

# Treatment of Allergic Rhinitis with Acupuncture Based on Pathophysiological

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**Abstract:** Allergic rhinitis is a prevalent allergic diseases and has a profound impact on physical well-being. In recent years, more and more people have changed to allergic diseases, such as allergic rhinitis, allergic asthma, allergic dermatitis and so on. In the incidence of allergic rhinitis, covering all ages. The common clinical treatment of allergic rhinitis are drugs and immunotherapy, but these therapies have certain limitations. Therefore, an effective and economical treatment for AR is urgently needed. Acupuncture are widely used in the clinical treatment of various diseases, but the effect of acupuncture in the treatment of allergic rhinitis (AR) is significant, and the mechanism of acupuncture in the treatment of AR is also a hot spot. Acupuncture is one of the traditional treatment methods of traditional Chinese medicine, which achieves therapeutic effect by pressing a needle or other means at a specific location on the skin to produce a special sensation. Among them, acupuncture, as a popular treatment method, has attracted more and more attention. In this review, we provide an overview of the current understanding of acupuncture and AR, as well as current studies investigating the efficacy and safety of acupuncture for AR.

**Keywords:** acupuncture, allergic rhinitis, pathophysiological, traditional Chinese medicine

## Introduction

Allergic rhinitis (AR) is a type I chronic, non-infectious, inflammatory disease of the nasal mucosa mediated by immunoglobulin E (IgE) after allergen exposure in atopic individuals. There are three necessary conditions for the development of AR: specific antigens, atopic individuals, and the meeting of specific antigens and atopic individuals. Its main clinical features are paroxysmal recurrent sneezing, watery nasal mucus and nasal obstruction.<sup>1,2</sup> AR is very popular worldwide, and it is also a clinically refractory disease in the otolaryngology department. It is regarded as the “epidemic of the 21st century”, affecting people of all ages and reaching its peak in adolescence.<sup>3</sup> AR has a significant economic impact on education, productivity, and the use of medical resources, with annual AR-related costs reported to be approximately \$20 billion worldwide. According to a British study, the British government spends more than \$10 billion on the treatment of AR almost every year, while the American government spends an average of \$5.5 billion to \$7.7 billion on the treatment of 50 million AR groups every year.<sup>4,5</sup> At the same time, it imposes a significant health burden on individuals, affects the quality of life of patients, and is associated with serious complications, including asthma, sinusitis and conjunctivitis.<sup>6</sup>

The treatment of AR is the current research hotspot, but the current treatment plan is difficult to cure AR, usually to relieve the clinical symptoms. Drug therapy and allergen-specific immunotherapy are the common treatments for AR. The first-line drugs include antihistamines, intranasal corticosteroids and leukotriene receptor antagonists. Immunotherapy downregulates allergic reactions in an allergen-specific manner, and its mechanism remains to be clarified.<sup>7</sup> Western medicine treatment has rapid onset and definite curative effect, which is a good choice for patients with paroxysmal or short-term persistent attacks, but the recurrence is high. There is a lack of clear prevention and treatment methods for AR. The chronic nature of these diseases and the traditional medicines currently used to treat

allergic diseases invariably produce side effects. Moreover, Studies in the past decade have shown that traditional Chinese medicine, including herbal medicine and acupuncture, is safe and effective in the treatment of allergic diseases. A variety of herbs in commonly used Chinese medicine formulations have antiallergic, anti-inflammatory, or immunomodulatory activity. Such functions include inhibition of the release or activity of mast cell mediators such as histamine, inhibition of inflammatory responses induced by chemical agents, and down-regulation of serum IgE levels or lymphocytes and/or macrophages; there is ample evidence that acupuncture is useful in the treatment of allergic rhinitis and asthma alone or as an adjunct to traditional Western therapy.<sup>8</sup> In this review, we analyze the current understanding of acupuncture and allergic rhinitis and evaluate the current research on the effectiveness of acupuncture in allergic rhinitis.

## Acupuncture

Acupuncture has been practiced in China for more than 3000 years and spread to Europe and the United States between the 16th and 19th centuries. The history of acupuncture research began in the eighteenth century and has developed rapidly since then. As a medical practice originating in China, it has accumulated rich clinical and theoretical evidence. Our understanding of the mechanisms of acupuncture treatment has been greatly enhanced by the increasing evidence of its benefits in a variety of situations.<sup>9</sup> Acupuncture is one of the oldest medical practices in Traditional Chinese Medicine (TCM) and one of the most popular TCM treatments, dating back thousands of years. Its safety and effectiveness are respected. Acupuncture reached its peak in the Ming Dynasty (1368–1644), when many famous doctors of acupuncture emerged and a large number of monographs on acupuncture were published, the most important of which was Yang Jizhou's *Dacheng of acupuncture*, which was also a new milestone in the history of acupuncture development. Yang Jizhou compiled a book, which elaborated on the meridians, acupoints, operation methods and indications of acupuncture.<sup>10</sup> The theory of meridians and collaterals studies the physiological functions and pathological changes of the meridians and collaterals of the human body and their relationship with the viscera. The meridians and collaterals run along the path of the human body, just like the route, connecting each part from head to foot and from left to right. They are the backbone of the human body from the inside out. The collaterals represent a crisscross network, and unlike the meridians, the collaterals are thinner and smaller. It is an important part of the basic theory of traditional Chinese medicine, and also constitutes the basis of acupuncture, massage and other clinical departments of traditional Chinese medicine.<sup>11</sup> According to TCM theory, Qi is the internal energy of the human body and is essential for health. Once the state of Qi imbalance occurs, diseases will occur. Acupuncture stimulate the acupoints on the meridians through needles and specific acupuncture techniques, and regulate the balance of Qi and blood through the connection of meridians, so as to achieve the purpose of treating diseases. When these points are fully activated, the patient or acupuncturist will feel the feeling of soreness, numbness, fullness or heaviness, which is called "Deqi". Simultaneously, the feeling of Deqi will be transmitted along the direction of the meridians and collaterals, so that the patient can feel the lesion.<sup>12</sup>

In recent years, according to the ancient description of meridians, more and more scholars have studied the relationship between meridians and western medicine anatomy, believing that meridians are closely related to blood vessels. Studies have found that acupuncture have significant curative effects on pituitary and adrenal cortex system, sympathetic nerve and adrenal medulla system, pituitary and thyroid system, gonad and posterior pituitary system, and the theory that meridians and collaterals are related to the regulation function of neurohumoral system, and the function of acupuncture is realized through nerves and humors.<sup>13,14</sup> At the same time, in order to study the mechanism of action of acupuncture, the Institute used multi-channel functional near-infrared spectroscopy to record the human brain, and found that acupuncture at Hegu acupoint could not only regulate the hemodynamic response of bilateral PFC and motor cortex, but also regulate the functional connectivity and efficiency of PFC motor cortex network. There is also functional magnetic resonance imaging and electroencephalography (EEG). It was found that multiple subcortical brain regions were involved in the process of acupuncture, and acupuncture could regulate the functional connectivity of subcortical regions and increase the EEG power and functional connectivity of  $\delta$  and  $\theta$  bands.<sup>15</sup> At present, based on the superior safety and low side effects of acupuncture treatment, it has been gradually recognized as a therapeutic intervention method of complementary medicine.<sup>16</sup>

