INCS, high certainty evidence indicated that IAT without bloodletting can increase total effective rate and low certainty evidence revealed that IAT without bloodletting probably lowered the serum IgE.

The implementation of IAT therapy in the included studies varied significantly. Four studies incorporated bloodletting therapy as part of IAT technique. Currently, there are no standardized guidelines for IAT therapy regarding details such as acupuncture frequency, needle retention time, total treatment duration, or acupuncture technique. Nevertheless, it is worthy to note that our study suggested there may be no difference in the effectiveness of integrating bloodletting therapy into IAT. Bloodletting therapy, as one of the oldest techniques in acupuncture, is an intervention that deliberately withdraws blood from a patient to treat or prevent disease.[49] Bloodletting is commonly applied in patients who have acute, heat, or stasis syndromes.[50] Relevant research has revealed that bloodletting by pricking the nasal mucosa can enhance mucosal metabolism, improve microcirculation and vascular function, and expel harmful substances from the bloodstream, thereby preventing excessive inflammatory responses.[51] However, bloodletting therapy may also increase the fragility of local capillaries, potentially leading to rhinorrhagia. Due to insufficient reports of adverse events in the included studies, it remains unclear whether bloodletting increases the risk of AEs. Future research should focus on standardizing IAT clinical practices and improving the management of AEs related to IAT therapy.

4.2. Agreements and disagreements with other reviews

Previous studies have extensively explored the efficacy of acupuncture in the treatment of AR, and they evaluated various acupuncture modalities including filiform acupuncture, ear acupressure, and acupoint herbal patching.[52-55] Yin et al. (2020) [56] compared results across different traditional acupuncture methods and found that acupuncture

therapy demonstrated comparable effectiveness to pharmacologic therapy. Similarly, Du et al. (2022) [55] revealed that filiform needle acupuncture effectively alleviated symptoms, improved quality of life, reduced medication usage, and promoted patient satisfaction, suggesting that acupuncture might be an effective and safe intervention for AR. However, Lee et al. (2009) [57] observed mixed outcomes, indicating limited effects for seasonal AR and suggestive benefits for perennial AR. However, most of the included trials in our study did not report the type of AR, making it impossible to conduct a subgroup analysis to observe the effectiveness of IAT in perennial and seasonal AR. In addition, the Biqiu acupoint, a special acupoint in IAT therapy where branches of the sphenopalatine ganglion are located, aligns with Fu et al.'s (2019) research on the effectiveness of sphenopalatine ganglion acupuncture (SGA) in treating AR.[58] This revealed that SGA is effective in relieving nasal symptoms and improving the quality of life for AR patients compared to western medicine, acupuncture of other areas, and sham acupuncture.

4.3. Strength and limitations of this review

To the best of our knowledge, this study is the first systematic review focusing on the effectiveness and safety of IAT for treating AR, thus providing a comprehensive evaluation of the available evidence. The findings suggest that IAT has shown promising benefit in AR symptom relief and may offer a viable alternative to pharmacological treatment for AR. In addition, our study adds to the evidence supporting acupuncture as an effective and safe treatment for AR.

This study also had some limitations. First, the quality of the included studies varied, with a majority of trials having some concern of risk of bias due to a lack of blinding or inadequate reports. Second, the short follow-up periods in many studies may have limited our ability to assess the long-term effects outcomes such as recurrence rates and quality of life. Third, our study makes some adjustments in terms of the primary outcome after consulting TCM practitioners, which contributes to the more concise and focused findings. In addition, since all of the studies were conducted in China, the external validity of the results is limited, and we should be more cautious when generalizing the findings to other populations.

4.4. Clinical and research implications

Future research investigating IAT for AR should address several critical areas to enhance methodological rigor. First, there is a pressing need for studies to be prospectively registered in recognized clinical trial databases to ensure transparency and minimize the risk of selective reporting and publication bias. Second, future trials should prioritize the implementation of blinding procedures and conduct rigorous sample size calculations to detect clinically significant effects of IAT. Furthermore, long-term follow-up assessments are essential to evaluate the sustained efficacy and safety of IAT, particularly in terms of recurrence rates and long-term symptom control.

4.5. Conclusions

This systematic review and meta-analysis indicated that IAT seems to be an effective and safe option for treating AR with comparable or superior outcomes to conventional western medicine for AR related symptoms. Future high-quality studies are required to validate these findings and the long-term effects and safety of IAT.

CRediT authorship contribution statement

Xiao-ying Chen: Conceptualization, Data curation, Investigation, Software, Writing – original draft, Writing – review & editing. **Qian-yun Wang:** Data curation, Formal analysis, Investigation, Software, Writing – review & editing. **Zhan-feng Yan:** Investigation, Methodology, Writing – review & editing. **Yu-yang Wang:** Data curation, Investigation, Validation. **Xing-ru Pan:** Investigation, Writing – review & editing. **Meng-yuan Ou:** Investigation. **Xue-han Liu:** Investigation, Methodology. **Jian-ping Liu:** Methodology, Writing – review & editing. **Xin-yan Jin:** Conceptualization, Investigation, Methodology, Project administration, Supervision, Visualization, Writing – review & editing.

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Declaration of competing interest

JpL and XyJ are editorial board members of the journal but their member status had no bearing on the editorial decision. The authors declare that they have no conflicts of interest.

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Ethical statement

All data in our study came from publicly available data. Our study did not recruit human subjects. Therefore, ethical approval was not required. Not applicable.

Data availability

The data that support the findings of this study are publicly available.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.imr.2024.101116.

Supplement 1. PRISMA 2020 checklist

Supplement 2. Symptom and physical sign scoring criteria and calculation equation for individual effect

Supplement 3. Searching strategy for electronic databases

Supplement 4. List of references excluded at full paper screen with reasons for exclusion

Supplement 5. Details of intranasal acupuncture therapy of the included studies

Supplement 6. Risk of bias of each outcome in the included RCTs

Supplement 7. GRADE certainty of evidence assessments for each outcome

Supplement 8. Secondary outcomes: total effective rate

Supplement 9. Secondary outcomes: RQLQ

Supplement 10. Secondary outcomes:endoscopic score of nasal signs

Supplement 11. Secondary outcomes: IgE

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