Bronchial asthma (abbr. as asthma below) is a chronic inflammatory disease of the airways involving the participation of multiple cells and cellular components, and inflammation is the main cause for airway hypersensitivity and spasm. Cytokines are a group of small molecular peptides and glycoproteins synthesized and secreted by activated immune or non-immune cells, which play an important part in immune regulation and mediation. Cytokine network imbalance may be one of the molecular bases for the pathogenesis of asthma. At present, Th1/Th2 cytokine disequilibrium is considered to play an important role in developing asthma. Therefore, regulating the disequilibrium becomes a new path of immunotherapy for the treatment of asthma.

Glucocorticoids are now the drugs with the most convincing effect in treating asthma, and their superiority and effectiveness in inhibiting airway inflammation from multi-links to alleviate it have been clearly demonstrated. However, some problems with respect to their adverse effect after long-term administration and impact on children's growth and development are still in dispute. Moreover, patients' poor compliance due to difficulties in handling the inhalation technique restricts their application to some extent. People expect to get new and effective anti-inflammatory agents to make up for the deficiency of hormonal therapy, therefore atomizing inhalation of ligustrazine injection (LI) was applied from January 2005 to January 2007 by the authors to explore

**CLINICAL EXPERIENCE**

**Effect of Ligustrazine Injection on Levels of Interleukin-4 and Interferon-γ in Patients with Bronchial Asthma**

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**ABSTRACT**  
**Objective:** To explore the effect of ligustrazine injection (LI) on serum levels of interleukin-4 (IL-4) and interferon-γ (IFN-γ) in patients with bronchial asthma and determine the mechanism of action of LI in preventing and treating asthma.  
**Methods:** Sixty-eight patients with mild or moderate bronchial asthma were assigned to two groups equally according to their sequence number, odd or even. The conventional treatment was administered to both groups, and LI was given to the treatment group by ultrasonic spray inhalation twice a day but not to the control group. The therapeutic course for all was 2 weeks. Further, 30 healthy subjects who had no history of smoking were enrolled as the normal control group. The clinical condition scores, frequency of attacks and dosage of Terbutaline inhaled were scored and recorded on the first day of hospitalization (before treatment) and after treatment. At the same time, the indexes of lung function, including forced expiratory volume in one second (FEV₁), forced expiratory volume in one second to forced vital capacity ratio (FEV₁/VC) and the peak expiratory flow (PEF) were determined before treatment. The levels of IL-4 and IFN-γ in peripheral blood were detected by ELISA before and after treatment, and compared with that of the healthy control group.  
**Results:** After treatment, the clinical condition scores were found to be lower, indexes of lung function were elevated, but serum level of IL-4 and ratio of IL-4/IFN-γ were reduced in both groups, showing significant differences as compared to those before treatment (P<0.05). However, the changes in all the indexes were more significant in the treatment group than in the control group, also showing statistical significance (P<0.05). No significant difference was revealed when IFN-γ levels were compared before and after treatment in both groups, though a lowering trend could be seen, significant difference could not be found in the comparison of IFN-γ levels between groups after treatment (P>0.05). **Conclusion:** LI shows good clinical effect in treating bronchial asthma, and its mechanism might be related to the suppression of the synthesis of IL-4, thus leading to the inhibition of TH2 cell subset preponderant response and immune equilibrium regulation.

**KEY WORDS** ligustrazine injection, asthma, lung function, TH1/Th2 disequilibrium, interleukin-4, interferon-γ

Bronchial asthma (abbr. as asthma below) is a chronic inflammatory disease of the airways involving the participation of multiple cells and cellular components, and inflammation is the main cause for airway hypersensitivity and spasm. Cytokines are a group of small molecular peptides and glycoproteins synthesized and secreted by activated immune or non-immune cells, which play an important part in immune regulation and mediation. Cytokine network imbalance may be one of the molecular bases for the pathogenesis of asthma. At present, Th1/Th2 cytokine disequilibrium is considered to play an important role in developing asthma. Therefore, regulating the disequilibrium becomes a new path of immunotherapy for the treatment of asthma.
the effects of Chinese herbal medicine on cytokines and on treating asthma.

