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Meta-analysis: reducing the recurrence rate of allergic rhinitis through oral administration of traditional Chinese medicine

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Abstract. – OBJECTIVE: A systematic review and meta-analysis were carried out to investigate the medical evidence of oral Chinese herbal medicine in reducing the recurrence of allergic rhinitis (AR).

MATERIALS AND METHODS: Through computer retrieval of PubMed, ScienceDirect, WOS, and other databases, relevant randomized controlled literature was obtained based on the inclusion criteria and retrieval strategies. The retrieval time was set from January 1, 2013, to December 31, 2022. The bias of the literature was evaluated using the bias evaluation module in Cochrane Manual Version 5.1.0, and the meta-analysis was conducted using RevMan software to verify the effectiveness of oral administration of traditional Chinese medicine (TCM) and its impact on reducing the recurrence rate.

RESULTS: The meta-analysis included 7 articles. In the meta-analysis of all articles, the effective treatment rate of oral administration of TCM reached 97.09%. Additionally, when comparing the recurrence rate of AR between patients taking Chinese medicine orally and other treatment groups, the recurrence rate of patients taking Chinese medicine orally was only 24.46%, which was significantly lower ($p<0.05$). Furthermore, the quality of life of patients taking Chinese medicine orally after treatment was significantly higher than that of patients in the control group (C), indicating the good safety of oral Chinese medicine.

CONCLUSIONS: Oral administration of TCM has demonstrated an effective reduction in the recurrence rate of AR, offering patients a good prognosis. This finding holds significant value for the clinical diagnosis and treatment of AR.

Key Words:
Traditional Chinese medicine, Allergic rhinitis, Soup, Recurrence rate.

Introduction

Allergic rhinitis (AR) is a prevalent condition in otolaryngology that is challenging to cure and prone to relapse after treatment. Common clinical symptoms of AR include nasal itching, frequent sneezing, and more. Although the onset of AR may not significantly affect patients' daily lives, prolonged illness could lead to severe conditions, such as sinusitis and otitis media. Additionally, long-term treatment may result in repeated visits to healthcare providers, increasing the economic burden and negatively impacting patients' quality of life. In current clinical treatment, drug treatment is often used to inhibit the deterioration of AR, because it cannot be eradicated. Therefore, based on the current clinical treatment status, some patients will choose surgical treatment to reduce the harm of AR at one time. However, surgical treatment can only bring short-term benefits, and its long-term effect is still poor. Western medicine believes that AR is a symptom caused by the stimulation of various inflammatory mediators, so symptomatic treatment is the main treatment. As the importance of traditional Chinese medicine (TCM) in clinical treatment continues to grow, several articles have suggested using TCM to treat AR. According to TCM, AR is caused by a malfunction of the patient's visceral functions. It is necessary to improve individual body performance to achieve the purpose of treating AR. From the current situation in clinical TCM treatment, AR is mainly treated by taking Chinese medicine orally, traditional Chinese patent medicines, and simple preparations and acupuncture and moxibustion (AM). Thus, existing

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articles have found that the treatment mode of oral administration of TCM can effectively reduce the recurrence rate of AR patients. Therefore, to clarify the effect of oral administration of TCM on the recurrence rate of AR, this study explores using oral administration of TCM in past AR treatment with the method of systematic review.

Materials and Methods

Literature Retrieval Strategy and General Information of Patients

In strict accordance with PRISMA guidelines and based on the developed retrieval strategy, the meta-analysis is shown in Table I. The literature search is conducted in PubMed, Science Direct, WOS, and other databases. "Perennial AR", "PAR", "Randomized controlled trial", "TCM", "Internal medicine", "Decoction", "Recurrence rate", and "Chinese medicinal herb" are used as keywords for literature retrieval. The search time period is limited to January 1, 2013, to December 31, 2022.

