

Astragalus Membranaceus prevents airway hyperreactivity in mice related to Th2 response inhibition

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Received 1 October 2007; received in revised form 11 November 2007; accepted 3 December 2007
Available online 8 December 2007

Abstract

Aim of the Study: Asthma is recognized as a common pulmonary disease throughout the world. To date, there has been a growing interest in herbal products in Traditional Chinese Medicine, which is considered to be effective to treat asthma. A Chinese herb *Astragalus Membranaceus* (AM) was found useful in treating allergic diseases. The purpose of this study is to determine whether this herbal injection could suppress allergic-induced AHR and mucus hypersecretion in allergic mice.

Materials and Methods: A mouse model of chronic asthma was used to investigate AM injection on the airway lesions in compared with glucocorticoids. The study was conducted on mice sensitized and challenged with ovalbumin and the whole body plethysmography was performed to assess AHR. The bronchoalveolar lavage (BAL), histopathology were examined.

Results: We found 28-day AM administration significantly decreased inflammatory infiltration and mucus secretion in the lung tissues of allergic mice. 28-day AM administration enhanced Ova-induced decreased IFN- γ , and the Ova-induced elevations of IL-5 and IL-13 in BALF were prevented by 28-day injection. We also showed 28-day AM injection markedly suppressed increased AHR in allergic mice.

Conclusions: Our results indicate *Astragalus Membranaceus* has a potential role in treating allergic asthma.

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Keywords: *Astragalus Membranaceus*; Asthma; IL-5; IFN- γ

1. Introduction

Asthma is recognized as a common pulmonary disease and a serious public problem throughout the world. In the last two decades, asthma morbidity and mortality have been increased (Masoli, 2004). Airway hyperreactivity (AHR), chronic pulmonary inflammation with infiltration of eosinophils in lung, and mucus hypersecretion in the airways are hallmarks of allergic asthma (Ray, 1999; Wills-Karp, 1999; Adamko, 2003). The onset and progression of allergic asthma is accompanied by a complex series of overlapping and concurrent inflammatory responses in the lung orchestrated by CD4+ Th2 lymphocytes (Gavett, 1994). These responses include T cell mediated help of antigen-specific immunoglobulin production particularly

IgG1 and IgE by B cells, expression of Th2 proinflammatory cytokines (e.g., IL-4, -5, -9, and -13) (Jenmalm, 1999; Kon, 1999). Among Th2 cytokines, IL-5 promotes differentiation and migration of eosinophils (Foster, 1996). IL-4 and IL-13 have been implicated in goblet cell hyperplasia, the development of AHR, and lung remodelling (Wills-Karp, 1998; Larche, 2003).

The treatment of asthma has been improved by the implementation of management guideline in recent years, with further development in the study for the mechanism of asthma. Inhaled corticosteroids and β 2-agonists are used as the first line of treatment of asthma, reducing airway inflammation and bronchial constriction effectively. Many other medicines such as theophylline, anticholinergics, leukotriene modifiers etc. have also been used to control asthma. However, the effects of those drugs are not satisfied in the clinical practice, because of local or systemic side effects (Sally, 2005). Therefore, there is a need for new or alternative approaches to the control of asthma. To

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date, there has been a growing interest in alternative medicine, particularly herbal products in Traditional Chinese Medicine (TCM), which is much more appropriate to the prevention and treatment of disease in chronic condition such as asthma (Yu, 2006).

Astragalus Membranaceus (AM) is a traditional Chinese herb which has been used for more than 2000 years in China. Physician in TCM system used AM that has been manufactured into injection to boost the body's general vitality and strengthening resistance to exogenous pathogens, which was regarded as a potent tonic for increasing energy levels and stimulating the immune system (Block, 2003). Scientific investigation in the last two decades has revealed much insight into the pharmacological functions of AM (Bedir, 2000; Mckenna, 2002). Several studies focused on its immunomodulatory properties, and AM was shown to increase human lymphocyte proliferation, cytotoxic T cell responses and IgG production (Wang, 2002). It stimulated murine splenocytes to proliferate and macrophages to produce proinflammatory cytokines (Lau, 1994; Yoshida, 1997). Recently, AM in combination with other herbs, was used in treating allergic rhinitis, asthma and atopic dermatitis (Suzuki, 1999; Ishimitsu, 2001; Cui, 2003). AM has recently become popular with Western herbalist and alternative health care providers. However, the role of AM in asthma therapy in Western medicine is still uncertain. More study is needed to investigate the action and mechanism of this herbal medicine.

