

REVIEW ARTICLE

Research Progress on the Mechanism of Acupuncture in the Prevention and Treatment of Allergic Rhinitis

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ABSTRACT

Objective • To research the mechanism of acupuncture and moxibustion in treating and preventing allergic rhinitis.

Methods • We searched PubMed; Google Scholar; Semantic Scholar; Academic Keys; Citation; Dimensions; EuroPub; Index (A & HCl); Compendex; Conference Proceedings Citation; and Science Citation Index. We reviewed the mechanism of acupuncture and moxibustion in the prevention and treatment of allergic rhinitis from the perspectives of Th1/Th2 balance regulation, IgE level reduction, lowering of inflammatory cell infiltration in the nasal mucosa, regulation of nasal neuropeptide (substance P) level, inhibition of Toll-like receptors, and NFκB protein expression.

Results • Acupuncture can play a therapeutic role in AR. Combining different aspects such as the influence on Th1 and Th2 subsets of cells, regulation of Th1/Th2 balance, reduction of IgE level, reduction of inflammatory cell infiltration in the nasal mucosa, regulation of nasal neuropeptide (substance P) level, inhibition of Toll-like receptor, and NFκB protein expression, the mechanism of action of acupuncture for AR can be elucidated more comprehensively.

Conclusion • Acupuncture and moxibustion can be used to treat allergic rhinitis in several ways. (*Altern Ther Health Med.* 2023;29(8):228-232).

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INTRODUCTION

The most recent definition of allergic rhinitis (AR) is “a non-infectious chronic inflammatory disease of the nasal mucosa primarily mediated by IgE following the body’s exposure to sensitized individual”.¹ It is clinically characterized by sudden or recurrent episodes of itching, sneezing, runny nose, and nasal congestion.² Under the combined effect of many factors (such as house pets, house decoration, air pollution, irritating gases, pollen, dust mites, mites, and so on), the incidence of AR worldwide is increasing year by year. It is estimated that AR patients worldwide have exceeded 500 million.³ AR has seriously affected people’s learning, work, and quality of life. Seeking safe and effective treatment is an urgent need at present. More and more AR patients are seeking alternative therapies that focus on acupuncture.⁴

In 2015, the latest guidelines for the treatment of AR developed by experts from the American Academy of

Otolaryngology-Head and Neck Surgery Foundation (AAO-HNSF) recommended acupuncture as one of the first-line of therapeutic options.⁵ This indicates that acupuncture therapy for AR has been basically recognized by the world medical community. To allow acupuncture treatment of AR to play a better role, research aimed at understanding its mechanism is indispensable (such as the impact of acupuncture on the immune system regulation function). Towards this end, the author collates and analyzes relevant research in recent years, and summarizes the findings.

MATERIALS AND METHODS

Research materials

A search through computerized literature databases including PubMed; Google Scholar; Semantic Scholar; Academic Keys; Citation; Dimensions; EuroPub; Index (A&HCl); Compendex, Conference Proceedings Citation; and Science Citation Index was conducted for relevant literature, with the search period ranging from January 1, 2000 to March 20, 2023.

Search method

The search method was a combined search strategy of subject terms and free words. The search terms used include rhinitis, allergic rhinitis, perennial allergic rhinitis,

acupuncture and moxibustion, electric-acupuncture, needling, acupoint, etc. After retrieving the eligible literature, the relevant references in each article were traced to check their eligibility for inclusion, to make this study as comprehensive as possible, and to reduce the possibility of missing out relevant literature. After importing the retrieved literature into NoteExpress management software for checking, we looked at the abstract of each article to exclude those that failed to meet the inclusion criteria and select the ones that met the criteria for analysis.

Inclusion criteria

The inclusion criteria are as follows: (1) Currently published research protocols on acupuncture for allergic rhinitis with clinical efficacy and mechanism studies as the main focus; (2) studies with blinded and non-blinded methods; (3) observation of efficacy and mechanism studies as the main purpose; (4) patients with clinical symptoms of allergic rhinitis, gender, case source, type and duration of disease are not limited; (5) the age of the research subjects should all be older than 18 years old, and the control group and the baseline data of the patients in the observation group should be well-balanced and comparable, and the primary diagnosis should involve the disease, and there should be clear diagnostic criteria as well as exclusion criteria.

Exclusion criteria

The exclusion criteria used are as follows: (1) the study focuses on the use of animals/animal models, clinical reports of adverse reactions and pharmacology, pharmacokinetics, and other non-clinical efficacy evaluation research; (2) the efficacy assessment index is not published in the treatment results; (3) the statistical analysis method is not clear; (4) the randomized control scheme is not clear in the clinical trials; (5) studies using purely descriptive research; (6) literature reviews, clinical case reports, and personal experience reports; (7) combined with other malefactors, personal experience reports; (8) Studies focusing on other diseases along with allergic rhinitis.