Inclusion and Exclusion Criteria

Literature inclusion and exclusion criteria

Inclusion criteria: (1) all subjects in the included articles met the diagnostic criteria for AR and underwent traditional Chinese medicine (TCM) syndrome differentiation; (2) the included studies utilized randomized controlled trial (RCT) designs, with the intervention group receiving only oral Chinese herbal medicine; (3) in the RCTs, the control group received only western medicine or TCM treatments (including oral TCM administration); (4) baseline data between the intervention and control groups were not statistically significant, indicating comparable groups; (5) study outcomes included comparisons of treatment efficacy and AR recurrence rates between groups, with a minimum follow-up period of 3 months post-treatment; (6) only English language studies were included.

Exclusion criteria: (1) studies of AR that did not include TCM syndrome differentiation; (2) non-clinical controlled studies; (3) studies where patients had concomitant severe chronic rhinitis or other oral and nasal conditions; (4) studies where patients had concomitant diseases including cardiac, hepatic and renal dysfunction; (5) studies where patients had other concomitant allergic diseases; (6) articles published repeatedly.

Data Extraction

Based on the predetermined criteria, three researchers systematically searched and screened the literature. Studies not meeting the inclusion criteria were excluded. Data extraction from the included studies was performed using a standardized form to collect the following information: (1) author and year of publication; (2) baseline characteristics of study participants, including sample size and treatment interventions; (3) outcome measures, including treatment efficacy rate and AR recurrence rate during follow-up.

Article Evaluation

The literature quality evaluation is conducted with reference to the risk of bias assessment tool recommended in Chapter 5.1 of the evaluator's manual. The evaluation indicators include: (1) the correctness of random sequence generation; (2) whether allocation concealment was performed; (3) the use of double blinding; (4) data integrity, including the number of participants lost to follow-up, causes, and handling results; (5) whether there was selective reporting of data; (6) whether there were sources of bias from other factors.

The risk of bias for the literature can be judged as high risk, low risk, or uncertain risk. When evaluating study quality, if one or more items are categorized as high risk, the overall study is considered to have a high risk of bias. If one or more items have uncertain risk, the study is deemed to have an uncertain risk of bias. Conversely, if all items have low risk, the study is considered to have a low risk of bias.

Statistical Analysis

In case of heterogeneity among the included studies, a descriptive analysis was utilized. In the absence of heterogeneity, the RevMan software (version 5.3, The Cochrane Collaboration, London, United Kingdom) was used to conduct meta-analyses. For meta-analyses, fixed-effect models were applied in the case of low or insignificant heterogeneity, while random-effect models were employed if substantial heterogeneity is detected. Standardized mean differences (SMDs) or mean differences (MDs) were used to pool continuous outcomes across studies. Dichotomous outcomes were synthesized using relative risks (RRs) or odds ratios (ORs) with 95% confidence intervals (CIs). Publication bias was assessed visually using funnel plots and statistically *via* Egger's test. Sensitivity analyses will be carried out to evaluate the robustness of conclusions by comparing results obtained from different effect models.

Table I. PRISMA guide and content distribution[7].

Section	Checklist item	Chapter location
Title	Identify the report as a systematic review, meta-analysis, or both.	Title
Abstract	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; conclusions and implications of key findings; systematic review registration number.	Abstract
Introduction		
Rationale	Describe the rationale for the review in the context of what is already known.	Introduction
Objectives	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Introduction
Methods		
Eligibility criteria	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	1.1
Information sources	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	1.1
Study selection	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	1.2
Data collection process	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	1.3
Data items	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	1.3
Risk of bias in individual studies	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	1.4
Summary measures	State the principal summary measures (e.g., risk ratio, difference in means).	1.4
Synthesis of results	Describe the methods of handling data and combining results of studies, if done, including measures of consistency for each meta-analysis.	1.5
Risk of bias across studies	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	1.4
Additional analyses	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	1.7
Results		
Study selection	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	2.1
Study characteristics	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	2.2
Risk of bias within studies	Present data on risk of bias of each study and, if available, any outcome level assessment	2.3
Results of individual studies	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	2.4, 2.5
Synthesis of results	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	2.4, 2.5
Risk of bias across studies	Present results of any assessment of risk of bias across studies.	2.6
Additional analysis	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression	2.4, 2.5
Discussion		
Summary of evidence	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Section 3, paragraphs 2, 3 and 4
Limitations	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Section 3, paragraph 5
Conclusions	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	3