The purpose of this study is to determine whether AM could suppress allergic-induced AHR and mucus hypersecretion in allergic mice. We employed a mouse model of chronic asthma, which replicates many features of the human disease, to investigate inhibitory effect of AM injection on the airway lesions compared with glucocorticoids. We found AM injection significantly inhibited the enhanced AHR and mucus hypersecretion, with blockade of eosinophil recruitment in airway. Elevated IL-5, IL-13 in BALF in asthmatic mice were markedly decreased while increased IFN- γ was observed. Our results indicate that AM have a potential role in treating exacerbations of asthma triggered by allergen.

2. Materials and methods

2.1. Preparation of AM extract

The aqueous extract of AM was prepared as follows. Fifty grams of powdered *Astragalus radix* were placed in 600 ml water, and boiled for 1 h. Then filtered, and the decoction was diluted in distill water to concentration of 1 g/ml. (each ml of solution contained 1 g crude drug of *Astragalus Membranaceus*). The extract and the voucher specimens of the herbs were kept at Chitai Qingchunbao Pharmaceutical Co. Ltd. (Hangzhou China).

2.2. Mice

Eight to ten weeks old male *C57BL/6* mice weighing 20–25 g were purchased from the Laboratory Animal Center of the Medical School of Zhejiang University (certificate no. 220010342,

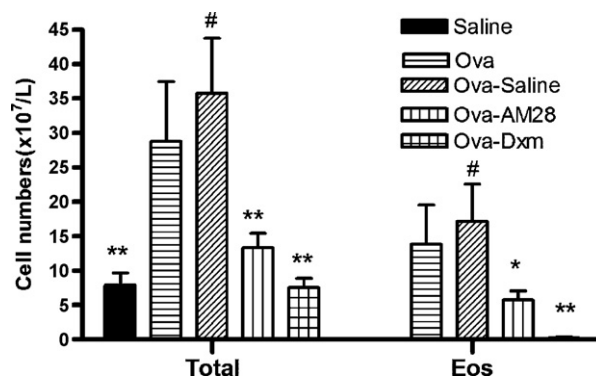


Fig. 1. Effect of AM injection on leukocytes in BALF of allergic mice. BALF was harvested on 48 h after last Ova challenge. Data are expressed as means $\pm$ S.E.M., $n=6$. ** $P<0.01$ vs. Ova; * $P<0.05$ vs. Ova; # $P>0.05$ vs. Ova. Saline: mice were sensitized and challenged with saline. Ova: mice were sensitized and challenged with Ova. Ova-AM28: Ova sensitized and challenged mice were treated with AM injection for 28 days at 10 g/kg per day. Ova-Saline: Ova sensitized and challenged mice were treated with Saline for 28 days. Ova-Dxm: Ova sensitized and challenged mice were treated with dexamethasone at 0.5 mg/kg 1 h before challenge.

conferred by the Zhejiang Medical Laboratory Animal Administration Committee). The present study was performed according to the internationally accepted principles for laboratory animal use and care as found in the US guidelines (NIH publication #85-23, revised in 1985). Fifty mice were divided into five groups, i.e., Ova group: mice were sensitized on the day 0 and day 14 by ip injection of ovalbumin (Ova) (Sigma-Aldrich, St. Louis, MO, USA) mixed with aluminum. At day 24, 25, and 26, mice were challenged by aerosolized 1% Ova in saline for 40 min. Saline group: mice were sensitized and challenged with saline. Ova-Saline group: mice sensitized and challenged as Ova group were administered with saline intraperitoneally for 28 days after first sensitization. Ova-AM28 group: mice sensitized and challenged as Ova group were administered with AM injection (Chitai Qingchunbao Pharmaceutical Co. Ltd., Hangzhou China) intraperitoneally for 28 days after first sensitization at dose of 10 g/kg per day. Ova-Dxm group: mice sensitized and challenged as Ova group were administered with dexamethasone at day 24, 25, and 26 before challenge at dose of 0.5 mg/kg.

2.3. Bronchoalveolar lavage fluid (BALF) of the lungs

At day 28, BALF was performed using 1 ml of PBS containing 2% FBS. Total BAL cellularity was determined with the use of a hemocytometer. Cytospin slides were fixed and stained by Wright-Giemsa staining. Differential cell counts by unbiased observers were based on counts of 200–300 cells using standard morphological criteria to classify individual leukocyte populations.

2.4. Airway hyperresponsiveness in response to methacholine

Airway responsiveness to methacholine (MeCh), was assessed by whole body plethysmography (Buxco Electronics,

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