METHODS

Subjects
Patients with asthma of mild or moderate degree were selected from the out- or inpatients of the authors’ hospital, according to the “Guidance on Prevention and Treatment of Bronchial Asthma” issued by the Special Group of Asthma, Chinese Association of Medicine. Sixty-eight patients, with forced expiratory volume in one second (FEV1)/the peak expiratory (PEF) ratio accounting for 60%-80% of the estimated value, or with a day-night variation of over 20%, were enrolled, none having received glucocorticoids or suffered from any upper respiratory infection in the last month.

They were assigned equally according to odd or even sequence numbers to two groups. The 34 patients in the treatment group were 21 males and 13 females; age 52-86 years, 66.2 ± 13.2 years on average; their course of disease was 5-17 years, average 10.2 ± 2.3 years. The 34 patients in the control group were 20 males and 14 females; age 49-80 years, 65.6 ± 12.8 years on average; their course of disease was 4-20 years, average 10.4 ± 2.5 years. The differences between the two groups in terms of age, sex, course and condition of illness were not significant (P>0.05).

Further, a normal control group consisting of 30 healthy subjects from the staff of the hospital was set up. They were 17 males and 13 females, age 48-78 years, 65.6 ± 12.7 years on average, none with smoking history.

Treatment
Conventional therapy administered to both groups included oxygen inhalation, aminophylline for alleviating asthma, and anti-infection therapy, etc. To the patients in the treatment group, LI injection (product of Tianjin Jinyao Co. Ltd., of Amino Acids, each milliliter containing 20 mg LI) was given additionally at a dose of 80 mg, which was added into 40 mL normal saline for ultrasonic atomizing inhalation twice a day, using medical ultrasonic atomizer type JSC-202 manufactured by Electronic Apparatus Factory of Anshan County, Liaoning Province, China. The therapeutic course for both groups was 2 weeks.

No patient in the two groups received glucocorticoids, but inhalation of Terbutaline, a β2 adrenergic receptor stimulator, could be given to them during asthma attacks.

Items and Methods of Observation
Clinical Condition Scores
Clinical symptoms and signs, including asthma, wheeze sound in lung and condition of night attacks, as well as the frequency and dosage of Terbutaline inhaled were scored and recorded for clinical efficacy evaluation before and after treatment.

The scoring of clinical conditions was worked out based on the following criteria: (1) the score of zero was given to patients who ended up with no symptoms, were able to sleep soundly and were capable of participating in all activities of daily life; (2) the score of 1 was given to patients with frequency of attacks or requiring Terbutaline inhalation for less than twice a week, unable to do heavy physical work, with possible mild asthma at night which did not affect their sleep; (3) the score of 2 was given to patients with frequent attacks or requiring Terbutaline inhalation over twice per week, with dyspnea when they were doing daily activities and sleep was often upset by asthma or cough; (4) the score of 3 was given to patients with daily or persistent attacks, unable to move about or take any compulsory passive posture, with sleep always disturbed due to frequent night attacks.

Lung Function Tests
Lung function tests, including FEV1, forced expiratory volume in one second to forced vital capacity ratio (FEV1%) and PEF, were performed before and after treatment in patients of the two groups, using the Sanyang type ST-300 apparatus from Japan. The inhalation of Terbutaline or other related treatments would be stopped 24 h before the test.

Serum Levels of IL-4 and IFN-γ Determination
Venous blood, at 3 mL per sample, was drawn from the cubital median vein on the first day of hospitalization and the day after 2 weeks of treatment. The serum was separated after 10 min of centrifugation, and preserved in a refrigerator (−80 °C). Using ELISA with the test kits purchased from Beijing Jingmei Bioengineering Co., Ltd., determination was operated strictly according to the kit instructions. The two indexes were also determined in the healthy controls.