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Research Article

Research Progress on the New Mechanism of Acupuncture Treatment for Allergic Rhinitis

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Abstract

Objective: To systematically review the latest research on the mechanism of action of acupuncture in the treatment of allergic rhinitis and to lay the foundation for the promotion of the international application of acupuncture.

Methods: A comprehensive search was performed on PubMed, Elsevier, Google Scholar, Web of Science, and CNKI databases with the keywords “acupuncture”, “traditional therapy”, “acupuncture”, “electroacupuncture”, “acupuncture” and “electro-acupuncture”, “traditional therapies”, “acupuncture”, “electroacupuncture”, “allergic rhinitis “ etc. Relevant papers published from January 1964 to August 2024 were collected to summarise the research progress in this field.

Results: Acupuncture achieves the treatment of allergic rhinitis by modulating inflammatory mediators, modulating neuropeptide, acupuncture pterygopalatine ganglion during the same period, and bi-directionally modulating the sympathetic and parasympathetic nerves, etc.

Conclusion: Acupuncture has precise efficacy in the treatment of allergic rhinitis with a clear mechanism, and this paper will promote the acupuncture treatment of allergic this article will promote the international clinical application of acupuncture for allergic rhinitis.

Keywords: Acupuncture; Allergic rhinitis; Mechanism; Research progress; Review

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According to literature, acupuncture has been used for clinical treatment in China for more than 1,000 years, however, its research on the therapeutic mechanism of allergic rhinitis has not been systematically and comprehensively evaluated. In this paper, based on the previous studies, a more in-depth review of acupuncture treatment of allergic rhinitis was carried out as follows.

Regulation of Inflammatory Mediators

In the process of Allergic Rhinitis (AR), the release of inflammatory mediators such as histamine and leukotriene by Mast Cell (MC) and basophil granulocyte (Bas) degranulation is the direct cause of nasal mucosal dysfunction and clinical symptoms. When stimulated by external antigens, MC release histamine, leukotriene and other inflammatory mediators, which accelerates the allergic reaction, leading to an imbalance in the immune status and aggravating the clinical symptoms of nasal congestion and sneezing in AR patients [1]. Therefore, inhibiting the expression of inflammatory mediators such as histamine and leukotriene and regulating their levels in the serum is one of the commonly used means of treating AR at present. In a large randomised controlled trial of acupuncture for the treatment of seasonal allergic rhinitis, Gellrich et al. Observed that acupuncture reduced intranasal non-specific inflammation and significantly lowered nasal concentrations of non-specific pro-inflammatory cytokines (IL-1b, IL-8, IP-10, MIP-1b, MCP-1) [2].

Regulation of HA expression

HA is one of the important mediators of AR development and exerts direct inflammatory and immunomodulatory effects by binding to its receptors to produce biological effects [3]. In the pathogenesis of AR, the receptors that bind to and function with HA include nasal mucosal HA receptors H1 (H1R) and H4 (H4R). H1R is closely related to allergic inflammatory reactions, reducing humoral immunity and enhancing cellular and autoimmunity.H1R also stimulates the release of inflammatory mediators such as HA and increases vascular permeability, and stimulates B-cells to produce IgE [4], further aggravating the symptoms of runny nose and itchy nose.H4R induces the production of Eotaxin3 and eosinophilic cationic proteins by HA and increases the polymerisation of EOS actin.H4R induces the production of EOS actin by HA and increases the polymerisation of EOS actin. The polymerisation of EOS actin increases the infiltration of EOS into the nasal mucosa, leading to an aggravation of the inflammatory response of AR [5]. Studies have shown that acupuncture can effectively down-regulate the expression of H1R and H4R proteins in nasal mucosal tissues, inhibit the release of inflammatory mediator HA, attenuate or block the inflammatory reaction, and play a therapeutic role in the treatment of AR[6].

