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Correlational study on atmospheric concentrations of fine particulate matter and children cough variant asthma

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Abstract. – OBJECTIVE: We explored the relationship between atmospheric concentrations of fine particulate matter and children cough variant asthma.

PATIENTS AND METHODS: 48 children all diagnosed with cough variant asthma were placed in the cough asthma group while 50 children suffering from typical asthma were place in typical asthma group. We also had 50 cases of chronic pneumonia (the pneumonia group) and 50 cases of healthy children (the control group). We calculated the average PM 2.5 and temperature values during spring, summer, autumn and winter and monitored serum lymphocyte ratio, $CD^{4+}/CD^{8+}T$, immunoglobulin IgE, ventilatory index and high-sensitivity C-reactive protein (hs-CRP) levels.

RESULTS: Our results showed that PM 2.5 values in spring and winter were remarkably higher compared to other seasons. Correlated analysis demonstrated that the onset of cough asthma group was happening in spring. The onset of typical asthma group happened mostly in winter, followed by spring. We established a positive correlation between the onset of asthma of cough asthma group and PM 2.5 value (r = 0.623, $p = 0.017$), and there was also a positive correlation between the onset of asthma of typical asthma group and PM 2.5 value (r = 0.714, $p = 0.015$). Our results showed that lymphocyte ratio and IgE level in the cough asthma group and the typical asthma group were significantly higher. $CD^{4+}/CD^{8+}T$ was significantly lower in the cough asthma group and the typical asthma group. The hs-CRP level in cough asthma, typical asthma and pneumonia groups were significantly higher than that of the control group. The FEV_1/predicted value, FEV_1/FVC and MMEF/predicted value in the cough asthma group and the typical asthma group were significantly lower than those in other groups, however when comparing between two groups respectively, the difference was not statistically significant.

CONCLUSIONS: Our findings showed that PM2.5 was related to the onset of children cough variant asthma. PM2.5 reduced immune regulation and ventilatory function.

Key Words:
PM2.5, Cough variant asthma, Immunization, Inflammation.

Introduction

With the World Environmental Conference of 2015 held in Paris, France, practical suggestions from both developed and developing countries were achieved. This included, among others, environmental pollution, energy shortages and global warming. Atmospheric particulate matter (PM), especially fine particles (PM2.5) are considered the main source of cardiovascular and respiratory system diseases[1]. This is due to their small diameter, their high absorption capacity for heavy metals, polycyclic aromatic hydrocarbons, methanol, SO_2, NO_2 and various pathogenic microorganisms, and their prolonged floating time[1]. Recently, asthma incidence is in a rising trend and experts are pointing their fingers toward the PM2.5 as the main suspect. Children with their incomplete respiratory system, big pulmonary ventilation volume per unit of time, weak immune regulating function and as individuals who are spending long hours outdoors are in the main victims of fine particles[2,3]. A limited number of studies on this subject is available and little is known about PM2.5 causing respiratory system

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disease[4]. Children cough variant asthma may be the omen of typical asthma[5], and we presumed that PM2.5 may cause cough asthma.

Patients and Methods

Patients

From October 2012 to October 2015 we selected 48 cases of children suffering from asthma and placed them in the cough asthma group. Consequently, we placed 50 cases of children with typical asthma in our typical asthma group. We also enrolled 50 children with chronic pneumonia (the pneumonia group) and 50 healthy children (the control group) at the same time. Inclusion criteria: (1) Age ≥ 5 years old and < 18; (2) In line with the definition of diagnosis of simple asthma[6] (the cough asthma group and the typical asthma); the pneumonia group was in line with the definition of diagnosis of simple chronic pneumonia[7]; (3) Effective medical treatment and controlled disease condition; (4) Complete clinical data. Exclusion criteria: (1) Concomitant diseases, such as tuberculosis, hereditary metabolic diseases, developmental abnormalities, untimely immunizations and autoimmune diseases; (2) Unfixed living; (3) Previous medication history, such as bronchodilators, and corticosteroids. The study was approved by our hospital Ethics Committee and obtained informed consents from guardians of children.

In the cough asthma group, there were 26 males and 22 females aging from 6 to 15 years (average = 10.3 ± 4.2 years). There were 27 males and 23 females in the typical asthma group, aging from 6.5 to 16.5 years (average = 12.4 ± 4.5 years). In our pneumonia, group we enrolled 26 males and 24 females aging from 6 to 16.5 years (average = 11.7 ± 4.3 years). We compared the gender and the age among groups, and the differences were not statistically significant ($p > 0.05$).

Detection Methods and Observation Index

All patients received standard medical treatment plans, such as inspection items, medication policy and follow-up requirements. According to the study, March, April and May were included in the spring; June, July, August were included in the summer; September, October and November were included in the autumn, and December, January and February were included in the winter. We obtained the average PM2.5 and temperature value in every quarter according to PM2.5 values and the average temperature value of daytime (6:00 to 18:00) and night (18:00 to 6:00 next day) by meteorological data of the day, excluding significant outliers. Two staffs finished the statistics. According to the disease history of children, two physicians jointly determined the seasons and time of onset of asthma and pneumonia.

Serum lymphocyte ratio, $CD^{4+}/CD^{8+}T$, immunoglobulin IgE, lung ventilation index (including the FEV_1/predicted value of enforced expiratory volume in one second, FEV_1/FVC, and MMEF/predicted value of maximum mid-expiratory flow rate) and high-sensitivity C-reactive protein (hs-CRP) levels were obtained. We collected 5 ml fasting peripheral venous blood, centrifuged it for 10 min at 2500 rps after keeping it in the refrigerator (4 C) for 2 h serum was transferred into sterile vials, and stored at -20°C. To obtain lymphocyte ratio we used conventional biochemical assays. For $CD^{4+}/CD^{8+}T$, IgE and hs-CRP we used double-antibody sandwich enzyme-linked immunosorbent assay (ELISA). Kits obtained from Beijing Hengda Parkson Biotechnology Co., Ltd., and operations were in strict accordance with the kit instructions.