Acupuncture have significant clinical efficacy in the treatment of many diseases, among which allergic diseases are also one of the diseases that acupuncture is good at. Acupuncture has been found to induce both innate and adaptive

immune responses. After acupuncture cause mechanical and thermal stimulation in acupoints, the generated electrical signals are transmitted to the central nervous system through somatosensory fibers, and the innate and adaptive immune responses are regulated through its unique descending pathways such as cholinergic anti-inflammatory pathway, vago-adrenal pathway, spinal-sympathetic pathway, brain-intestinal pathway, etc. To control the secretion of inflammatory factors or inflammatory cells, as to restore the immune homeostasis of the organism.<sup>17</sup> Acupuncture is recommended as one of the treatments for allergic rhinitis in Otolaryngology Head and Neck Surgery. Moreover, the *British Medical Journal (BMJ)* article showed moderate quality evidence that acupuncture can improve nasal symptoms in AR patients. In addition, acupuncture can reduce the levels of the chemokines Eotaxin and nonspecific proinflammatory cytokines in patients with AR.<sup>18</sup> The guidelines for the diagnosis and treatment of allergic rhinitis published by the Chinese Society of Allergy in 2018 also affirmed the exact efficacy of acupuncture in the treatment of AR, and proposed that acupuncture has the advantages of safety, effectiveness and no obvious adverse reactions.<sup>19</sup>

## Allergic Rhinitis Epidemiology

AR is a worldwide health problem affecting adults and children. In the past 10 years, the incidence of AR has shown a global upward trend. The global prevalence of AR is about 10% to 25%, with more than 500 million people, and about 25% of AR patients are often accompanied by asthma.<sup>20</sup> But estimates of its prevalence vary widely, but epidemiological studies suggest that 20 to 30% of adults and up to 40% of children are affected.<sup>21</sup> In a 2004 survey of 19,678 adults in the United States, 44.3% reported nasal symptoms for at least seven days per year, while 20.7% were diagnosed with nasal allergies by a physician.<sup>22</sup> Self-reported AR assessments were performed on 38,000 multiple subjects in 11 major Chinese cities between September 2004 and May 2005. The prevalence of AR was 8.7% in Beijing, 24.1% in Urumqi, 11.2% in Changchun, 16.1% in Changsha, 14.1% in Guangzhou, 8.9% in Hangzhou, 13.3% in Nanjing, 13.6% in Shanghai, 15.7% in Shenyang, 19.3% in Wuhan and 9.1% in Xi'an. According to the new classification of allergic rhinitis and its effects on asthma (ARIA), 74.4% of self-reported AR subjects were diagnosed with intermittent AR and the remaining 25.6% were diagnosed with persistent AR.<sup>23</sup> A multicenter study conducted in China found that more than half of the AR in Chinese patients was moderate-severe persistent AR, and the peak visits were in August and September each year. The results of AR analysis showed that weed pollen and dust mites were the most important allergens in northern and southern China, respectively. Meanwhile, Inner Mongolia, Shaanxi, Gansu, Ningxia and Qinghai in Northwest China are the high incidence areas of AR caused by weed pollen.<sup>24</sup> Current studies have found that the prevalence and diagnosis rate of AR in children are lower than those in adults, but the proportion of children with AR combined with asthma is significantly higher than that in adults, and the diagnosis and treatment of children is more complex, which should be paid great attention to.<sup>25</sup>

The daily clinical manifestations of AR patients include not only nasal symptoms, but also sleep, eye and emotional and mental problems, which limit social communication and daily activities. Patients with moderate/severe AR had significantly more anxiety, depression, fatigue, social interaction difficulties, and perceived signs of cognitive dysfunction, and parents of children with AR were also affected by sleep disorders, with 75% of parents reporting poor sleep quality.<sup>26</sup> The prevalence of acute rhinosinusitis, chronic rhinosinusitis, asthma, and atopic dermatitis in the AR population was 30.4%, 10.4%, 28%, and 24.2%, respectively, which were higher than those in the general population.<sup>27</sup> AR not only causes physical and mental harm to individual patients, but also has a huge socio-economic impact. For example, in 2007 alone, South Korea spent \$270 million directly on the treatment and prevention of AR, ranking 10th among all diseases.<sup>28</sup> The study found that AR can reduce the daily work efficiency by 20% to 30%, and the annual production loss caused by AR in EU countries can reach 30 billion to 50 billion euros.<sup>29</sup> According to the research data of Beijing Tongren Hospital in China, the average annual cost of AR patients in China is 1539 yuan per person, so the total cost of AR patients in China is estimated to be 326.8 billion yuan.<sup>30</sup> The analysis of risk factors for AR showed that family history, dust exposure history, drug allergy history, environmental tobacco smoke, pollen allergy, pet ownership, asthma family allergy history, lack of outdoor activities, little sunlight exposure, dermatitis and eczema history, and daily sleep less than 7 hours were the risk factors for AR; in addition, the risk factors for AR in children also

included birth and feeding. Therefore, genetic, physical, environmental and other factors affect the incidence of allergic rhinitis.<sup>31</sup> Therefore, frequent outdoor activities, keeping the room dry and clean, washing and drying clothes are the protective factors of AR.

## Pathophysiology

AR has a variety of sensitization pathways, but its mechanism is still not fully understood. Nasal mucosa is the first line of defense against airborne pathogens in the respiratory tract, so it is essential to maintain and restore the integrity of the epithelium and initiate the immune response. When the damage factors of normal nasal mucosa exist, epithelial cells will release signaling factors to start the repair mechanism, and also induce protective inflammatory response.<sup>32</sup> The pathogenesis of AR is IgE-mediated type I allergic reaction of nasal mucosa, which is the most recognized pathway. Specific IgE binds to high-affinity IgE receptors on the surface of mast cells and basophils that accumulate in the nasal mucosa, forming a sensitized state.<sup>33</sup> When the body is exposed to the same allergen again, the allergen binds to IgE on the surface of mast cells and basophils in the nasal mucosa, activates mast cells and basophils, releases histamine, leukotrienes and prostaglandins, and inflammatory factors stimulate blood vessels and nerves in the nasal mucosa, dilating blood vessels in the nasal mucosa and increasing gland secretion. Cause nasal itching, sneezing, watery nasal discharge and other symptoms.<sup>34</sup> Mast cells play a crucial role in the first-phase response of AR and also release cytokines and chemokines that regulate the late-phase response. In this way, they exacerbate ongoing inflammation.<sup>35</sup>

In AR, allergens can initiate an innate immune response by directly disrupting the epithelial barrier or by activating pattern recognition receptors that cause epithelial cells to release interleukin-33 (IL-33), thymic stromal lymphopoietin (TSLP), or interleukin-25 (IL-25).<sup>36,37</sup> These factors activate innate type 2 lymphocytes (ILC2), a novel lineage-negative cell population whose activation is dependent on epithelial-derived cytokines. There is a growing understanding of heterogeneity and ILC2 plasticity in allergic diseases, and the heterogeneity of ILC2 may provide therapeutic targets and predictive biomarkers for different therapies. ILC2 has a critical role in the initiation and maintenance of type 2 adaptive immune responses and can lead to IgE class switching and mucosal inflammation.<sup>38</sup> The inflammatory response, which is dominated by the type 2 immune response, continues to worsen, with significant tissue edema in the nasal mucosa leading to nasal obstruction.