MECHANISM OF ACUPUNCTURE IN THE PREVENTION AND TREATMENT OF ALLERGIC RHINITIS

Acupuncture adjusts the Th1/Th2 balance

Immune imbalance between Th1/Th2 cells is an important factor in the development of AR. Th1 cells mainly secrete IL-2, IL-12, TNF- α , and interferon- γ (IFN- γ),⁶ among which IFN- γ is a characteristic factor, which can inhibit the synthesis of IL-4-mediated IgE and inhibit the differentiation of Th cells into Th2 cells.⁷ Th2 cells mainly secrete IL-4, IL-5, IL-10, IL-13, and granulocyte-macrophage colony stimulating factor (GM-CSF).⁸ IL-4 is a characteristic factor, which can induce specific IgE production in the B cells. In AR patients, the Th1 cytokine IFN- γ is significantly decreased, while the Th2 cytokine IL-4 is significantly increased, indicating that the imbalance of Th1/Th2 cell axis and the over-secretion of

IL-4 are important factors in the pathogenesis of AR.⁹ Through the secretion of cytokines, the Th1 and Th2 regulate and inhibit each other, so that Th1/Th2 is in a state of balance.⁷ Th1 cells mainly secrete cytokines such as IFN- γ , IL-2, and IL-12, while Th2 cells mainly secrete cytokines such as IL-4, IL-5, IL-6, IL-9, IL-13, and IL-15.¹⁰

Depending upon the functions and the types of cytokines they secrete, T helper lymphocytes (Th cells) in human body can be divided into 4 subtypes, namely, Th1, Th2, Th17, and Treg cells. In recent years, a large number of studies have suggested that the pathogenesis of AR may be closely related to Th1/Th2 imbalance, which is manifested by the low function of Th1 subgroup and the hyperfunction of the Th2 subgroup.¹¹ IFN- γ secreted by Th1 cells can inhibit the synthesis of IgE mediated by IL-4 and inhibit the differentiation of Th cells into Th2 cells. IL-4 secreted by Th2 can not only induce IgE synthesis in human B cells but also promote the differentiation of Th cells into Th2 cells.

Zhang et al.¹² studied the effect of acupuncture and moxibustion on serum IL-4 and IFN- γ in patients with perennial allergic rhinitis (PAR), and found that the level of IFN- γ before and after acupuncture treatment was significantly negatively correlated with the symptoms and signs of patients. Meanwhile, the level of IL-4 is positively correlated with the symptoms and signs of patients, and acupuncture can increase the level of IFN- γ in serum and reduce the level of IL-4, so as to restore the balance of Th1/Th2. Gong et al.¹³ observed the effect of intranasal acupuncture on AR, the protein expressions of substance P (SP), vasoactive intestinal peptide (VIP), and neuropeptide Y (NPY) in rabbit nasal mucosa, and the changes of serum immunoglobulin E (IgE), interleukin-4 (IL-4), and interferon- γ (IFN- γ) contents. The mechanism of improving AR by intranasal acupuncture was discussed. The results showed that intranasal acupuncture could alleviate the symptoms of AR in rabbits, which may be related to the improvement of neurogenic inflammation by regulating the expressions of SP, VIP, and NPY in nasal mucosa and the contents of IgE, IL-4, and IFN- γ in serum.

Through a clinical trial, Chen et al.¹⁴ aimed to explore the mechanism of acupuncture on hypothalamus-pituitary-adrenal (HPA) axis in patients with moderate or severe persistent AR. The results of the trial will provide evidence for the effects of chronic, long-term, and repetitive stimulation in patients with moderate to severe persistent AR and the effects of acupuncture on the HPA axis in such patients.

Acupuncture reduces IgE levels

In the pathogenesis of allergic rhinitis, IgE is the most important antibody that mediates the degranulation of inflammatory cells and causes nasal symptoms, thus reducing IgE level. Hence, this is one of the effective mechanisms for the treatment of this disease.¹⁵ Numerous studies have shown that acupuncture can effectively reduce serum IgE levels in patients with AR.

McDonald et al.¹⁶ conducted a randomized, sham-controlled acupuncture treatment for adults with persistent

AR, where 151 subjects were recruited and randomly divided into real acupuncture group, sham acupuncture group, and non-acupuncture group. Various cytokines, neurotrophins, proinflammatory neuropeptide, and immunoglobulins were measured in saliva or plasma from baseline to 4-week follow-up. The results of this study indicated that the specific IgE decreased only in the real acupuncture group, and symptoms such as nasal itching, nasal congestion, sneezing, runny nose, itchy eyes, and sleep deprivation was significantly improved. These results also suggest that acupuncture can play a sustained immunomodulatory role by reducing IgE levels.

