JTCM 中医杂志 Journal of Traditional Chinese Medicine

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J Tradit Chin Med 2018 February 15; 38(1): 61-66
ISSN 0255-2922

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RESEARCH ARTICLE

Effect of Xiaochuanping powder on the inflammatory response and airway remodeling in asthmatic rats

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Supported by Natural Science Foundation of China: Intervention Mechanism of the Method of Tonifying Qi And Promoting Blood Circulation and Resolving Phlem on Airway Remodeling after COPD (No. 81473675); Based on p38MAP Signal Pathway Yiqi Huoxue Huatan Method was Explored the Mechanism Study of Bronchial Asthma Airway Remodeling (No. 81774301); Excellent Young Talent Fund Project of Colleges and Universities in Anhui Province: Study on the Mechanism of Airway Remodeling of Asthma Model In Rats With Xiaochuanping Powder (No. 2011SQRL093)
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Accepted: September 13, 2017

Abstract

OBJECTIVE: To observe the effect of Xiaochuanping powder (XP), a traditional Chinese prescription for the treatment of cough and asthma, on serum concentrations of eosinophil cationic protein (ECP), tumor necrosis factor (TNF)-α, and interleukin (IL)-4, eosinophil counts, as well as expression of matrix metalloproteinase (MMP)-9, tissue inhibitor of metalloproteinase (TIMP)-1 in the lung tissues of asthmatic rats.

METHODS: Sixty clean-grade Sprague–Dawley rats were divided randomly into six groups: normal control (NC), asthma model, Guilong Kechuanning (GK) group, as well as high-, intermediate-, and low-dose XP groups. Rats were sensitized with ovalbumin (OVA) to trigger asthma. Serum concentrations of ECP, TNF-α and IL-4, eosinophil counts, as well as expression of MMP-9 and TIMP-1 in lung tissues were evaluated using an immunofluorescence method. mRNA expression of MMP-9 and TIMP-1 was determined using real-time quantitative polymerase chain reaction.

RESULTS: Compared with the asthma-model group, serum concentrations of ECP, TNF-α, and IL-4, and eosinophil counts decreased significantly in the high- and intermediate-dose XP groups and GK group (all $P < 0.01$). Protein expression of MMP-9 and TIMP-1 decreased significantly in the high- and intermediate-dose XP groups and GK group (all $P < 0.01$). Transcription of MMP-9 and TIMP-1 mRNA and the ratio of expression of MMP-9: TIMP-1 in lung tissue were significantly lower ($P < 0.01$).

CONCLUSION: XP can reduce TNF-α secretion, suppress the infiltration / activation of eosinophils, reduce serum concentrations of ECP and IL-4, reduce the protein and mRNA expression of MMP-9 and TIMP-1 in lung tissue, and regulate the balance between expression of MMP-9 and TIMP-1. In these ways, XP alleviated the inflammation and remodeling of the airways.

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Keywords: Asthma; Airway remodeling; Eosinophils; Eosinophil cationic protein; Matrix metalloproteinase 9; Tumor necrosis factor-alpha; Tissue inhibitor of metalloproteinase-1; Xiaochuanping powder

INTRODUCTION

Bronchial asthma is a common, recurrent, protracted, and persistent respiratory disease. Inflammation and remodeling of the airways are important pathologic features of asthma. They can promote each other, jointly inducing the development and exacerbation of asthma.[1-4] About 1%-18% of the populations of different countries are affected by asthma. Worldwide, > 300 million people are plagued by asthma, and the incidence and severity of asthma are increasing annually.[5]

Western Medicines such as glucocorticoids and β2-agonists have shown good efficacy in the early management of acute severe asthma by controlling symptoms, reducing damage to delicate lung tissue, and improving quality of life. However, Western Medicines cannot cure asthma. Furthermore, they often cannot be used for long periods or at high doses, especially in older adult people and young children.[6] In comparison, Traditional Chinese Medicine (TCM) have several advantages in the prevention and treatment of asthma due to their documented efficacy, few side-effects, applicability to different populations, and low price. In recent years, their role in asthma control has been recognized increasingly.[7-9]