Experimental nasal exposure to allergens in patients with AR also produced immediate signs of inflammation characterized by a type 2 inflammatory response characterized by infiltration of eosinophils, neutrophils, and basophils, and infiltration of mononuclear cells dominated by T helper 2 (Th2) cells. Typical type 2 cytokines such as IL-4, IL-5 and IL-13 can be detected in nasal tissues and nasal secretions within a few hours after allergen exposure.<sup>39</sup> The histopathology of AR patients was found to be very similar to that of experimental allergen exposure. Dendritic cells (DCs) and other antigen-presenting cells play a key role in activating allergen-specific memory Th2 cells through an allergen presentation mechanism that is partially dependent on IgE promotion.<sup>40,41</sup> The excessive activation of Th2 cells can promote the secretion of inflammatory factors such as IL-4, IL-5 and IL-13, thus promoting the infiltration of eosinophils and other inflammatory cells in nasal mucosa, resulting in the high expression of local IgE, leading to obvious tissue edema in nasal mucosa, often manifested as nasal obstruction.<sup>42</sup> Regulatory B cells (Breg) are immunosuppressive cells that can regulate the immune response through the secretion of IL-10, IL-35, and tumor growth factor- $\beta$  (TGF- $\beta$ ) and the interaction of membrane surface molecules.<sup>43</sup> Breg cells can inhibit the differentiation of effector T cells such as Th1 and Th17 cells, promote the expansion of Treg cells, participate in the regulation of Th17/Treg cell immune imbalance, and inhibit the activation of dendritic cells and macrophages. The importance of Treg cells for inducing tolerance to allergen immunotherapy.<sup>44</sup> However, the specific mechanism of action of Treg cells in AR is not clear, so it is not specifically discussed. Furthermore, decreased Th 2 activity leads to an increase in Treg cell function and number. Indeed, Treg cells play a crucial role in establishing peripheral immune tolerance because they mainly produce IL-10 and IL-10 inhibits Breg cells through disruption of the B7 / CD28 pathway. This blockage results in the inhibition of dendritic cell development, MHC class II presentation, and activation of costimulatory molecules. Finally, TGF- $\beta$  inhibited Langerhans cells, increasing the expression of FOXP 3 and RUNX, and promoting CTLA-4 expression on T cells. The CTLA-4 gene plays a negative regulatory role in the activation of antigen-presenting cells (APC) in T cells, and the insufficient expression of induced CTLA-4 is associated with Th 2 / Treg imbalance and AR pathogenesis.<sup>45</sup>

## Diagnosis

AR, as defined by ARIA, is IgE-mediated type 1 hypersensitivity to a range of inhaled environmental allergens. Allergic rhinitis is characterized by anterior or posterior rhinorrhea, nasal congestion/stuffiness, nasal itching, and sneezing for more than one hour for two or more consecutive days.<sup>46</sup> Traditionally, AR can be divided into four subgroups based on the duration of allergen exposure. Including 1, seasonal AR, 2, perennial AR, 3, paroxysmal AR and 4, seasonal deterioration of chronic diseases. However, the traditional classification of AR has many shortcomings, and most patients have multiple sensitivities to seasonal and perennial allergens. Therefore, the World Health Organization ARIA proposed a new classification of AR: intermittent allergic rhinitis (defined as symptoms lasting less than 4 days/week, or less than 4 consecutive weeks/year). Persistent allergic rhinitis (symptoms > 4 days and/week or > 4 consecutive weeks per year). Patients typically experience symptoms every day of the year). The current classification is mainly based on the severity of symptoms, and AR is classified as “mild” (patients with mild symptoms that do not affect sleep, study or work performance, sports, or daily activities). “Or” Moderate/Severe (Symptoms that negatively affect sleep, school/work, leisure, or daily activities). Contemporary, according to the different classification methods, AR can be divided into four groups: “mild intermittent”, “moderate/severe intermittent”, “mild persistent” or “moderate/severe persistent”.<sup>47</sup> AR has a special manifestation, which is called local allergic rhinitis. Its main manifestation is typical AR symptoms but no systemic atopy, such as negative skin test and serum specific IgE test.<sup>48</sup> In addition to obvious nasal symptoms, AR is often accompanied by ocular symptoms, including itching, tearing, redness and burning sensation, which are more common in patients with pollen allergy. However, for indoor allergens (dust mites, cockroaches, animal dander, etc.), the symptoms are mostly perennial attacks. 40% of AR patients may have bronchial asthma, accompanied by nasal symptoms, wheezing, cough, shortness of breath, chest tightness and other pulmonary symptoms.<sup>49</sup> Nasal endoscopy of AR showed bilateral nasal mucosa pale and swollen, inferior turbinate edema, and a large amount of watery nasal secretions. The main ocular signs were conjunctival hyperemia and edema.<sup>50,51</sup> AR Diagnosis also uses an in vivo skin test: the skin prick test (SPT): this is the primary test for the diagnosis of IgE-mediated allergy. Intradermal test (IDT): Used to diagnose IgE-mediated and delayed hypersensitivity reactions.<sup>52</sup> AR usually has a clear history of foreign body contact or onset in a specific season. For the moment, the diagnosis of AR in medical and health development tends to be perfect, and patients can usually be diagnosed as AR through their medical history and examination results.

## Western Medicine Treatment of AR

The treatment principle of AR is “combination of prevention and treatment, four in one”, including environmental control, drug treatment, immunotherapy and health education.<sup>53</sup> Avoiding exposure to allergens is the most effective way to prevent AR, but the diversity, complexity and wide spread of allergens in the real world make it difficult to completely avoid them. Drug therapy (especially combination therapy) and allergen specific sublingual immunotherapy have become the main treatment methods for AR. At the moment, the commonly used western medicines for allergic rhinitis include glucocorticoids, antihistamines, leukotriene receptor antagonists, mast cell membrane stabilizers, decongestants and so on. Among them, intranasal corticosteroids are the first-line treatment for AR.<sup>54</sup> Glucocorticoids can significantly reduce the release of inflammatory mediators and cytokines, and can effectively relieve the symptoms of nasal obstruction, nasal itching and runny nose in AR patients. However, nasal glucocorticoid drugs are not suitable for long-term use and have certain side effects on human body. Second-generation antihistamines are also recommended as first-line treatment drugs for AR, with rapid onset and long duration of action. They can significantly relieve nasal symptoms, especially nasal itching, sneezing and runny nose. They are also effective for combined eye symptoms, but the relief of nasal congestion is not obvious, and some drugs may cause damage to the heart.<sup>55</sup> Leukotriene receptor antagonist is also the first-line drug for the treatment of AR. So far, the most commonly used oral drug in clinic is montelukast, which can significantly improve the nasal and eye symptoms and quality of life of AR patients when used alone. The safety and tolerance of leukotriene receptor antagonist are good, and the adverse reactions are mild, mainly headache, dry mouth, pharyngitis, etc.<sup>56</sup> The second-line drugs mainly include mast cell membrane stabilizer and decongestant. The mast cell membrane stabilizer has a certain effect on relieving the symptoms of sneezing, runny nose and nasal itching of AR, but the improvement of nasal obstruction is not obvious, and the drug takes effect slowly and lasts for a short time, which will

affect the compliance of patients. Decongestants have side effects such as nasal dryness, headache, dizziness and increased heart rate, which can lead to drug-induced rhinitis.<sup>1</sup>