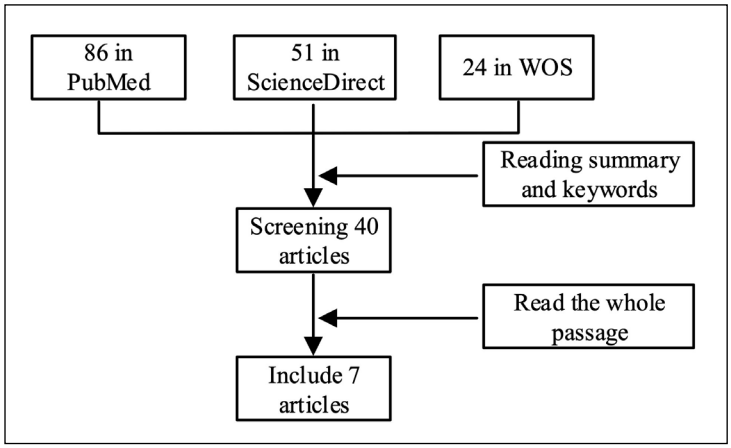

Figure 1. Process of document retrieval and screening.

Results

Literature Search Results

The initial literature search yielded 161 articles related to oral TCM for AR treatment, with 86, 51, and 24 articles identified from PubMed, ScienceDirect, and Web of Science databases, respectively. Following the search, three reviewers independently screened the retrieved studies per the pre-specified eligibility criteria. Full-text articles were then assessed to determine final inclusion. Any disagreements during the screening and full-text review stages were resolved *via* discussion. Ultimately, 7 studies met the inclusion criteria and were included in the meta-analysis. Figure 1 provides a PRISMA flow diagram detailing the study selection process.

Article Information

There were 7 articles[8-14] for analysis, and the duration of the literature was from 2013 to 2022. The author, age, and relative information of the seven articles are shown in Table II. Among the seven articles included in the analysis, the treatment group (G) used TCM decoction as a treatment method, while the control group (C) used Western medicine and TCM therapy.

Included in Literature Quality Evaluation

The methodological quality and risk of bias of included studies were assessed using the Cochrane risk of bias tool, as shown in Figure 2. None of the 7 included studies[8-14] adequately described the method for random sequence generation, resulting in an unclear risk of selection bias. Allocation concealment was mentioned in 2 studies[8-10], accounting for 28.6% of included trials; the remaining 5 studies did not mention allocation concealment, indicating an unclear risk. Only 2 studies[10,13] explicitly stated the use of double blinding of participants and study personnel, suggesting a high risk of performance bias in the other 4 studies[8,9,11,12,14], which did not report on blinding. A study[12] was rated at high

Table II. Basic information of included documents.

First author	Literature years	Number in C	Number in G	Treatment mode in C	Treatment mode in G
Zhao et al[8]	2019	47	51	Bimin decoction	Fluticasone nasal spray and loratadine tablets
Umali and Chua[9]	2017	12	12	Ehretia Microphylla (Tsaang Gubat)	Loratadine
Chan and Chien[10]	2014	83 / 83	83	Cure-allergic-rhinitis Syrup / Yu-ping-feng San	Placebo
Kim et al[11]	2019	56	56	So-Cheong-Ryong-Tang	SCRT or placebo
Hajiheydari et al[12]	2017	37	34	Nepeta bracteata	Placebo
Zhang and Wang[13]	2022	50	50	Tuomin Zhiti Decoction	Loratadine
Wang et al[14]	2015	45	45	CHM	Acupuncture

