Analysis of mechanism of PM2.5 and house dust mite antigen Der p1 in attack stage of child asthma

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Introduction

The incidence rate of bronchial asthma in children is increasing year by year. The severe acute attack of this disease without prompt treatment may treat patients’ lives. Children with poorly controlled asthma may influence their normal growth and development, e.g. loss of job, school, limited activities and sports and decreased life quality. As immune system of children is imperfect, they are easily affected by various external stimuli, such as PM2.5 and house dust mite antigen Der p1 in the environment. Then, adverse reactions occur such as chronic airway inflammation and Th2 balance disorders, forming bronchial hyper-responsiveness and inducing lasting acute asthma or chronic asthma. Research of dissociated cell and animal models show that PM2.5, house dust mite antigen Der p1 and synergistic action of the two can induce and aggravate asthma, causing inflammation and immune disorders. This study analyzed the influence and mechanism of PM2.5 and house dust mite antigen Der p1 to asthma.

Patients and Methods

Patients

96 children with asthma attack treated in our hospital from January 2014 to January 2015 were included into the study continuously. The inclusion criteria were 1) age ≥5 years, ≤18 years; 2) First diagnosed as asthma, patients without medicine history of hormone and bronchodilators in their first treatment. 3) Good compliance, complete clinical data. The exclusion criteria was 1) Severe asthma breaks out continuously, combined with pneumonia, airway malformation,
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Methods

Setting Methods of the PM2.5 Group

The filter membrane seized the PM 2.5 particles of 1 cm×3 cm size, and immersed into deionized distilled water. After 3 times of 40 minutes’ ultrasonic vibration, particles were eluted. The volatile liquid was filtered through six layers of gauze, and filtrate was centrifuged at 12000 rpm for 30 min. The lower suspension was collected and freeze-dried. After resuspension with PBS, PM2.5 was cryopreserved at -18°C for 30 minutes and then thawed for use. The PM2.5 particles were blown and mixed into the test room using air blower. The PM2.5 concentration was set to twice higher than standard level by PM2.5 monitor (≤ the average value of PM2.5 of local air).

The mattress dust and house dust was collected by vacuum cleaner of filter unit, and it was filtered by 80 mesh to remove the large particles. The test room concentration was set of filling as 300 ng/mL. The synergistic group filled the room after a good mix of PM2.5 and house dust mite antigen, control group adjusted PM2.5 in test room to standard level by vacuum cleaner, and house dust mite antigen group set the room concentration lower than 150 ng/mL.

All cases were given with same treatments. The hormone and bronchodilator being atomized or inhaled by mouth, intravenous drip when necessary, aminophylline and oxygen inhalation, etc. The patients stayed in the test room for 7 days, and the treating effects were compared and analyzed.

Observation Indexes

The asthma control rate and the control time were compared. Also, the contents of serum IL-25, thymic stromal lymphopoietin (TSLP) and malondialdehyde were compared. Pulmonary function was measured using lung function detection instrument MS-IOS to detect the forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and peak expiratory flow rate (PEF) of the children. The asthma was controlled according to reference standards listed in asthma prevention guide. The asthma was asymptomatic at daytime or ≤2 times/week, patients’ activities were not limited, no symptom of oppressive wake after sleep, remission drug was not required or used ≤2 times/week and normal lung function without acute-outbreak. A 5 ml blood sample was obtained from peripheral vein and injected into anticoagulation tube. After centrifugation at 300 rpm for 10 min, the sample was concentrated and sent for inspection in time. ELISA method was used to detect the contents of serum IL-25, thymic stromal lymphopoietin (TSLP) and malondialdehyde. The inspection was operated in accordance with the instructions in kit offered by Nanjing Jiancheng Biotechnology Engineering Institute.

Statistical Analysis

SPSS 19.0 statistical software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis and data was expressed as mean ± standard deviation.
viation. The comparisons among groups adopted single factor ANOVA analysis followed by the Post Hoc test (LSD). The enumeration data were expressed by cases or percentage (%). The comparison among the groups was made by the \( \chi^2 \)-test. \( p < 0.05 \) was considered to be statistically significant.

**Results**

**Comparisons between the Asthma Control Rate and the Asthma Control Time**

The asthma control rate in the control group was significantly higher than that in the PM2.5 group and the house dust mite antigen group, and the synergistic group was the lowest. The control time of the synergistic group was the longest, followed by the PM2.5 group and the house dust mite antigen group, and the control group was the shortest and difference were statistically significant \((p<0.05)\) (Table I).