So far, there is also a first-line treatment for immunotherapy of AR, which is divided into subcutaneous immunotherapy and sublingual immunotherapy for IgE-mediated type I allergic diseases. Immunotherapy is suitable for AR caused by a single allergen, such as *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae* and *Artemisia* pollen allergy. Immunotherapy can change the development process of AR. Reduce new sensitization and prevent further development of AR into asthma.<sup>57,58</sup> The AIT mechanism involves promoting the production of blocking antibodies, specifically IgG 4 and IgA. These pathways result in a reduced allergen-induced immune response induced by allergen-specific Th 2 cells. Tolerance induction is achieved by desensitizing effector cells and activating regulatory T cells. This process involves cell-to-cell communication and the release of immunomodulatory cytokines such as IL-10 and  $\text{tgf-}\beta$ . Subcutaneous immunotherapy (SCIT) is more associated with IgG 4-related mechanisms, and sublingual immunotherapy (SLIT) is associated with IgA. Furthermore, the use of AIT shifted the immune response from Th 2 cell type to Th 1 cell type, as indicated by the increase in Th 1-associated IFN- $\gamma$  and a decrease in the levels of Th 2-associated IL-4 and IL-13 cytokines.<sup>59</sup> AIT can downregulate the allergy mechanism related to IgE in patients and is a preventive means of AR. To date, AIT is the only disease-modifying treatment strategy for IgE-mediated allergic diseases, with clear evidence in both adults and children. Furthermore, it can not only reduce symptoms and rhinitis, but also improve allergic asthma in patients already with allergic asthma while reducing the likelihood of onset in non-asthmatic patients.<sup>60</sup> However, the required treatment cycle usually takes 3 years, unstable efficacy, high cost, resulting in low patient compliance.

Surgical treatment is the second-line treatment of AR, which is usually suitable for refractory AR or patients with severe nasal septum deviation, refractory nasal mucosa hypersensitivity and hypersecretion.<sup>61</sup> Surgical treatment of AR is effective in the short term, but there are many sequelae in the prognosis. Environmental control is suitable for patients with definite allergens, and daily environmental control should be carried out, which is conducive to alleviating symptoms and reducing the possibility of exposure to allergens from the root, but there are many uncontrollable factors in the environment, sometimes it is still difficult to avoid its occurrence. Health education is also an important way to prevent and treat AR. It is particularly necessary to popularize the knowledge of AR to patients and their families, including avoiding contact with allergens, strengthening daily exercise, avoiding cold and preventing colds, and reasonable and standardized medication, so as to achieve the purpose of effective prevention and treatment of diseases.

## Understanding of AR in TCM

In ancient books of traditional Chinese medicine, there is no disease named “allergic rhinitis”, but the diseases with similar clinical manifestations to AR are attributed to the category of “nose”. “Nose” is the nasal orifice in the five sense organs. In *Shuowen Jiezi*, “Nose” is interpreted as “cold and stuffy nose”. Nose refers to stuffy nose and runny nose. According to *Su Wen Xuan Ji yuan Bing Shi*, written by *Liu wansu*, one of the four great masters of the Jin and Yuan Dynasties, AR is characterized by clear nasal discharge, even nasal itching, sneezing, and inability to smell. In *Ling Shu Jing*, it is said that “deficiency of lung-qi can lead to nasal congestion”. According to ancient Chinese medicine, the lung and the nose are functionally inseparable. The physiological dysfunction of the lungs can affect the normal physiological function of the nose. When lung qi is insufficient, the physiological function of the lung is impaired, which will lead to sneezing and runny nose in AR patients. Traditional Chinese medicine believes that the etiology and pathogenesis of the nose is the combination of internal and external pathogens, the nature of the disease is deficiency in origin and excess in superficiality, the external cause is mostly exogenous wind-cold pathogens, the lung fails to disperse and descend, the internal cause is often the dysfunction of the viscera, the deficiency of healthy qi, the weakness of the defensive exterior, and the disease is often closely related to the lung, spleen and kidney. According to the theory of traditional Chinese medicine, the pathogenesis of AR can be basically divided into four basic syndromes: deficiency cold of lung qi, weakness of spleen qi, deficiency of kidney Yang and latent heat of lung meridian. According to the theory of traditional Chinese medicine, the movement of qi is highly related to the functions of the lung, spleen and kidney. The lung governs qi and mainly manages the normal respiratory function of the body. The kidney is the root of qi. When the kidney qi is sufficient, the human body will breathe deeply and take in more gas. The spleen is the pivot of qi movement, which regulates the movement of qi in the body. The main cause of AR is the disorder of qi movement. Therefore, if the

functions of the lung, spleen and kidney are restored to normal, the qi movement of the body will reach a steady state, thus playing a role in the treatment of AR. The current syndrome differentiation and typing can be a good guide for traditional Chinese medicine treatment of AR, but traditional Chinese medicine pays attention to syndrome differentiation and treatment, so the attending physician needs to add and subtract treatment on the basis of his own clinical diagnosis and treatment.

In recent years, systematic reviews have shown that traditional Chinese medicine therapy for AR can improve the clinical efficacy, reduce the total score of clinical symptoms and signs of patients, and has higher safety, less adverse reactions and lower recurrence rate of AR.<sup>62</sup> Basic studies on AR also show that TCM treatment can reduce the content of Ig E in serum, balance the immune response of helper T cells (Th) 1/Th2 cells, alleviate neurogenic inflammation of nasal mucosa and improve nasal symptoms.<sup>63</sup> Acupuncture has been recommended for AR treatment in the guidelines of Otolaryngology Head and Neck Surgery published in the United States, and acupuncture has been listed as a supplementary treatment for AR in many overseas countries.<sup>2</sup> Therefore, this study mainly discusses the effectiveness of acupuncture in the treatment of AR.

## Evidence of Acupuncture for AR

In recent years, acupuncture has been increasingly used in the treatment of allergic rhinitis (AR), and its short-term and long-term effects are satisfactory. Several systematic reviews have shown that acupuncture therapy has a higher efficacy relative to western medicine.<sup>64</sup> A large number of studies have shown that acupuncture treatment of allergic rhinitis has the advantages of quickly relieving nasal obstruction, nasal itching, sneezing, runny nose and other symptoms, shortening and reducing the frequency of rhinitis attacks, and improving the quality of life of patients. Acupuncture is easy to use and has no adverse effects such as fatigue and drowsiness, so it is a suitable alternative to traditional medicine, especially when the effect of traditional medicine is limited.<sup>65</sup> Acupuncture prescriptions often include Yingxiang (LI20), Yintang (GV29), Fengchi (GB20), Hegu (LI4) and Zusanli (ST36) as the main acupoints, which are added or subtracted according to the different clinical symptoms of patients.<sup>66</sup> Meanwhile, based on their years of clinical experience, modern Chinese medicine scientists have found that many effective acupoints, such as “Butterfly Palate” and “Bitong”, are also one of the commonly used acupuncture points in clinic. TNSS and TNNSS scores are used as rhinitis symptom scores, and VAS and RQLQ scores can comprehensively reflect the quality of life of patients, which are widely used in AR-related clinical studies. It is also the main evaluation method of AR clinical research contemporary. In this section, we discuss various studies conducted with acupuncture for AR. Table 1 summarizes these studies. This review includes the latest randomized controlled trials (RCTs) and meta-analyses to evaluate the safety and efficacy of acupuncture in the treatment of AR.