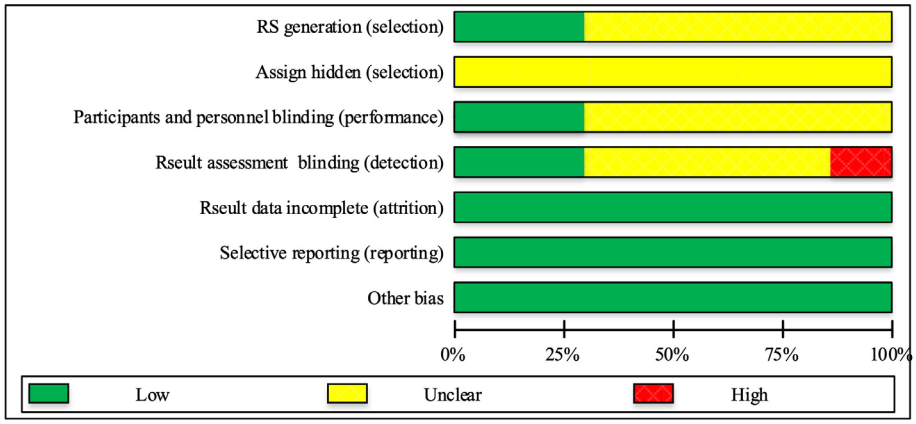

Figure 2. Risk assessment of inclusion literature bias.

risk for detection bias as the blinding procedure was violated during outcome assessment. Regarding attrition bias, all 7 studies were considered low risk as there were no missing outcome data reported. No selective outcome reporting was detected in any studies, yielding a low risk of reporting bias. No other sources of bias were identified.

Results of Meta-Analysis of Patients' Treatment Effectiveness

A total of 7 studies[8-14] involving 744 patients with AR were included in the meta-analysis, comprising 413 patients in the treatment group (G) receiving Chinese herbal medicine and 331 patients in the control group (C) receiving loratadine. Across all included studies, 401 patients in G and 295 patients in C were considered effectively treated, with treatment efficacy rates of 97.09% and 89.12% in G and C, respectively.

The treatment effects of groups G and C were analyzed based on the main AR symptoms and signs. The aim was to evaluate differences in efficacy between Chinese herbal medicine and loratadine for AR. As shown in Figure 3, no significant heterogeneity was detected among studies for the meta-analysis of main symptom and sign outcomes (p=0.38, I^2=9%). When aggregating all studies, treatment group G showed significantly greater improvement compared to control group C for main symptom scores. However, there was no significant difference between groups in scores for physical signs.

Then the effectiveness between Chinese herbal medicine and placebo in the treatment of patients with AR, the difference was analyzed. Figure 4 shows the results of the meta-analysis, where it can be seen that there is no heterogeneity between the main symptoms and signs of patients in the two groups (p=0.95, I^2=0%). In Figure 4,

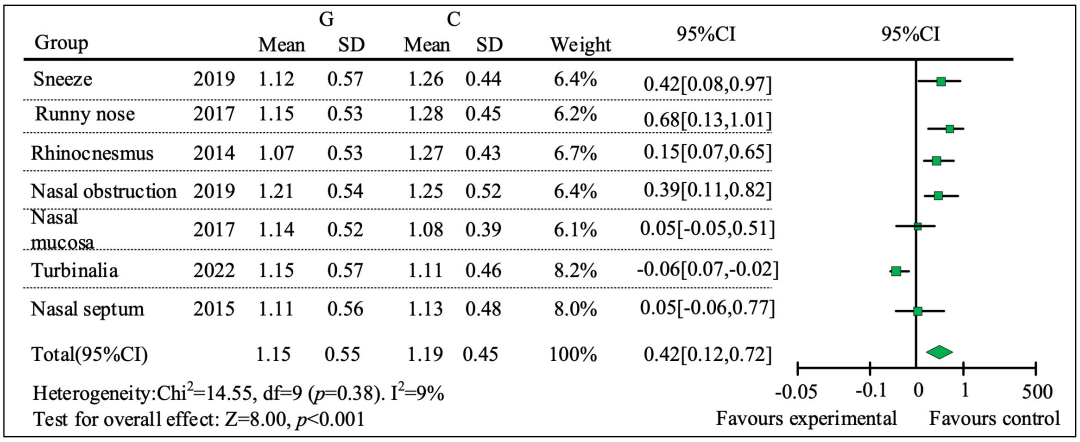

Figure 3. Analysis of the difference between oral administration of TCM and loratadine tablets.