Xiaochuanping powder (XP) is a TCM composed of medicinal materials such as Shanyao (*Rhizoma Dioscoreae Oppositae*), Bihu (*Gekko Swinhonis*), Baizhu (*Rhizoma Atractylodis Macrocephalae*), Muhudie (*Semen Qroxyli*) and prepared Mahuang (*Herba Ephedra Sinica*). XP has been used in the Department of Respiratory Medicine of the First Affiliated Hospital of Anhui University of Chinese Medicine (Hefei, China) for many years, with confirmed efficacy.[10]

In the present study, we evaluated changes in serum levels of eosinophil cationic protein (ECP), tumor necrosis factor (TNF)-α and interleukin (IL)-4, eosinophil counts, as well as differences in the expression of matrix metalloproteinase (MMP)-9 and tissue inhibitor of metalloproteinase (TIMP)-1 in lung tissues by applying different interventions in a rat model of asthma. Our results could provide theoretical and experimental evidence for asthma treatment using XP.

MATERIALS AND METHODS

Animal groupings

Sixty clean-grade Sprague-Dawley rats [30 males and 30 females; (200 ± 20) g] were purchased from the Laboratory Animal Center of Anhui Medical University. The study was approved by the experi-mental animal ethics committee of Anhui University of Chinese Medicine. They were divided randomly into six groups of 10: normal control (NC); asthma model; Guilong Kechuanning (GK; a TCM used to treat cough and asthma); high-dose XP; intermediate-dose XP; low-dose XP. The animals were bred in a conventional manner at (25 ± 1) °C for 7 d before being experimented upon.

Drugs

XP was composed of the following medicinal materials: Shanyao (*Rhizoma Dioscoreae Oppositae*; 20 g), Bihu (*Gekko Swinhonis*; 8 g), Baizhu (*Rhizoma Atractylodis Macrocephalae*; 10 g), Muhudie (*Semen Qroxyli*; 10 g) and prepared Mahuang (*Herba Ephedrae*; 6 g). These medicinal materials were purchased from the TCM Pharmacy in the First Affiliated Hospital of Anhui University of Chinese Medicine. Using a conventional method, a decoction with a crude drug concentration of 0.55 g/mL was prepared. GK granules were manufactured by Golong Medicine (No. Z20103119; Shanxi, China).

Reagents and equipment

Ovalbumin (OVA) was purchased from Sigma-Aldrich (A5253; Saint Louis, MO, USA). Aluminum hydroxide was obtained from Shanghai Dong Shan Chemical Plant (Shanghai, China). Kits to measure levels of TNF-α, IL-4, ECP, expression of MMP-9 and TIMP-1, and to obtain the eosinophil count, were purchased from Shanghai Yuanye Biotechnological (Shanghai, China). TRIzol® Reagent was obtained from Invitrogen (14105; Carlsbad, CA, USA). A RevertAid ™ First Strand cDNA Synthesis kit was from Thermo Scientific (00145205; Waltham, MA, USA). An automatic embedding and slicing system was purchased from Leica (Wetzlar, Germany). A microplate reader was obtained from Bio-Rad Laboratories (Hercules, CA, USA). A microscope image-analysis system was obtained from Olympus (Tokyo, Japan). A PikoReal™ 96 RealTime Polymerase Chain Reaction (PCR) system was purchased from Thermo Scientific. A desktop high-speed refrigerated centrifuge (JW-3021HR) was obtained from Jiaven (Anhui, China).

Modeling and drug administration

In the NC group, sensitization and asthma induction were undertaken using physiologic (0.9%) saline. In the other groups, sensitization was triggered by 10% OVA (1 mL; i.p.); after day-15, asthma was induced by aerosol inhalation with 1% OVA (5 mL) for 20-30 min on a daily basis for 2 weeks consecutively. The OVA challenge was regarded as being successful if the rats developed symptoms of irritability, dyspnea, sneezing, wheezing and cyanosis, as well as bending their back and scratching their ears.[10]

After 6 consecutive days of asthma induction, physiologic saline was administered (i.g.) to rats in NC and asthma-model groups. In the high-dose XP, intermediate-dose XP, low-dose XP, and GK groups, the corresponding drugs were administered (i.g.) at a daily dose (in g/kg body weight) of 0.5 (10-fold higher than the dose for human adults), 0.375 (7.5-fold), 0.25 (5-fold), and 0.375 (7.5-folds) respectively, for 8 consecutive days.

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