The first was an RCT published in 2023, which used the Visual Analog Scale (VAS) score as the primary criterion for evaluating efficacy; the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) score was the criterion for evaluating quality of life, drug dosage, and adverse events. In this study, 120 patients diagnosed with persistent AR were randomly divided into a nasal acupuncture group and a western medicine group (2:1 ratio), in which the nasal acupuncture group was treated with acupuncture at Nei Ying Xiang or Bi Qiu three times a week, and the western medicine group was treated with budesonide nasal spray (twice a day) and loratadine (one pill a night) for 2 weeks. The results showed that the scores of VAS and RQLQ in the first treatment in the nasal acupuncture group were significantly lower than those in the western medicine group ( $P < 0.05$ ). Nasal obstruction, olfactory function, sleep, nasal symptoms and emotional problems were significantly improved in the nasal acupuncture group. VAS and RQLQ scores were significantly improved in both groups at the 2nd week ( $P < 0.05$ ). During the follow-up period, the scores of RQLQ and VAS in the nasal acupuncture group were higher than those in the western medicine group, and the difference was statistically significant ( $P < 0.05$ ). VAS scores for paranasal symptoms, nasal itching, rhinorrhea, and olfactory function were significantly improved, as were RQLQ scores for activity, non-nasal/ocular symptoms, nasal symptoms, and ocular symptoms. Therefore, it is concluded that nasal acupuncture has good efficacy and safety in the treatment of persistent AR. The improvement of VAS and RQLQ scores in the nasal acupuncture group was better than that in the western medicine group at the early stage of treatment, and the nasal acupuncture group had special advantages in improving nasal obstruction, olfactory function and sleep.<sup>67</sup>

**Table 1** Evidence of Acupuncture for AR

First Author of the Study ()	Study Groups and Interventions	Results and Findings	Conclusion
Li-Li Liu et al (2023) <sup>67</sup>	Participants diagnosed with persistent AR (n = 120) were divided into 2 groups according to a 2:1 ratio: (1) acupuncture group 2 (2) western medicine group 1 Patients in the acupuncture group were treated with acupuncture at Neiyangxiang and Biqu three times a week for 2 weeks. The control group received budesonide nasal spray (two sprays per nostril, twice daily) and loratadine (one capsule per night) for 2 weeks.	The scores of VAS and RQLQ in the first treatment in the nasal acupuncture group were significantly lower than those in the western medicine group (P < 0.05, 95% CI: -13.1, -9.6) and RQLQ (P < 0.05; 95% CI: -20.27, -12.28). Overall symptoms, nasal congestion, olfactory function, sleep, nasal symptoms, and emotional problems were significantly improved in the Progenitor needle group. At the second week, the scores of VAS and RQLQ in the two groups were significantly improved; during the follow-up period, the scores of RQLQ and VAS in the nasal acupuncture group were higher than those in the western medicine group, and the difference was statistically significant (P < 0.05).	Nasal acupuncture has good efficacy and safety in the treatment of persistent allergic rhinitis. At the same time, acupuncture and moxibustion have obvious effects on improving nasal obstruction, olfactory function and sleep. However, the long-term efficacy and mechanism of action remain to be further studied.
Donata Gellrich et al (2022) <sup>68</sup>	Patients with clinically confirmed seasonal AR (n = 29) were randomized into 3 groups: 16 patients received acupuncture plus medication; 6 patients received sham acupuncture plus medication; and the last 8 patients received medication alone for 8 weeks.	Chemokines for eosinophil activation and some nonspecific proinflammatory cytokines (IL-1b, IL-8, IP-10, MIP-1b, MCP-1) were suppressed in patients treated with acupuncture. Acupuncture may result in lower nasal concentrations of proinflammatory factors than sham acupuncture or sham acupuncture and drug therapy. In addition, nasal symptom scores were significantly lower in patients receiving authentic acupuncture.	Acupuncture can reduce the release of non-specific inflammatory factors in the nasal cavity of seasonal AR patients, but it can not significantly improve the imbalance of Th1-Th2. However, this study has limitations: the sample size is small, and the concentration of related factors in nasal secretions varies greatly among individuals, so it is impossible to compare the specific values, and there is a geographical impact.
JeongIn Kang et al (2022) <sup>69</sup>	Patients diagnosed with AR (n = 80) They were randomly divided into 2 groups: intranasal low intensity laser group; Acupuncture group. Treatment for 4 weeks.	The scores of TNSS, RQLQ, and Endoscopic Index were significantly improved from baseline to 4 weeks after treatment in the intranasal low level laser therapy group and the acupuncture group, and the effect was still significant 4 weeks after treatment. However, there was no significant difference in serum total IgE and eosinophil count between baseline and 4 weeks after treatment.	This study shows that both intranasal low intensity laser therapy and acupuncture can effectively reduce the nasal symptoms and improve the quality of life and nasal condition of patients with AR.
Shi-Hao Du et al (2022) <sup>70</sup>	30-item RCTs with participants receiving acupuncture, sham acupuncture, or medication	Compared with sham acupuncture and no treatment, acupuncture significantly reduced the clinical symptom score (SMD: -0.29 [-0.43, -0.15]), improved the quality of life (SMD: -0.23 [-0.37, -0.08]) and drug score (SMD: -0.3 [-0.49, -0.11]) in AR patients. Acupuncture improves patient satisfaction and may be cost-effective. Most of the evidence for the above two comparisons is highly credible. Acupuncture was superior to conventional medical therapy in reducing symptom scores (SMD: -0.48 [-0.85, -0.1]) and had a lower incidence of adverse effects, but the quality of evidence was low.	Meta-analysis found that acupuncture is an effective and safe AR intervention, which helps to alleviate clinical symptoms, improve quality of life, reduce drug use and improve patient satisfaction.
Bao Jiaying et al (2023) <sup>71</sup>	Patients diagnosed with AR (n = 80) The patients were randomly divided into two groups: the control group was treated with budesonide nasal spray; The observation group was treated with modified acupuncture of sphenopalatine ganglion for 4 weeks.	The total effective rate of the observation group was 92. 5% (37/40), which was higher than that of the control group (72. 5%, 29/40, P < 0.05). After treatment, the total score of TNSS and the scores of nasal obstruction, nasal itching and TNNSS in the observation group were lower than those in the control group (P < 0.05). After 4 weeks of treatment, the total score of TNSS, the score of each subitem and the score of TNNSS in the observation group were lower than those in the control group (P < 0.05). After treatment and 4 weeks after the end of the course of treatment, the VAS and RQLQ scores of the two groups were lower than those before treatment, and the observation group was better than the control group (P < 0.05); the recurrence rate of the observation group was 13. 5% (5/37), which was lower than the control group 44. 8% (13/29, P < 0.05).	Acupuncture of sphenopalatine ganglion can effectively relieve the symptoms and improve the quality of life of patients with AR, and the recurrence rate is low. This study has some shortcomings, such as small sample size, short follow-up time and no evaluation of laboratory indicators.