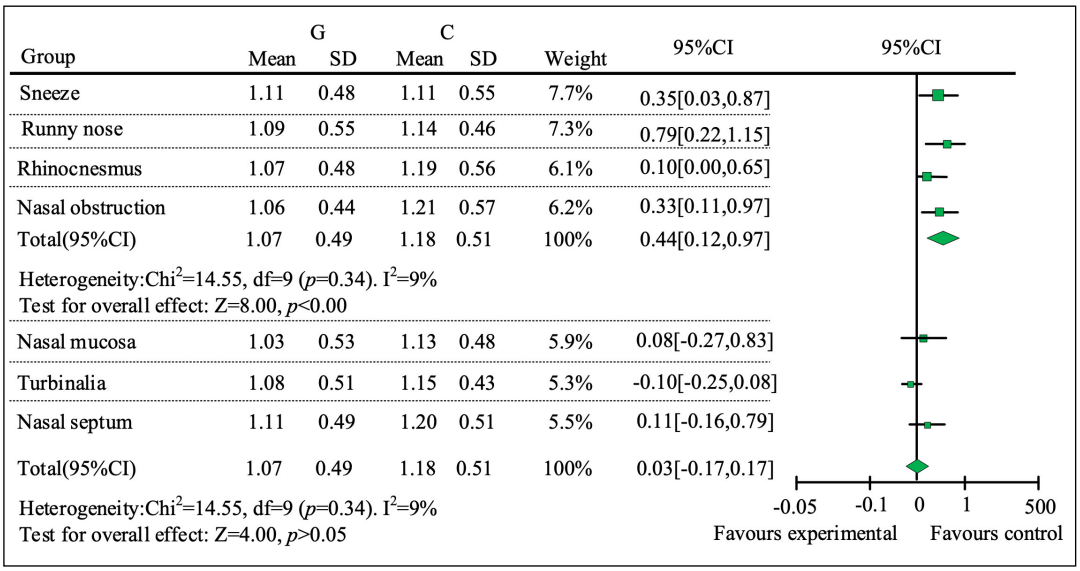

Figure 4. Analysis of the difference between oral Chinese medicine and placebo treatment.

the blocks in the patient's main symptoms and signs evaluation are on the right side of the invalid vertical line with X=1. That is, the score of main symptoms and signs of patients in C was higher than that in G. The difference in main symptom and physical sign scores between the two groups was statistically significant (p<0.05), OR=-0.58, 95% CI [0.12, 0.97], Z=8.00, p<0.001. Physical sign scores had no obvious difference (p>0.05), OR=-0.03, 95% CI [-0.17, 0.17], Z=4.00, p>0.05.

Finally, in the evaluation of treatment effect, the difference between oral administration of TCM and treatment of TCM was analyzed. The results of the meta-analysis are shown in Figure 5. The main symptoms and signs of the two groups were not heterogeneous (p=0.62, I^2=5%). In Figure 5, the main symptoms of the two groups were significantly different (p<0.05), and there was no statistically significant difference in physical sign scores (p>0.05).

Meta-Analysis of Patients' Quality of Life

The study analyzed the application of oral TCM in reducing AR recurrence rate by comparing quality of life outcomes between the two