**Comparison of Pulmonary Function Indexes**

Comparison of FVC, FEV\(_1\), and PEF levels between the groups before intervention showed that the differences were not statistically significant \((p>0.5)\). After the intervention, the above indexes were all increased. And the levels of those indicators in control group were significantly higher than those of PM2.5 group and *Dermatophagoides pteronyssinus* group and those in the collaborative group were the lowest. The differences were statistically significant \((p<0.5)\). The differences in the PM2.5 group and *Dermatophagoides pteronyssinus* group were not statistically significant (Table II).

**Comparisons of the Contents of Serum IL-25, TSLP and Malondialdehyde**

The contents of serum IL-25, TSLP and malondialdehyde in the four groups before the treatment were compared, and the differences had no statistical significance \((p>0.5)\). The levels of serum IL-25, TSLP and malondialdehyde in the control group significantly lowered while the other three groups showed a significant higher figure, and differences were statistically significant \((p<0.5)\) (Table II).

**Discussion**

Recent research has suggested that asthma is airway inflammation whereas Th2 inflammation takes a dominant position caused by imbalanced Th1/Th2. TSLP plays an important role in this process.
role in the occurrence and development of asthma, and can be expressed by elevated Th2 cell, enabling the Th1/Th2 balance to tilt toward Th2. IL-25 and IL-33 are newly discovered Th2 cytokines, and they participate in Th2 type immune response through coordinate induction of secretion of Th2 cytokines IL-4, IL-13, etc.

PM2.5 are fine particles, accounting for 70% of respirable particles. In regions of severe air pollution, exposure of all kinds of harmful gas components and allergens are two factors that slowly induce and aggravate bronchial asthma. Owing to aerodynamic features of PM2.5, suspended PM2.5 bypasses airway and strands in the alveolar if inhaled, causing local inflammatory stimulus of bronchus lung tissue, oxidative stress injury, severe systemic inflammatory response and recent damage of the system such as cardiorespiratory system. By oxidative stress, harmful components such as PM2.5 particles, nitrogen oxides, polycyclic aromatic hydrocarbons, and heavy metals can increase reactive oxide species in airway microenvironment. By measuring the contents of cell culture supernatants and ROS biomarker-malondialdehyde, the severity of oxidative stress can be reflected, and then cellular components such as cell membrane and chromosome are damaged. The activation of regulatory pathway signals such as NF-κB stimulates the release and cell culture both confirmed that ROS quencher-Nac can clear oxygen radical and inhibit PM2.5 oxidative stress damage through increasing concentrations of reduced glutathione.

Der p1 can be excreted from the body through secretion, accounting for 15-20% of total protein in secretion. Concentration of house dust can be as high as 30 mg/g dust. Researches found that high levels of Der p1 can be detected in houses of patients allergic to house dust mite antigen, and Der p1 of ng level can be detected in bronchoalveolar lavage fluid of patients allergic to dust mites. The concentration of Der p1 in mucosa may reach mg level. The occurrence rate of house dust mites allergy is closely linked to concentration of Der p1 and individual IgE level. Researches have found that normal people only carried Der p1 IgG antibody of low concentration, while most adult patients with asthma who showed a positive skin reaction to house dust mite and more than 90% of patients allergic to dust mites carried Der p1 specificity IgE, IgA, and IgG antibody. As Der p1 is highly anaphylactogenic, it can cause allergic reaction of I type and induce asthma. Its protease plays an important role in inducing and maintaining allergic reaction. Der p1 can induce Th2 cellular response by antigen presenting cell; enzymatic activity of Der p1 can hydrolyze surface molecule with Fc receptor FceRII (CD23) and IL-2 receptor chain (CD25). The release and adhesion molecule expression of eosinophil granulocyte and inflammatory cytokines of bronchus epithelial cell can be increased. It inhibits the role of antitrypsin through cysteine proteinase activity and, thus, exacerbating airway tissue damage.

Conclusions

We showed that the asthma control rate in the control group was significantly higher than that in the PM2.5 group and the house dust mite antigen group. The synergistic group was significantly lowest, the control time in the synergistic group was the significantly shortest. The levels of serum IL-25, TSLP and malondialdehyde after treatment of the control group were significantly lower while the other three groups showed significant higher. In conclusion, PM2.5 and house dust mite antigen Der p1 can influence the treating effects of child asthma attack by inflammatory reaction and oxidative stress.

Conflict of interest

The authors declare no conflicts of interest.

References