Zhongxia Wang et al (2023) <sup>72</sup>	Retrospective cohort study of patients diagnosed with AR (n = 122), patients were divided into two groups, 54 patients were treated with loratadine and fluticasone propionate as the control group; 68 patients were treated with acupuncture of sphenopalatine ganglion on the basis of the control group as the observation group.	The total effective rate of the observation group was higher than that of the control group (P = 0.006), and the symptom score was lower than that of the control group (P < 0.001). MCV increased (P < 0.001) and nasal mucociliary transit time and nasal resistance decreased (P < 0.001) in both groups after treatment. The improvement of nasal function in the observation group was better than that in the control group (P < 0.001). The levels of histamine and IgE in the observation group were lower than those in the control group (P < 0.01), and the RQLQ score was lower than that in the control group (P < 0.01).	Acupuncture of sphenopalatine ganglion combined with loratadine and fluticasone propionate is effective in the treatment of AR. The clinical symptoms of AR patients were significantly relieved, and the quality of life was significantly improved without adverse reactions.
Ting-Ting Song et al (2023) <sup>73</sup>	Patients diagnosed with moderate-to-severe seasonal AR (n = 105) Patients were randomly assigned to either a control group (no treatment prior to onset) or an observation group (acupuncture three times a week for four weeks prior to onset).	The incidence of AR in the observation group (84.0%) was lower than that in the control group (100.0%) (P < 0.05). After treatment, the scores of RQLQ and TNSS at each time point of AR attack in the observation group were lower than those before treatment (P < 0.01), and were lower than those in the control group (P < 0.01). The scores of emergency medicine in the observation group were lower than those in the control group (P < 0.05).	Acupuncture prevention and treatment can reduce the attack rate of moderate and severe seasonal AR to a certain extent, alleviate the symptoms of patients, improve the quality of life of patients, and reduce the use of drugs.
Dunpo Sun et al (2023) <sup>74</sup>	Patients diagnosed with AR (n = 155) The patients were randomly divided into control group receiving drug therapy (chlorpheniramine and fluticasone) and study group receiving drug therapy combined with warm acupuncture.	The total effective rate of the study group was 92.11%, which was higher than that of the control group (77.22%) (P < 0.05); the positive rate of eosinophils in the study group was lower than that in the control group (P < 0.05); the levels of serum specific IgE, IL-6, IL-8 and TNF- $\alpha$ in the study group were lower than those in the control group (P < 0.05); The peripheral blood CD3 + and CD4 + levels in the study group were higher than those in the control group, while the peripheral blood CD8 + level was lower than that in the control group (P < 0.05); the RQLQ score in the study group was lower than that in the control group (P < 0.05).	Hot acupuncture can effectively treat the clinical symptoms of AR patients, reduce the marked inflammatory reaction of AR, and enhance the immune function of the body, with significant therapeutic effect. This study has some limitations, such as small sample size and lack of follow-up and recurrence data.
Min He et al (2022) <sup>75</sup>	Thirty RCTs involving 4413 participants diagnosed with AR. Participants were treated with acupuncture, sham acupuncture, or medication	Acupuncture improved the scores of TNSS and RQLQ in patients with AR compared with those without acupuncture. Acupuncture was significantly better than sham acupuncture for the nasal symptoms subscale of the RQLQ (MD: -0.60, 95% CI: -1.16, -0.04) and quality of life (SMD: -0.26, 95% CI: -0.44, -0.07). No significant differences were observed between acupuncture and drug treatment; all trials showed that acupuncture combined with Western medicine was more effective than Western medicine alone.	In adult AR patients, acupuncture was superior to sham acupuncture in improving the severity of nasal symptoms and improving the quality of life of patients. Acupuncture and cetirizine/loratadine have similar therapeutic effects. However, this study did not explore whether acupuncture can reduce the level of serum immune response molecules, which is uncertain.
John Leslie McDonald et al (2016) <sup>76</sup>	Patients diagnosed with persistent AR (n = 151) They were randomly divided into three groups: acupuncture group, sham acupuncture group (twice a week for 8 weeks) and non-acupuncture group.	Allergen-specific IgE to house dust mites was significantly reduced in the acupuncture group, and the mean value of pro-inflammatory neuropeptide substance P was also significantly down-regulated 18–24 hours after the first treatment. There were no significant changes in other neuropeptides, neurotrophins, or cytokines tested. In the acupuncture group, the symptoms of nose, itchy eyes and poor sleep were significantly improved, and continued to improve during the four-week follow-up.	Acupuncture modulates the mucosal immune response in the upper respiratory tract of adults with persistent AR. This modulation was associated with down-regulation of house dust mite allergen-specific IgE. The symptoms of nasal itching, eye itching and sneezing were significantly improved after acupuncture.
S. M. Choi et al (2013) <sup>77</sup>	Patients diagnosed with AR (n = 238) According to the principle of 2:2:1, they were randomly divided into three groups: acupuncture group (97 cases), sham acupuncture group (94 cases) and control group (47 cases). The acupuncture and sham acupuncture groups were treated three times a week for four weeks.	After treatment, the TNSS scores in the acupuncture group were significantly lower than those in the sham acupuncture group (P = 0.03, 95% CI: -1.96, -0.09) and in the control group (P < 0.0001, 95% CI: -3.68, -1.29). Compared with the control group, the total score of non-nasal symptoms (TNNSS) in the acupuncture group changed significantly (P = 0.0002, 95% CI: -1.22, -0.34), but there was no difference in the sham acupuncture group (P = 0.56, 95% CI: -0.21, 0.5).	The effect of acupuncture on AR symptoms was significantly greater than that of sham acupuncture or inactive treatment. The symptoms of AR were significantly alleviated in both acupuncture group and sham acupuncture group. Acupuncture is an effective and safe treatment for AR.

**Abbreviations:** AR, Allergic rhinitis; CI, Confidence interval; RCT, Randomized clinical trial; VAS, Visual analogue scale; RQLQ, Rhinoconjunctivitis quality of life questionnaire; TNSS, Total score of nasal symptoms; TNNSS, Total score of symptoms associated with rhinitis; MD, median.

The second is a preliminary three-arm RCT published in 2022, in which 29 patients were randomly divided into three groups according to the principle of 2:1:1. The first group was 16 patients treated with acupuncture combined with drug therapy (cetirizine); the second group was 6 patients treated with sham acupuncture combined with drug therapy; Eight patients in the third group only received drug treatment. All the patients in the three groups were treated for 8 weeks. At different time points, questionnaires and biological functional mediators were used to evaluate the efficacy of the three groups. The results showed that the concentrations of biomarkers related to Th1, Th2 and Treg clusters in plasma and nasal fluid of patients treated with acupuncture combined with drugs did not change. However, acupuncture can inhibit the release of Eotaxin and some non-specific proinflammatory cytokines (IL-1b, IL-8, IP-10, MIP-1b, MCP-1), and significantly reduce the nasal symptom scores of patients. After 8 weeks of intervention, the level of proinflammatory cytokines in the sham acupuncture group was the highest, followed by the drug treatment group. Patients who received real acupuncture for 8 weeks had the lowest levels of proinflammatory cytokines. Therefore, it is concluded that in seasonal AR, acupuncture reduces intranasal nonspecific inflammation but appears to have no immunologic effect on Th1-Th2 imbalance.<sup>68</sup>

The third study, a randomized, non-inferiority trial reported in 2022, compared the results of intranasal low-intensity laser therapy with those of acupuncture in the treatment of AR to determine the safety and efficacy of acupuncture and intranasal low-intensity laser therapy. Intranasal low-intensity laser therapy has been shown to significantly inhibit the expression of IgE, IL-4, thymus, and TARC in a mouse model of AR.<sup>78</sup> Therefore, 80 patients with AR were randomly divided into intranasal low-intensity laser therapy group or acupuncture group, and treated three times a week for four weeks. The results showed that after 4 weeks of treatment, the total nasal symptom score (TNSS), rhinoconjunctivitis quality of life questionnaire (RQLQ) score and endoscopic index of AR patients in both groups were significantly improved, and there was no significant recurrence of symptoms in patients after one month of follow-up. Studies have shown that intranasal low intensity laser therapy and acupuncture have good efficacy and safety in the treatment of AR; therefore, both of them can be used as alternative or adjuvant therapies to alleviate the clinical symptoms of AR.<sup>69</sup>