Brinkhaus et al.¹⁷ used a randomized, controlled, multicenter trial to conduct a controlled study of acupuncture and cetirizine on 422 AR patients who were sensitive to birch pollen and grass pollen. The results showed that acupuncture achieved the goal of treatment by significantly reducing the serum IgE level.

Hauswald et al.¹⁸ evaluated the clinical effect of acupuncture and moxibustion and its influence on the immune system by comparing the efficacy of acupuncture and loratadine on patients with mite allergy. Twenty-four patients with persistent allergic rhinitis caused by dust mites were treated with acupuncture (15 cases) and loratadine (9 cases), respectively. The data were evaluated by subjective and objective rhinoconjunctivitis symptom scores, specific and total IgE, interleukins (IL-4, IL-10), and IFN- γ as markers of Th1 or Th2 cell activity. The results showed that the efficacy of acupuncture group and loratadine group was similar. Changes in specific or total IgE were decreased in both groups. McDonald et al.¹⁶ observed the effects of acupuncture on dust mite specific IgE, substance SP, and symptoms of persistent AR, and found that acupuncture could regulate the mucosal immune response of upper respiratory tract in adults with persistent AR. This regulation may be attributed to the down-regulation of specific IgE levels of house dust mite allergens by acupuncture.

Acupuncture reduces the infiltration of inflammatory cells in nasal mucosa

Reduction of eosinophil infiltration in nasal mucosa.

Eosinophil is an important effector cell in the pathogenesis of AR. Studies have shown that the positive rate and distribution degree of EOS in nasal secretions are significantly higher than those in normal people and non-AR patients.¹⁹ Studies have shown that an important pathological feature of patients with AR is the infiltration of a large number of eosinophils in the nasal mucosa. Eosinophils synthesize and secrete a large number of bioactive substances, which plays a crucial role in the pathophysiology of patients with AR²⁰ which is consistent with the pathogenesis of AR. In nasal secretions, the infiltrated EOS are activated and release eosinophil cationic protein, interleukins, major basic protein, leukotriene, platelet activating factor, and tumor necrosis factor,²¹ which are nerve and vascular active substances that cause vascular engorgement and increases sensitivity reaction in glands and nasal mucosa.²² It is an important

indicator of inflammation in allergic diseases and plays an important role in the pathogenesis of diseases.²³ Acupuncture treatment of AR can improve nasal symptoms by reducing the local accumulation of eosinophils.

Jo et al.²⁴ conducted a randomized blinded trial study on 40 patients with PAR to study the possibility of electrothermal moxibustion (EM) in the treatment of PAR, and compared EM with acupuncture (AC) to evaluate the feasibility of using this technology in a wider range. Results showed that the total nasal symptom score (tns) and the average score of rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) was significantly improved before and after treatment in the electrothermal moxibustion group and the acupuncture group ($P < .05$), total IgE and eosinophil count were decreased after treatment compared with those before treatment ($P < .05$). The results indicated that EM is a safe alternative treatment for patients with PAR.

Kang et al.²⁵ conducted a randomized controlled trial on the treatment of AR using intranasal low-level laser therapy, and randomly divided 80 AR patients into intranasal low-level laser treatment group and acupuncture treatment group. Each group was treated for 20 min, 3 times a week, for 4 weeks. The results showed that the total nasal symptom score (tns), RQLQ, and the nasal endoscopic index improved in the two groups after 4 weeks of treatment. In terms of tns, the low-level intranasal laser treatment was not inferior to acupuncture treatment. After treatment, the total IgE level and eosinophil count in the two groups was lower than those before treatment ($P < .05$). The results showed that the curative effect of low-level laser treatment was not lower than acupuncture treatment.

Acupuncture reduces mast cells in nasal mucosa glands. Mast cells (MCs), derived from hematopoietic stem cells, are a class of non-specific immune cells that are widely distributed in tissues and organs throughout the body and are the target cells of allergic reactions. MCs release inflammatory mediators such as histamine, leukotriene, bradykinin, and eosinophilic chemokine. It causes acute allergic reactions such as runny nose, nasal itching, sneezing, and nasal congestion.²⁶ Since the 1990s, studies on the effects of acupuncture and moxibustion on mast cells in allergic rhinitis have gradually increased and made some progress.²⁷ Chen et al.²⁸ compared real acupuncture and sham acupuncture in 140 patients with a history of AR and positive skin prick test (SPT). The changes of serum allergen specific immunoglobulin E (sIgE), mast cells, eosinophils, and T cells were observed. The results of this trial demonstrated the efficacy of acupuncture in the treatment of AR and verify whether the effectiveness of acupuncture is related to the feeling of qi by needles.

