

Acupuncture treatment for patients with asthma

Zogopoulos P^{1,2*}, Sagris K³, Gkorgkolis V⁴, Kollias S², Pankos A², Vretakos G² and Rologis D²

¹Department of Medical Acupuncture, Metropolitan Hospital, Athens, Greece

²Department of Neurosurgery, Metropolitan Hospital, Athens, Greece

³Intensive Care Unit, Metropolitan Hospital, Athens, Greece

⁴St. Andrews Centre for Plastic Surgery and Burns, Broomfield Hospital, Chelmsford, UK

Abstract

Acupuncture is a treatment modality for a wide range of disorders and diseases. Although, it has been widely practised in Asia for many centuries, western medicine has focused on its therapeutic potential only over the last few decades. Extensive investigations are currently being conducted worldwide, regarding acupuncture's indications, efficacy and mechanisms of action. We present a review of available experimental and clinical data, to date, regarding acupuncture's efficacy as an adjunctive treatment for patients with asthma.

Introduction

Bronchial asthma is a chronic airway inflammatory disease, characterized by airway hyperresponsiveness that leads to airflow obstruction or even bronchospasm, and chronic inflammation [1]. Common symptoms include coughing, wheezing, shortness of breath and chest tightness [2]. Acupuncture treatment has been proven effective for many different diseases and disorders, including airway disorders such as bronchial asthma.

Materials and methods

We searched all available publications on electronic medical database PubMed, regarding acupuncture's efficacy in treating patients with asthma. Search terms were "acupuncture" and "asthma". In total, 27 studies met the inclusion criteria (16 clinical and 11 experimental studies).

Results

Experimental data

Many experimental animal studies (mostly on rats and mice) have documented the efficacy of acupuncture treatment in alleviating asthma symptoms and have shed light on the mechanisms of action and the neurobiology behind these beneficial effects. Most commonly used experimental model is that of ovalbumin-induced bronchial asthma.

Specifically, acupuncture treatment led to a significant suppression of airway hyperresponsiveness, chronic lung inflammation and mucus secretion in animal models of asthma (after injection and inhalation of ovalbumin) [3,4]. It also inhibited airway remodeling, decreased airway resistance and increased lung dynamic compliance, since acupuncture treatment resulted in a remarkable decrease of the airway wall thickness and smooth muscle thickness [4,5]. These effects were mediated by an inhibition of Ca(v) 3.1 T-type calcium channel protein expression in airway smooth muscle cells [6].

A significant decrease in serum concentrations of certain pro-inflammatory cytokines, such as interleukin (IL)-1 β , IL-33 and tumor

necrosis factor - α (TNF- α) compared to untreated asthmatic mice (control group) was also observed after acupuncture treatment [4]. Moreover, acupuncture reduced the CD4 +IL-17A+ cell proportion and counts and increased CD4+Foxp3+ cell counts in bronchoalveolar lavage fluid [3,4]. Acupuncture also reduced ovalbumin-specific IgE levels, as well as Th17 cytokine levels (such as IL-17A, IL-17F and IL-22) in the serum, compared to control group [3].

Hematoxylin and eosin staining of bronchoalveolar lavage fluid after acupuncture treatment has revealed significantly reduced inflammatory infiltration and aggregation of a variety of inflammatory cells (eosinophilic granulocytes, neutrophils and lymphocytes) around airways, compared to control group [3,7-9]. These beneficial effects of acupuncture on asthma treatment may be mediated by suppression of acetylcholine signalling both during its synthesis, as well as its release, since acupuncture treatment reduced acetylcholine synthetase pulmonary expression and restored pulmonary expression of muscarinic receptors (mAChRs) M1 & M2 (especially in the bronchiolar epithelium), that play a pivotal role in acetylcholine release inhibition [9]. Furthermore, acupuncture significantly reduced expression of protein kinase B (PKB/AKT) in lung tissues and consequently reduced inflammatory reaction and airway remodelling [8].

Acupuncture treatment in experimental rat asthma models significantly inhibited transforming growth factor β 1 (TGF- β 1) expression in the lung tissues (both in bronchoalveolar lavage fluid and serum) compared to the control group [5,10]. Moreover, TGF- β 1 expression levels were even lower than those of the medication group (aminophylline administration), thus, suggesting that this effect could play a pivotal role in airway remodeling improvement [5]. TGF- β 1 is a polypeptide that belongs to the family of cytokines and performs many cellular functions (such as control of cell proliferation, differentiation

*Correspondence to: Zogopoulos Panagiotis, Department of Medical Acupuncture, Metropolitan Hospital, Athens, Greece, E-mail: p.zogopoulos@yahoo.com

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and apoptosis), especially regarding the immune system [11]. In another ovalbumin-induced murine asthma model, acupuncture treatment enhanced hypothalamic-pituitary-adrenal (HPA) axis activity and thus, increased adrenocorticotrophic hormone and cortisol secretion in the plasma [12]. These effects on TGF- β 1 expression and HPA-axis activity could explain, at least in part, the anti-inflammatory properties of acupuncture and particularly the attenuation of airway inflammation in asthma patients [12].