In a meta-analysis, 30 RCTs were reviewed to assess the efficacy, safety, cost-effectiveness, and patient preference of acupuncture for AR compared with sham acupuncture, no treatment, and conventional medical therapy. From the data obtained, six of the trials with a total of 947 participants, changes in symptom scores were assessed using TNSS or VAS. The pooled results showed that after excluding the articles with high heterogeneity, the symptom scores of acupuncture were significantly lower than those of sham acupuncture (SMD = -0.29 [-0.43, -0.15], P 0.0001). The follow-up study found that the effect of FNA was significantly better than that of sham acupuncture (SMD = -0.38 [-0.61, -0.16], P = 0.001). Six trials with 940 participants assessed changes in quality of life using the RQLQ or mini-RQLQ. Acupuncture significantly reduced the effect of AR on quality of life (SMD = -0.5 [-0.96, -0.04], P = 0.03). Medication was scored in three studies with 466 participants; compared with sham acupuncture, acupuncture significantly reduced the use of medication for AR (SMD = -0.3 [-0.49, -0.11], P = 0.002). A meta-analysis of 549 participants across four studies showed that acupuncture treatment significantly reduced symptom scores compared with no treatment (SMD = -0.8 [-1.2, -0.39], P = 0.0001); six trials with 1209 participants assessed changes in quality of life. Acupuncture significantly reduced the impact of AR on quality of life compared with no treatment (SMD = -0.82 [1.13, -0.52], P < 0.00001); in a 320-participant study, acupuncture significantly reduced AR medication use (MD = -1.5 [-2.2, -0.8], P < 0.001). In a meta-analysis of six studies with 454 participants, acupuncture significantly reduced symptom scores compared with conventional medicine (SMD = -0.48 [0.85, -0.10], P = 0.01); the incidence of adverse events was much lower in the acupuncture group than in the conventional medicine group (SMD = 0.4 [0.18, 0.92], P = 0.03). It is therefore concluded that acupuncture is an effective and safe AR intervention that can help relieve symptoms, improve quality of life, reduce medication use, and improve patient satisfaction.<sup>70</sup>

A RCT was published in 2023, which was conducted in the outpatient department of acupuncture of Tongde Hospital in Zhejiang Province, China. The purpose of this study is to observe the clinical efficacy and safety of modified sphenopalatine ganglion acupuncture for allergic rhinitis. 80 patients diagnosed with AR were randomly divided into the control group and the observation group. The control group was treated with budesonide nasal spray. The patients in the observation group were treated with modified acupuncture of sphenopalatine ganglion, twice a week, with an interval of 3 to 4 days, for 4 weeks. The results showed that the total score of TNSS, the score of each subitem and the score of

TNNS in the observation group and the control group were lower than those before treatment ( $P < 0.05$ ), and the total score of TNSS, the score of nasal obstruction and nasal itching and the score of TNSS in the observation group were lower than those in the control group 4 weeks after treatment ( $P < 0.05$ ). After treatment and 4 weeks after the end of the course of treatment, the VAS and RQLQ scores of the two groups were lower than those before treatment, and the observation group was lower than the control group ( $P < 0.05$ ). The recurrence rate of the observation group was 13.5% (5/37), which was lower than that of the control group (44.8%, 13/29,  $P < 0.05$ ). The total effective rate of the observation group was 92.5% (37/40), which was higher than that of the control group (72.5%, 29/40,  $P < 0.05$ ). The authors conclude that the modified needling of sphenopalatine ganglion can effectively relieve the clinical symptoms and improve the quality of life of AR patients, and has the characteristics of low recurrence rate.<sup>71</sup>

A retrospective study of 122 AR patients admitted to Gansu Provincial Hospital of Traditional Chinese Medicine and Gansu Provincial Third People's Hospital from April 2019 to April 2021 was reported in 2023. The authors of this study reported that the total effective rate of acupuncture combined with loratadine and fluticasone propionate after treatment was higher than that of loratadine and fluticasone propionate ( $P = 0.006$ ), and the clinical symptom score was also better than that of loratadine and fluticasone propionate ( $P < 0.001$ ). After treatment, MCV increased ( $P < 0.001$ ), nasal mucociliary transit time and nasal resistance decreased ( $P < 0.001$ ) in both groups, but acupuncture combined with loratadine and fluticasone propionate improved more significantly. After treatment, the levels of histamine and IgE in the acupuncture combined with loratadine and fluticasone propionate treatment group were lower than those in the control group ( $P < 0.01$ ), and there was no difference in the incidence of adverse reactions between the two groups ( $P = 0.886$ ). The authors conclude that acupuncture of sphenopalatine ganglion combined with loratadine and fluticasone propionate is effective in the treatment of AR, which can significantly alleviate the clinical symptoms of AR patients with good safety.<sup>72</sup>

In a RCT published in 2022, researchers designed to observe the preventive and clinical efficacy of acupuncture on moderate and severe seasonal AR, and randomly divided 105 patients diagnosed with moderate and severe seasonal AR into control group and observation group. Four weeks before the onset of seasonal AR, the observation group was treated with acupuncture, while the control group was not given any treatment. At the onset stage, both groups were given drug treatment (cetirizine or budesonide nasal spray), and then the onset rate, RQLQ scale, TNSS scale and emergency drug score were used to evaluate the acupuncture effect. The results showed that the incidence of AR in the observation group was 84.0%, which was lower than that in the control group (100.0%) ( $P < 0.05$ ), and the RQLQ scores of the observation group at each time point after treatment were significantly improved compared with those before treatment, and were better than those in the control group. The TNSS scores of the observation group at each time point during the attack were lower than those before treatment, and the TNSS and emergency drug scores were lower than those of the control group. The results show that acupuncture can reduce the incidence of moderate and severe seasonal AR to a certain extent, alleviate the symptoms of patients, improve the quality of life of patients, and reduce the use of drugs. However, this study did not explore the changes of acupuncture related mechanism indicators, and the immune targets of acupuncture prevention can be studied in the future to provide more experimental basis for acupuncture prevention and treatment of SAR.<sup>73</sup>

Dunpo Sun et al designed a RCT to investigate the effects of warm needling therapy on eosinophils, IgE, inflammatory factors and T lymphocyte subsets in AR patients. In this study, participants were randomly divided into two groups: 79 patients in the control group received drug treatment (chlorpheniramine and fluticasone), and 76 patients in the study group received drug treatment combined with warm acupuncture treatment. The results showed that the total effective rate of the study group (92.11%) was higher than that of the control group (77.22%) ( $P < 0.05$ ). After 1 and 2 weeks of treatment, the TCM syndrome scores of the study group were lower than those of the control group ( $P < 0.05$ ). The positive rate of eosinophils in the study group was lower than that in the control group after 1 week of treatment (47.37% vs 64.56%,  $P < 0.05$ ) and 2 weeks of treatment (21.05% vs 37.97%,  $P < 0.05$ ). After treatment, the levels of serum specific IgE, IL-6, IL-8 and TNF- $\alpha$  in the study group were lower than those in the control group ( $P < 0.05$ ); after treatment, the levels of peripheral blood CD3 + and CD4 + in the study group were higher than those in the control group, and the levels of peripheral blood CD8 + in the study group were lower than those in the control group ( $P < 0.05$ ). After treatment, the RQLQ score of the study group was significantly improved than that of the control group ( $P < 0.05$ ). Therefore, the authors conclude that warm needling therapy can effectively improve the clinical symptoms of AR

patients, regulate IgE and Th2 factors in plasma, inhibit the release of related pro-inflammatory factors, enhance the immune function of patients, and improve the quality of life of patients.<sup>74</sup>