Acupuncture regulates nasal neuropeptide (substance P) levels. With the deepening of research, the understanding of the pathogenesis of AR has improved. It is now known that pathogenesis of AR not only includes the type I hypersensitivity reaction mediated by IgE but also the neural, endocrine, and inflammatory reaction mechanisms.²⁹ In recent years, some

studies have shown that neurogenic inflammation is one of the key pathogenic links of AR.³⁰ There are abundant peptidergic nerve endings in the nasal mucosa. According to different functions, neuropeptides are mainly divided into four types, namely, sensory neuropeptide such as substance P (SP), NKA (Neurokinin A), neurokinin B (NKB), and calcitonin gene-related peptide (CGRP); parasympathetic neuropeptides such as vasoactive intestinal peptide (VIP); sympathetic neuropeptides such as neuropeptide Y (NPY); and inflammatory neuropeptides such as bradykinin.³¹

Neuropeptides exert their biological effects mainly by binding to their corresponding receptors. In 1983, SP and SP nerve were found in nasal mucosa,³² and SP can participate in the pathogenesis of AR through various ways. For example, SP can interact with mast cells and cause abnormal permeability and secretion function of nasal mucosa.³³ It can promote the chemotaxis and degranulation of eosinophils and enhance the infiltration of inflammatory cells, leading to tissue edema, vasodilatation, and glandular hyperplasia.³³

At present, relevant studies have proved that acupuncture can reduce SP levels in patients with AR, thereby improving nasal symptoms. Jung et al.³⁴ conducted a randomized controlled study on the effects of acupuncture and moxibustion on mice, and the results showed that both of them could significantly reduce the content of SP in nasal mucosa. Moreover, the effects of acupuncture group and moxibustion group were better than those of western medicine (levocetirizine) group. Gong et al.¹³ observed the effect of intranasal acupuncture on neurogenic inflammation in rabbits with AR, and the results showed that acupuncture could alleviate the symptoms of AR in these rabbits, which may be related to the improvement of neurogenic inflammation by regulating the expressions of SP, VIP, and NPY in nasal mucosa and the contents of serum IgE, IL-4, and IFN- γ .

Acupuncture inhibit Toll-like receptor and NF κ B protein expression

Toll like receptors (TLRs), as a kind of transmembrane receptors that can recognize highly conserved pathogen-related molecular patterns (PAMP), is widely distributed and mainly expressed on cells involved in host defense function such as mononuclear macrophages, granulocytes, dendritic cells, lymphocytes, endothelial cells, epithelial cells, etc.³⁵ Cui et al.³⁶ observed that ovalbumin or nasal drops sensitization could not induce AR and the increase of serum IgE in TLR4 knockout mice, indicating that TLR4 was involved in the pathogenesis of AR. Jung et al.³⁷ reported that acupuncture or moxibustion can play an anti-allergic role by reducing the expression of NF- κ B, SP, and inducible nitric oxide synthase in nasal mucosa of AR rats.

CONCLUSION

In conclusion, acupuncture can play a therapeutic role in AR from multiple aspects. Combining existing research findings including the influence on Th1 and Th2 subsets of cells, regulation of Th1/Th2 balance, reduction of IgE level,

reduction of inflammatory cell infiltration in nasal mucosa, regulation of nasal neuropeptide (substance P) level, inhibition of Toll-like receptor, and NF κ B protein expression, we can analyze and discuss the mechanism of action of acupuncture for AR more comprehensively. However, there are still some problems in current studies such as the small study scope, small sample size, low-level repetition, lack of standardization, and low reliability. In future studies, unified treatment methods can be adopted to conduct large sample randomized controlled trials to integrate various individual factors that have been concluded in this study to explore the network effect mechanism of acupuncture therapy for AR and further promote research development.

Looking forward, the future will focus on a few aspects of research related to AR. First, according to the “cell experiment-animal experiment-clinical experiment” step, animal experiments proved effective and the mechanism of acupuncture therapy clinical should be clearly elucidated and verified as soon as possible. The second is to focus on the material basis of effective treatment of AR by acupuncture. Reasonably designed and rigorously operated multi-target observation clinical and experimental studies will help to reveal the underlying mechanism of acupuncture and promote the anti-allergy acupuncture therapy with precise efficacy across the globe.

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The authors declare that they have no conflicts of interest.

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