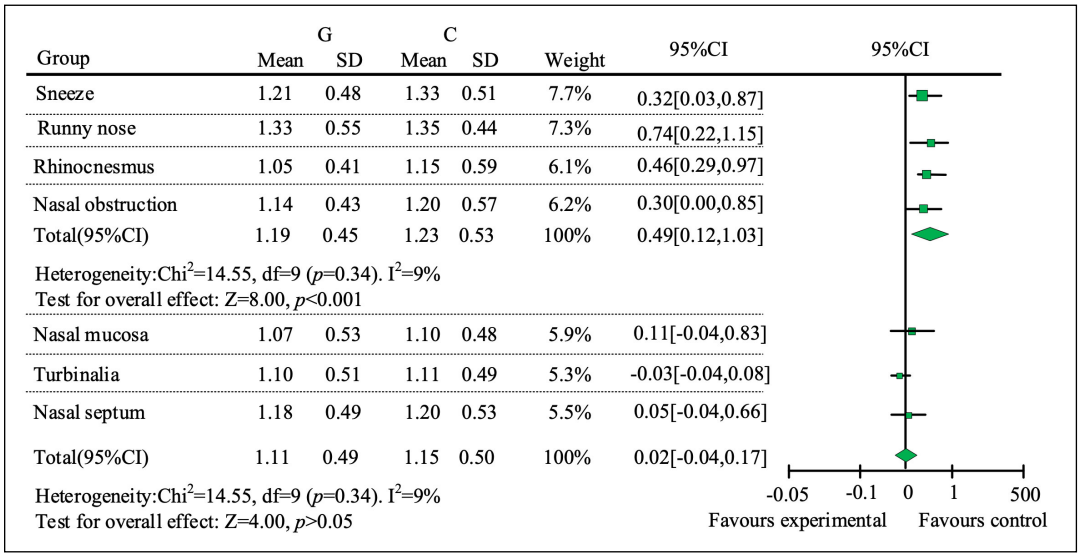

Figure 5. Analysis of the difference between oral administration of TCM and treatment of TCM.

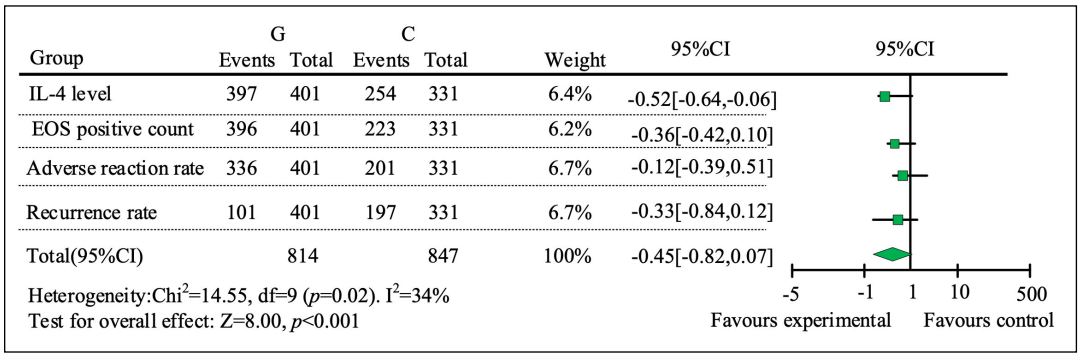

Figure 6. Analysis results of quality of life of two groups of patients.

groups. As shown in Figure 6, oral TCM significantly reduced patients' IL-4 level, eosinophil count, and recurrence rate compared to the control group ($p<0.05$, OR=-0.45, 95% CI [-0.82, 0.07], Z=8.00, $p<0.001$).

A meta-analysis was also conducted on AR recurrence rate using the included studies. Figure 7 presents the results. Heterogeneity analysis showed low heterogeneity among the included randomized controlled trials ($p=0.02$, $I^2=34\%$), so a fixed effects model was used. In Figure 7, the effect sizes for all 7 studies were to the left of the invalid line at X=1, indicating oral TCM significantly reduced AR recurrence versus control (combined OR=0.42, 95% CI [0.12, 0.72], Z=8.00, $p<0.001$).

Literature Publication Bias Analysis

To assess the publication bias of the included studies, a funnel plot was generated, as shown in Figure 8. The funnel plot was symmetrical around the central axis at OR=0.52, with most studies distributed across the top. This shape indicates that the included studies have a low risk of publication bias.

A Galbraith plot was also constructed to further evaluate potential publication bias (Figure 9). All included studies fell within the 95% confidence bounds, again demonstrating no significant bias in the literature (Table III-IV).

Discussion

AR is a common nasal disease. AR patients are prone to mucosal edema and itching, which seriously affects their normal life. In recent years, with the increasing frequency of environmental changes, the prevalence of AR has shown a growing trend worldwide. The current literature suggests that AR occurs in individuals after exposure to allergens, as allergens induce inflammatory reactions in the nasal mucosa. In contrast, according to TCM, AR is caused by a deficiency of the lung, spleen, and kidney, leaving patients more susceptible to wind and cold.