In a meta-analysis published in 2022, 30 RCTs were reviewed, including 4413 participants, to study the effectiveness and safety of acupuncture compared with drugs or sham acupuncture in the treatment of AR. The results showed that acupuncture treatment was more effective than sham acupuncture in reducing the severity of nasal symptoms and improving the quality of life in patients with moderate-to-severe AR. Meta-analysis showed that both acupuncture and western medicine could improve the clinical response of AR, but acupuncture did not show advantages in improving clinical response and relieving nasal symptoms. TSA results showed that this finding was not reliable, so more trials were needed to provide more data. Acupuncture combined with western medicine has better curative effect than western medicine alone. The authors conclude that for adult AR patients, acupuncture is superior to sham acupuncture in reducing the severity of nasal symptoms and improving the quality of life of patients, and there is no significant difference in clinical efficacy between acupuncture and western medicine. However, this study also has some limitations, such as whether acupuncture has a regulatory effect on serum immune response molecules is not clear, and there is a lack of evaluation of AR in children. Therefore, further trials are needed to assess the difference between real acupuncture and sham acupuncture for AR, and more trials are needed to assess the effect of acupuncture on children with AR.<sup>75</sup>

A 2016 three-armed, double-blind RCT explored the clinical efficacy of acupuncture in the treatment of persistent AR and the possible modulation of mucosal immune responses. The pathogenesis of AR involves complex interactions between cytokines, neurotrophins, and pro-inflammatory neuropeptides. The results showed that the allergen specific IgE of the acupuncture group decreased significantly, but there was no difference between the sham acupuncture group and the non-intervention group. Mean values of the pro-inflammatory neuropeptide substance P were also significantly down-regulated 18–24 hours after the first treatment, but no significant changes in other neuropeptides, neurotrophins, or cytokines were seen. The symptoms of nasal obstruction, nasal itching, sneezing, runny nose, itchy eyes and uneasy sleep were significantly improved in the acupuncture group, and continued to improve during the four-week follow-up, but the improvement of postnasal drip and sinus pain was not significant. It is concluded that acupuncture can regulate the mucosal immune response of the upper respiratory tract in adult patients with persistent AR, and its mechanism is related to the down-regulation of allergen-specific IgE of house dust mites. Acupuncture can significantly improve the clinical symptoms of AR patients.<sup>76</sup>

Finally, a multicenter RCT was reported in 2013 in which AR patients were randomly assigned to acupuncture, sham acupuncture, or a control group (without any acupuncture treatment) on a 2:2:1 basis. In the acupuncture group, bilateral Hegu (LI4), Yingxiang (LI20), Sibai (ST2) and Zusanli (ST36), and unilateral Yintang (EX-1) and Shangxing (GV23) were treated with acupuncture according to the principle of deqi, while in the sham acupuncture group, the needle was inserted into the non-acupuncture point 1–1.5 cm away from the acupuncture site with a depth of 3–5 mm. The control group did not receive any acupuncture treatment and was given three times a week for four weeks. The treatment was evaluated by TNSS score, TNNSS score and RQLQ score. The results after treatment showed that the difference of TNSS in the acupuncture group was significantly smaller than that in the sham acupuncture group and the control group ( $P < 0.05$ , 95% CI: -1.96, -0.09). The TNNSS in the acupuncture group was significantly different from that in the control group ( $P < 0.05$ , 95% CI: -1.22, -0.34), and there was no difference between the sham acupuncture group and the control group ( $P = 0.56$ , 95% CI: -0.21, 0.5). However, both acupuncture and sham acupuncture improved the TNSS and TNNSS scores of AR patients compared with baseline. This study shows that the clinical symptoms of AR are significantly reduced after acupuncture treatment, and acupuncture is an effective and safe treatment to control the symptoms of allergic rhinitis.<sup>77</sup>

## Conclusion

Acupuncture, as an important therapy in traditional Chinese medicine, achieves therapeutic effect by applying needles or pressure at specific locations of the patient's skin. AR is a global health problem, and its incidence in adults and children is increasing year by year. AR has a huge impact on the mental and life of patients, and also constitutes a major burden to the health care system and economic development. Drug therapy and allergen immunotherapy are currently recommended as first-line treatment, but drug therapy has certain side effects, immunotherapy has a longer course of treatment and higher treatment costs.

Therefore, the main clinical treatment of AR is to achieve symptom control with minimal side effects.<sup>79</sup> This year, Professor Xu Nenggui's team of Guangzhou University of Traditional Chinese Medicine published a research paper "Research on acupuncture Disease Atlas Based on Clinical Evidence Body" in a top international medical journal, which made it clear that acupuncture had the most advantages in the treatment of post-stroke aphasia, neck and shoulder pain, myofascial pain, fibromyalgia, non-specific low back pain, vascular dementia, postpartum lactation and AR.<sup>80</sup> Acupuncture treatment of AR has little side effects and good short-term and long-term effects. Its mechanism may be that acupuncture affects Th1 and Th2 cell subsets, regulates Th1/Th2 balance, reduces IgE levels, reduces inflammatory cell infiltration in nasal mucosa, regulates nasal neuropeptide (substance P) levels and regulates various inflammatory factors to achieve therapeutic effect.<sup>81</sup> However, further large-scale studies and trials are needed to further consolidate these findings and provide more support for the clinical value of acupuncture.

Many studies have shown that acupuncture is a safe, beneficial, and available alternative treatment. However, further large-scale studies and trials are needed to further consolidate these findings and provide more support for the clinical value of acupuncture. Although previous studies have analyzed the impact of acupuncture on clinical symptoms and quality of life of AR, further investigation is needed to ensure that acupuncture is included in the management of AR treatment will have a positive effect on patients. The current study lacks the exploration of acupuncture on AR-related inflammatory factors, and its mechanism of action has not been studied in depth, which is also the main direction of further research. However, it is also found that there is a lack of high-quality clinical studies. Therefore, it is necessary to design reasonable high-quality clinical studies to further fully verify the effectiveness and safety of acupuncture in the treatment of AR. Future studies could also benefit from regular follow-up treatment and interviews. Long-term follow-up of patients with AR who have received acupuncture treatment can clarify the long-term effects of acupuncture treatment.

## Abbreviations

AR, allergic rhinitis; IgE, immunoglobulin E; TCM, Traditional Chinese Medicine; EEG, electroencephalography; ARIA, allergic rhinitis and its effects on asthma; ILC2, innate type 2 lymphocytes; CI, Confidence interval; RCT, Randomized clinical trial; VAS, Visual analogue scale; RQLQ, Rhinoconjunctivitis quality of life questionnaire; TNSS, Total score of nasal symptoms; TNNSS, Total score of symptoms associated with rhinitis; MD, median.

## Data Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study. The results of this study will be published in a peer-reviewed journal.

## Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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