Regulation of LTs expression

Leukotrienes (LTs) is common lipid inflammatory mediators, and during the development of AR, HA and other related inflammatory mediators are released, which acts on vascular endothelial cells and epithelial cells and induce the release of adhesion molecules, thus contributing to the release of LTs. Studies [7] found that LTs can

effectively diastole vascular smooth muscle and increase vascular permeability, and at the same time, LTs can activate EOS, increase the adhesion properties of EOS, and stimulate the secretion of mucus. LTs are closely related to metabolic reactions, and they play a direct role in symptoms such as nasal congestion and runny nose associated with AR. Therefore, inhibiting the expression of inflammatory factors LTs, reducing vascular permeability and causing vasoconstriction is one of the ways to treat AR.Toll-like receptor (TLR)4/nuclear factor-κB (NF-κB) signalling pathway is a classical neuroinflammatory pathway, and inhibition of this signalling pathway can significantly attenuate the production and release of inflammatory mediators, and alleviate inflammatory allergy in the body [8]. Studies have demonstrated that acupuncture can inhibit the expression of LTs by regulating the TLR4/NF-κB signalling pathway [9], which can effectively reduce the content of LTs in the nasal cavity of AR rats, thereby reducing the inflammatory response and exerting a certain degree of alleviation of the symptoms associated with AR [10].

Regulation of Neuropeptides

Neuropeptide are key substances in the development of neurogenic inflammatory reactions, and they are mainly found in the class C sensory nerve endings of the nasal mucosa. Nasal mucosa epithelium, blood vessels and glands are surrounded by abundant neuropeptide fibres, which includes substance P (SP), vasoactive intestinal peptide (VIP), neuropeptide Y (NPY), etc. Changes in neuropeptide affect the severity of inflammation and indirectly regulate the inflammatory response. Changes in neuropeptide affect the severity of the inflammatory response and indirectly regulate the state of the immune response, playing an important role in the pathogenesis of AR [11]. Various neuropeptide are differentially expressed in the nasal mucosa of AR patients and animal models, and the acupuncture intervention can play a therapeutic role in the treatment of AR by regulating neuropeptides [12].

Regulation of Substance P (SP)

Substance P is a cleavage product of pro-tachykininogen, a primary RNA transcript encoded by the TAC1 gene that is spliced to produce four mRNAs, each of which contains one copy that can be processed into a biologically active fragment of substance P [13]. When a non-specific stimulus (e.g. histamine) acts on the cell membrane of a neuron, the receptor ionisation channel on the cell membrane will be stimulated, and then the afferent nerve will release e.g. substance P (substance P, SP), which causes a series of inflammatory symptoms.SP, as a neuropeptide neurotransmitter, plays a significant role in allergic reactions for its function of inducing the histamine release. After allergen stimulation, the sensitivity of SP-containing nasal mucosal class C ganglia is enhanced, and nitric oxide is produced through the specific expression of IgE receptors and the redifferentiation of inflammatory factors, which leads to vasodilatation of the nasal mucosa and an increase in nasal resistance [14]. In addition, SP and its receptors are widely present in nasal mucosal cells, blood vessels, and glands, and they can act directly on MCs and activated macrophages to degranulate their surfaces and release inflammatory factors such as LTs and HA. The released factors indirectly cause vasodilatation and oedema of the nasal mucosal tissues by altering vasodilatation pressure and plasma osmolality through the action on the nasal mucosal microvessel, which can exacerbate the symptoms of nasal congestion [15]. SP also plays a major role in the degranulation of MC and the release of transmitters [16]. SP is mainly mediated by its specific receptor NK-1R (neurokinin-1 receptor, NK-1R), which can be activated by the microvascular and glandular compartment of MCs and activated macrophages. SP mainly acts through its specific receptor NK-1R (neurokinin-1 receptor), and it has been found that MC near the nasal mucosa expresses the receptor NK-1R, and the expression of NK-1R was found to be increased in patients with AR, which suggests that SP may play an important role in CS-induced metamorphic reactions [17]. The level of SP in the nasal mucosa is significantly elevated in the event of AR, and acupuncture is able to inhibit the expression of SP in the nasal mucosa by modulating the sensory reflexes and therefore alleviating the symptoms in the nose. Acupuncture can inhibit the expression of SP in the nasal mucosa by regulating the sensory nerve reflexes, thus alleviating nasal symptoms [18]. Acupuncture can reduce the sensitivity of nasal sensory nerves and down-regulate the level of pro-inflammatory neuropeptide by regulating the neuroimmune activity [19]. Nasal mucosal SP levels are significantly elevated during the development of AR [20]. Acupuncture can inhibit the expression of nasal mucosal SP by regulating the sensory reflexes to alleviate the nasal symptoms [21].