Protein electrophoresis and mass spectrometry in experimental animal models of asthma have shown that acupuncture can regulate the inflammation signaling pathway at several different key points by regulating specific proteins [13]. In particular, it can downregulate proinflammatory proteins [such as S100 calcium-binding protein A8 (S100A8), receptor for advanced glycation endproducts (RAGE) and S100 calcium-binding protein A11 (S100A11)] and upregulate anti-inflammatory proteins [such as Clara cell 10 kD protein (CC10), Annexin-A5 (ANXA5) and soluble RAGE (sRAGE)] [13]. Furthermore, acupuncture can significantly increase Fas mRNA expression (Fas protein is a member of the TNF-receptor superfamily and is implicated in the regulation of programmed cell death), while Bcl-2 mRNA expression is significantly reduced (Bcl-2 is an integral outer mitochondrial membrane protein that blocks the apoptotic death of some cells such as lymphocytes) [7].

Clinical data: Several randomized, controlled, clinical trials in patients with asthma have proven acupuncture's clinical efficacy in terms of symptoms remission, as well as respiratory functional status. Patients with allergic asthma who received acupuncture treatment in combination with their standard medication exhibited significantly improved disease-specific and health-related quality of life (as assessed with the asthma quality of life questionnaire and Short-Form-36 questionnaire), compared to patients who received standard medication alone [14].

Randomized, controlled clinical trials in children with asthma showed that acupuncture treatment resulted in a significant reduction of subjective asthma symptoms and of inhaled steroids and β 2 agonists use, compared to the control group, for as long as acupuncture treatment was administered, but these beneficial effects were not sustained after acupuncture's discontinuation [15].

In a randomized, controlled, clinical trial in patients with mild to moderate asthma, acupuncture treatment led to a decrease in eosinophils and neutrophils and an increase in macrophages [16]. Patients experienced less coughing, wheezing, dyspnea and nocturnal awakening episodes and used significantly less rescue medication (short- and long-acting β -2 agonists and inhaled corticosteroids) [16]. Finally, patients exhibited significant improvement in peak expiratory flow, peak expiratory flow variability, functional capacity and general health status [16,17].

A meta-analysis on randomized controlled clinical trials of acupuncture for asthma patients found that acupuncture can significantly improve peak expiratory flow (PEFR), forced vital capacity (FVC) and the Tiffeneau-Pinelli index (FEV1/FVC), although FEV1 was not found to be affected in a statistically significant manner [18]. However, there have been reports from randomized, controlled clinical trials that FEV1 can also be significantly improved with acupuncture, up to the same extent or even superior to inhaled bronchodilation [19,20].

Acupuncture treatment in patients with bronchial asthma was found to be equally effective to inhaled salbutamol in terms of acute symptoms' control and could achieve immediate relief within 30

minutes of needle insertion [21]. It also led to a significant decrease of IgA concentration in the saliva and nasal secretions, as well as a significant decrease of total serum IgE, IL-2R+ T lymphocytes and eosinophils counts in the peripheral blood [22]. On the other hand, a significant increase of CD3+, CD4+, and CD8+ T lymphocytes, as well as an increase of IL-8 and a significant decrease of IL-6 and IL-10 concentrations in the peripheral blood were observed, suggesting that acupuncture can have a regulatory effect on cellular and mucosal immunity in asthma patients [22,23].

Discussion

Bronchial asthma is a serious health problem with nearly 5%-10% of the global population suffering from it [24]. Particularly, incidence of asthma and asthmatic bronchitis among children is estimated to be even higher (between 10% and 20%) [15]. Despite numerous available medications for bronchial asthma (such as inhaled corticosteroids, long acting beta agonists and antileukotriene agents), there is no definitive treatment and symptoms' control is usually only temporary or even not feasible. Therefore, new therapeutic regimens that combine both high efficacy and minimum side-effects are still necessary and acupuncture treatment can play that role.

Acupuncture treatment for allergic bronchial asthma in addition to standard care is associated with additional costs but also with greater efficacy regarding symptoms' control and, thus, improvement of quality of life as has been depicted through Asthma Quality of Life Questionnaire (AQLQ) score improvement [25,26].

There is a hypothesis that acupuncture may inhibit re-uptake of neurotrophic factors (such as brain-derived neurotrophic factor, nerve growth factor and leukemia inhibitory factor) that are synthesized in bronchial epithelial and immune cells and consequently inhibit synthesis and release of substance P in dorsal root ganglia [27]. Substance P is known to cause contraction of airway smooth muscle cells, increase of mucous secretion, capillary extravasation and release of inflammatory mediators, which all contribute to airway hyper-reactivity [27]. Thus, through the inhibition of this cascade acupuncture can exhibit its beneficial effects in asthma patients.

There have been reports in the literature that acupuncture failed to improve clinical status and functional respiratory indexes of asthma patients [28-31]. A general big concern regarding acupuncture trials is the lack of a rigorous study design, patient selection bias and poor study quality and reporting. As the interest for acupuncture is constantly increasing internationally and more and more patients seek alternative treatments for their condition, strict methodological criteria should be adopted for all trials on acupuncture and furthermore, acupuncture practice should only be restricted to experienced and specially trained physicians who can guarantee both safety and effectiveness of this treatment modality.

Conclusion

Acupuncture can effectively protect lung function and prevent airway inflammation, thereby playing an important role as an adjunctive treatment modality for asthma patients. Furthermore, it is a cost-effective treatment with no serious adverse effects, when practised by an experienced and certified acupuncturist.

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