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Multifactor dimensionality reduction analysis of syndrome characteristics of chronic persistent asthma

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Abstract *Objective:* To analyze the syndrome characteristics in patients with chronic persistent asthma.
Methods: 365 patients (121 males, 244 females, 60.8 ± 29.1 years old) with chronic persistent asthma were enrolled in this cross-sectional study. The information of syndrome, symptoms, signs, tongue coating and pulse were collected from all patients. The syndrome characteristics of chronic persistent asthma were examined through the multifactor dimensionality reduction (MDR) analysis and the results were verified by the Chi-square test.
Results: The results of the MDR analysis and the Chi-square test showed the following positive correlation of the interaction among: the deficiency syndrome of the lung and spleen and deep pulse, disinclination to talk due to lack of *qi*, fatigue, lassitude and thick tongue coating; the deficiency syndrome of the lung and kidney and dizziness and disinclination to talk due to lack of *qi*, fatigue, lassitude and pallid complexion; the syndrome of phlegm-heat obstructing the lung and rapid pulse, abdominal distension, disinclination to talk due to lack of *qi*, frequent urination and lassitude; the syndrome of phlegm-dampness obstructing the lung and disinclination to talk due to lack of *qi*, greasy coating, fatigue and lassitude. ($P < .05$ for all).
Conclusion: The syndrome of chronic persistent asthma is characterized by fatigue and lassitude due to dysfunction of the lung, spleen and kidney.

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Introduction

Asthma is a commonly-seen chronic inflammatory disease of the airways characterized by variable and recurring symptoms, airflow obstruction and bronchospasm.[1] It is also a complex disease involving many cells and mediators.[2] Asthma affects 300 million people worldwide,[3] with an increasing prevalence in Western Europe (5%) and the USA (7%) in particular.[4,5] Despite the fact that there is still no cure for asthma, it has been established in a great number of small and large studies that many patients can reach a good asthma control with controller treatment.[6] Generally speaking, medications used to treat asthma are divided into two classes: quick-relief medications used to treat acute symptoms and long-term control medications used to prevent further exacerbation.[7] The therapeutic options available for patients with asthma depend on the severity of the condition. Although the symptoms can be controlled by drug treatment in most patients, effective low-risk, non-drug strategies could constitute a significant advance in asthma management.[1–3] Therefore, an increasing number of patients with asthma are attracted by complementary and alternative medicine (CAM).[8] A survey showed that roughly 50% of asthma patients used some forms of traditional Chinese medicine (TCM) therapy.[9]

Chronic persistent asthma is the key period in terms of the prognosis of the disease. Guided by holistic concepts and syndrome differentiation, TCM has shown the potential to modulate it with herbal treatment acupuncture, massage, health care and other methods.[10] As we know syndrome is one type of specific functional condition which shows the response of the body to pathogenic factors. It would be helpful to consider TCM syndrome differentiation and treatment as one of the factors to deal with in chronic persistent asthma.

Multifactor dimensionality reduction (MDR) analysis is one kind of nonparametric methods without genetic model. MDR analysis tells all the possible combinations between-factors. According to the standard threshold, the combination of every two factors is divided into the high risk group or low risk group. The purpose is to classify the risk level of the combined factors and to bring high-dimensional data down to a one dimensional model.[11] Therefore, the MDR method is beneficial to the objective rigorously to reflect the syndrome characteristics. According to the perspective of TCM, literature review, expert questionnaire survey and group interviews, a cross-sectional study was designed to explore the syndrome characteristics of chronic persistent asthma, which might be of great value to secondary prevention and TCM comprehensive intervention strategy for chronic persistent asthma.

Methods

Subjects

365 outpatients with chronic persistent asthma were enrolled from the China-Japan Friendship Hospital, Xiyuan Hospital affiliated to the China Academy of Chinese Medical Sciences, Dongzhimen Hospital affiliated to the Beijing University of Chinese Medicine, and Beijing Hospital of Traditional Chinese Medicine affiliated to the Capital Medical University from October 2012 to April 2013. Of them, 190 cases were from the China-Japan Friendship Hospital, 62 from Xiyuan Hospital, 93 from Dongzhimen Hospital, and 20 from Beijing Hospital of Traditional Chinese Medicine.

Diagnostic criteria

Asthma was diagnosed according to the *National Guidelines for the Diagnosis and Management of Asthma in China*.[12] TCM syndrome was differentiated according to *the Clinical Research Guideline of New Drugs for Traditional Chinese Medicine*.[13]

Inclusion and exclusion criteria

Chronic persistence asthma is referred to weekly occurrence of symptoms at various frequencies and/or degrees (wheezing, shortness of breath, chest tightness, coughing, etc.). Patients would be required to complete the baseline asthma diary. Written informed consent was obtained from each participant. Participants of both genders aged at 18—90 years were recruited from above 4 hospitals. Standard of diagnosis is listed as follows: (1) Common signs and symptoms of asthma include: recurrent wheezing, coughing, breathing problem, chest tightness; (2) Reasons of attack or seriousness; (3) Scattered or diffuse expiratory wheezing sound heard in the lung on attack; (4) Above symptoms relieved or disappeared after treatment; (5) Conditions other than asthma ruled out; (6) In case of absence of typical symptoms, lung function tests employed to confirm. These include positive challenge test, positive bronchodilator test (an increase in FEV1 of $\geq$12% and $\geq$200 mL), and mutation rate of PEF $\geq$ 20% one day/two weeks. Participants were excluded if they suffered from other diseases with breathlessness or dyspnea, such as bronchiectasis, cor-pulmonale, pulmonary fibrosis, tuberculosis, pulmonary abscess, lung cancer, chronic obstructive pulmonary disease and so on. Female participants were not eligible if they were in the state of pregnancy or lactation. The following conditions were also the excluded items: complicated with serious life-threatening diseases, such as heart and brain blood vessel disorders, liver, kidney and hematopoietic system disease and psychotic patients.

Clinical design and data-collecting methods

Clinical information of patients with chronic persistent asthma in the study were collected from the TCM Clinical Research Information Sharing System. Different hospitals share the information through virtual network transmission.

Research procedures

(1) Case Report Form (CRF) was formulated; (2) Those graduate students who had passed the required examination were employed in the research team. All the staff were familiar with the study method, techniques and content through training; (3) Pre-investigation: The expected weak points of the study were investigated and the CRF table was improved; (4) Information acquisition: Patients'