Regulation of Vasoactive Intestinal Peptide (VIP)

VIP is a parasympathetic peptide derived from the pterygopalatine ganglion, which has a strong vasodilator effect. When AR develops, high expression of VIP in the nasal mucosa leads to increased glandular secretion and increased nasal mucosal oedema [22]. In addition, VIP also interferes with the balance of Th1/Th2 in the body, which is mainly manifested in the inhibition of the secretion of specific factors such as IFN-γ by Th1 cells and the activation of Th2 cells to promote their secretion of IL-4 sensitising factors, which ultimately leads to the enhancement of the body's hypersensitivity inflammatory response and the aggravation of AR-related symptoms [23]. Research [24] shows that acupuncture inhibits the expression of VIP in patients by regulating parasympathetic excitability, thereby contracting nasal mucosal blood vessels and reducing glandular secretions and blood flow in the nasal mucosa and cavernous body to achieve the purpose of treating AR.

Regulatory Neuropeptide Y (NPY)

NPY is a sympathomimetic neuropeptide, mainly released from the endings of the sympathetic nervous system, and is an important substance in the regulation of gland secretion and vasoconstriction in the nasal cavity.NPY has a strong vasoconstrictive ability, and it can effectively and persistently inhibit vasodilatory factors and antagonise their normal expression and differentiation.NPY can also effectively reduce the capacity of the microvessel in the nasal cavity by regulating the neuropeptide Y1 receptor, and indirectly acquire anti-inflammatory ability by regulating NPY via Y1 receptor [25]. NPY can also reduce the volume of microvessel in the nasal cavity by regulating the neuropeptide Y1 receptor in vivo, and indirectly acquire anti-inflammatory ability through the regulation of Y1 receptor [25]. Acupuncture intervention can increase the level of NPY by increasing the sympathetic excitability, and the increase in NPY expression leads to vasoconstriction of the nasal mucosa and a decrease in glandular secretion, thus improving the symptoms of AR [24]. The three neuropeptide, SP, VIP and NPY, are physiologically antagonistic to each other, SP, VIP has the function of vasodilatation of blood vessels, mucous membranes, and glands, while NPY is the opposite, acupuncture can effectively regulate the balance of neuropeptides in the body, such as SP, VIP, and NPY, and regulate the balance of the body's endocrine secretion, improve the symptoms of the patients, and improve the patients' quality of life [26].

Acupuncture Pterygopalatine Ganglion

The pterygopalatine ganglion is a branch of the parasympathetic nerve, which also has the distribution of sympathetic and sensory nerves. Acupuncture pterygopalatine ganglion can avoid completely cutting off the pterygopalatine nerve to directly change the overexpression of the parasympathetic nerve, and achieve the therapeutic effect of improving the symptoms of the nasal region while avoiding the adverse effects [27]. It has been suggested that stimulation of the pterygopalatine ganglion activates the preganglionic or postganglionic fibres of the parasympathetic nerves, causing their neural electrical activity to exceed their intrinsic discharge frequency and blocking the efferent parasympathetic signals, thus decreasing parasympathetic expression [28]. The Chinese AR Diagnostic and Therapeutic Guidelines also recommended acupuncture on the Butterfly-Palate nerve node for the treatment of allergic rhinitis [29]. It has also been suggested that acupuncture on the pterygopalatine ganglion leads to changes in the levels of sensory nerve-related SP and sympathetic nerve-related NPY, while parasympathetic nerve-related VIP does not change significantly [30]. The mechanism of acupuncture pterygopalatine ganglion in the treatment of allergic rhinitis is as follows: ① Acupuncture pterygopalatine ganglion can regulate the sympathetic and parasympathetic nerves in the same period and in both directions, and it mainly exerts stimulating and excitatory effects on the sympathetic nerves of the nasal cavity, but has little effect on the parasympathetic nerves, maintains the balance between the two and improves the effect of nasal ventilation rapidly and dramatically; ② the excitatory signals produced by acupuncture pterygopalatine ganglion are transmitted to the brain through the sensory nerves, and then to the brain through causing somatic visceral reflexes. By causing somatic visceral reflexes, neuro-endocrine-immune regulation, thus improving nasal pathology and reducing rhinitis symptoms; (3) Acupuncture pterygopalatine ganglion plays a role in balancing the autonomic nervous system and reducing neural sensitivity through cholinergic anti-inflammatory effects; (4) Acupuncture pterygopalatine ganglion can reduce the release of serum P substances in patients with allergic rhinitis, and alleviate the over-sensitive state of the nasal mucosa [31,32].

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