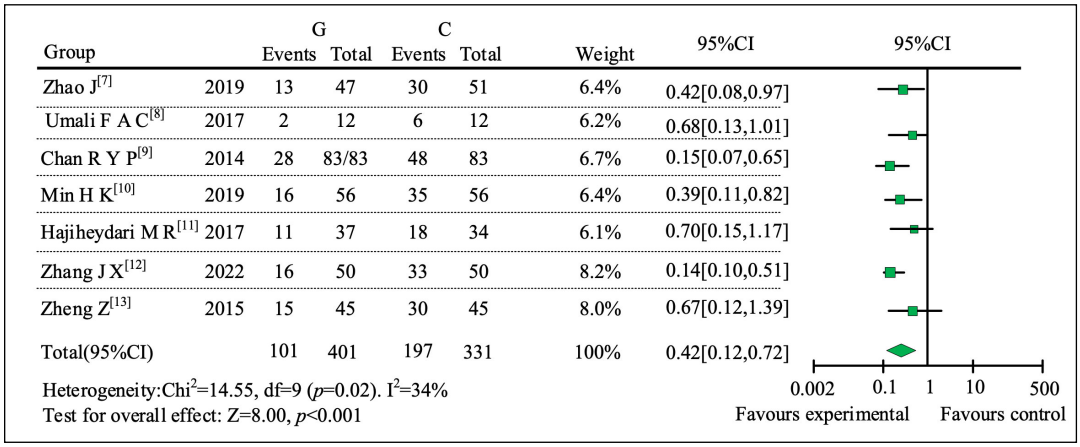

Figure 7. Forest map analysis results of recurrence rate of two groups of patients.

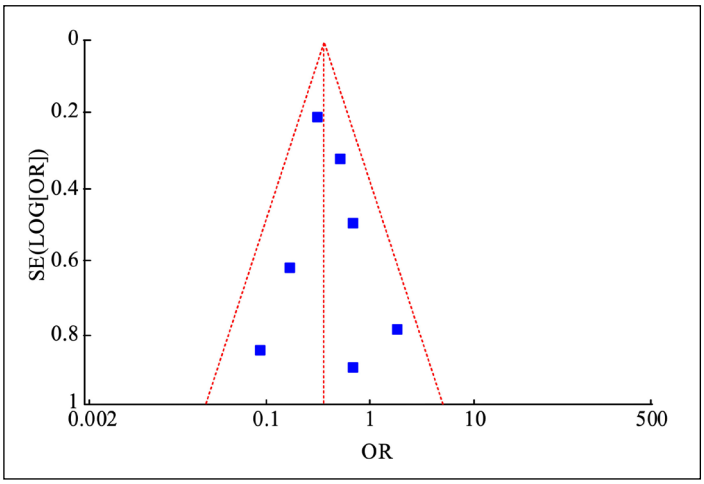

Figure 8. Funnel chart for comparison of adverse reaction rates between the two groups.

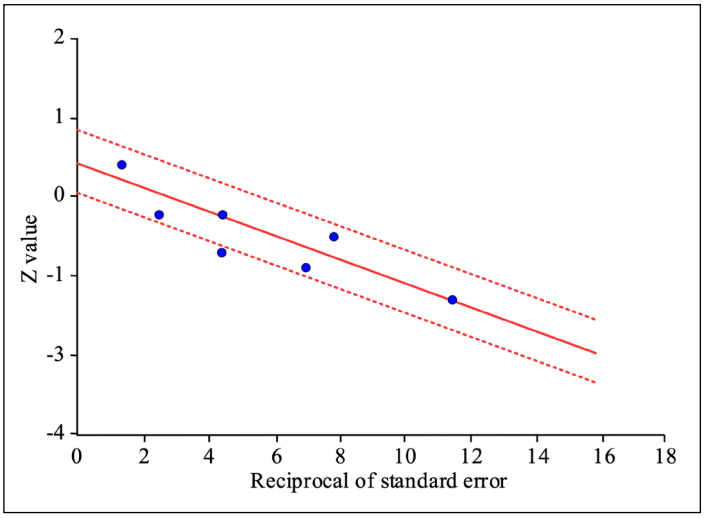

Figure 9. Galbraith chart in Comparison of adverse reaction rates between the two groups.

Table III. Difference in treatment effectiveness between two groups of patients.

Group	Before treatment	After treatment	χ^2	*p*
G	0	21 (95.45%)	0.135	<0.05
C	0	18 (81.82%)	0.534	<0.05
χ^2	/	2.153	/	/
p	/	<0.05	/	/

Table IV. Difference in recurrence rate between the two groups.

Group	Rhinobyon	Shed tears	Total
G	2	2	4
C	5	7	12
χ^2	.0324	0.943	1.137
p	<0.05	<0.05	<0.05

In clinical diagnosis and treatment, AR patients show frequent sneezing and clear mucus-like water for a long time, which will affect the sleep quality of patients in serious cases. Patients with AR for a long time will have complications like sinusitis and asthma. It can even lead to malignant tumors such as nasopharyngeal carcinoma. Therefore, achieving effective diagnosis and treatment of AR is an important direction in the clinical practice of rhinology. Based on current clinical practice, AR cannot be cured, but it can be managed with medication. Although surgery is sometimes recommended, the long-term efficacy results for patients suggest that their quality of life may remain suboptimal. TCM has rich experience in treating AR. From the current treatment effects, TCM can achieve syndrome differentiation and treatment. It will improve individual immunity by enhancing the patient's physique and treating AR. From previous studies, it can be seen that TCM decoctions have good effects in treating AR, with high safety, and can significantly reduce the late recurrence rate of AR. Therefore, to more clearly understand the effect of TCM decoctions on the recurrence rate of allergic patients, this study adopted a systematic review method to verify the efficacy and safety of TCM oral treatment for AR.

In the meta-analysis of the literature, this study first evaluated differences in treatment effectiveness between all patients. Comparing oral Chinese medicine to loratadine tablets revealed that patients taking oral Chinese medicine had significantly lower main symptom and sign scores than those taking loratadine. That is, compared to Western medicine, oral TCM more effectively reduced patients' clinical symptoms and had better therapeutic effects. In comparing oral Chinese medicine to a placebo, patients taking oral Chinese medicine had significantly different main symptom scores from those taking a placebo. This is because the placebo has no therapeutic effect, so it can only alleviate AR incidence in patients to a certain extent, while oral TCM can significantly improve patients' individual immunity. Comparing oral TCM to acupuncture and moxibustion (AM) showed that AM could reduce main symptom and sign scores to some extent. However, oral TCM was more effective at reducing patients' main symptoms and signs. It was previously suggested that AM and plasters could alleviate pain, but TCM treatments have stronger medicinal properties and provide better therapeutic effects compared to these alternatives.

To evaluate the AR recurrence rate, a meta-analysis of oral TCM administration was conducted on studies[8-14]. In comparing patient quality of life and recurrence rate, the recurrence rate in the TCM group was significantly lower than the control group. Reviewing the included studies shows that most controls used loratadine tablets or a placebo. However, existing studies have found TCM more effective than Western medicine in post-treatment rehabilitation and safety. Moreover, TCM reduced IL-4 levels, eosinophil counts, and adverse reactions, and maintained these improvements long-term.

Conclusions

To sum up, oral administration of TCM can effectively treat AR and reduce patient recurrence rates. Compared to other TCM modalities, oral TCM improved treatment efficacy and lowered recurrence more effectively. Oral TCM also showed greater therapeutic effects and recurrence reduction than Western medicine. Currently, oral TCM represents a highly efficacious approach to reducing AR recurrence. However, this study has limitations. The strict literature search criteria yielded a small pool of included studies (8-14), which precludes fully elucidating the impacts of oral TCM on AR. Future studies should expand the search terms to identify more research on AR treatment and strengthen the evidence base.

Conflict of Interest

The Authors declare no conflict of interests.

Funding

There are no financial disclosures of the authors.

Ethics Approval

Not applicable.

Informed Consent

Not applicable.

Authors' Contributions

YZ, LQ, and RW contributed to the conception and design and were involved in drafting the manuscript. They have been involved in critically revising the articles. All authors have thoroughly reviewed and endorsed the final manuscript.

Availability of Data and Materials

The data are available on request from the corresponding author.

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