For pulmonary function tests we used Gretel portable ventilation small spirometer manufactured by the Geratherm (Geschwenda, Germany). Children's noses were pinched so they respired through their mouths. We tightened mouth with no leak, cooperated with the password to complete the breath and breathing action. Children respired as much as possible, then with the greatest strength, breathed out with the fastest speed. It was completed by two professional inspectors while one person assessed, and analyzed the average value of two fully qualified results.

Statistical Analysis

We used SPSS 20.0 statistical software (SPSS Inc., Chicago, IL, USA) to record and analyze the data. After the normal inspection of quantitative data, we used mean±standard deviation to represent it. Comparisons between groups were performed using a single factor ANOVA analysis. For comparisons within the two groups, we employed LSD and Bonferroni tests. We used the number of cases or (%) to represent qualitative data, and comparisons between groups were done by χ^2 analysis. For correlation between the onset of asthma and season and time χ^2 analysis was used. $p < 0.05$ showed that the differences were statistically significant.

Table I. The comparison of PM2.5 and temperature of different seasons within three years.

	The first year			The second year			The third year		
	PM2.5 (μg/m³)	Temperature in day (°C)	Temperature in night	PM2.5	Temperature in day	Temperature in night	PM2.5	Temperature in day	Temperature in night
Spring	82.6 ± 23.5	12.6 ± 3.8	6.6 ± 2.5	83.6 ± 24.4	12.4 ± 3.6	6.3 ± 2.3	85.5 ± 23.3	12.2 ± 3.4	6.2 ± 2.4
Summer	43.9 ± 25.8	23.3 ± 5.9	10.6 ± 3.3	44.7 ± 26.6	24.7 ± 6.2	10.4 ± 3.2	45.2 ± 24.9	24.5 ± 6.3	10.2 ± 2.7
Autumn	45.6 ± 23.7	13.3 ± 4.2	7.2 ± 2.6	46.9 ± 22.5	14.5 ± 4.3	7.3 ± 2.8	46.6 ± 23.4	14.2 ± 4.1	7.5 ± 2.3
Winter	125.6 ± 36.7	4.7 ± 1.5	-3.6 ± 2.4	132.7 ± 39.4	4.6 ± 1.3	-3.4 ± 2.2	135.5 ± 34.2	4.7 ± 1.2	-3.6 ± 2.3

Results

Correlation Between the Onset of Asthma and Season, Time

PM2.5 concentrations during spring and winter seasons were significantly higher than that of summer and autumn, and the difference was statistically significant ($p<0.05$). Day and night time temperature during summer was the highest while we had the lowest day and night time temperature in winter. The difference between spring and autumn was not significant. Comparing PM2.5 and temperature during three years revealed no statistically significant differences ($p > 0.05$), suggesting a relatively stable external environment (Table I). In the cough asthma group, the onset of 20 cases happened during spring; 25 cases happened in winter and 3 cases happened in other seasons. The onset of 11 cases happened in spring daytime and 9 cases in spring nighttime. In 12 cases the onset happened during winter daytime and 13 cases at nighttime. In the typical asthma group, the onset of 12 cases happened in spring and 36 cases happened in winter while 2 cases happened in other seasons. In the typical asthma group, the onset of 6 cases happened in spring daytime while 6 cases happened at nighttime. The onset of 19 cases happened in winter daytime and 17 cases at night. Related analyses demonstrated that when the onset of cough asthma group happened in spring and winter, the difference was not statistically significant ($\chi^2 = 1.046$, $p = 0.306$); it had nothing to do with time ($\chi^2 = 0.218$, $p = 0.641$). The onset of the typical asthma group happened mostly during winter, followed by spring and the difference was statistically significant ($\chi^2 = 23.077$, $p < 0.001$) while it had no link with time ($\chi^2 = 0.028$, $p = 0.868$). There was a positive correlation between the onset of asthma in the cough asthma group and PM2.5 value ($r = 0.623$, $p = 0.017$); the same was true between the onset of asthma of typical asthma group and PM2.5 value ($r = 0.714$, $p = 0.015$).

The Comparisons of Serum Lymphocyte Ratio, $CD^{4+}/CD^{8+}T$, IgE and hs-CRP

Lymphocyte ratio and IgE level in the cough asthma group and the typical asthma group were significantly higher than those of other groups. $CD^{4+}/CD^{8+}T$ was significantly lower than that of other groups and the difference was statistically significant ($p < 0.05$). When we compared the cough asthma group and the typical asthma group, the difference was not statistically significant ($p > 0.05$). The hs-CRP level in the cough asthma group, the typical asthma group and the pneumonia group were significantly higher than that of the control group ($p < 0.05$). When compared within two groups the difference was not statistically significant ($p > 0.05$) (Table II).

Table II. The comparisons of serum lymphocyte ratio, $CD^{4+}/CD^{8+}T$, IgE and hs-CRP.

Group	Lymphocyte ratio (%)	$CD^{4+}/CD^{8+}T$	IgE (ng/ml)	hs-CRP (mg/L)
Cough asthma group	45.6 ± 4.9	1.5 ± 0.4	75.5 ± 16.7	8.4 ± 2.6
Typical asthma group	48.7 ± 4.3	1.3 ± 0.6	86.9 ± 14.7	12.3 ± 3.7
Pneumonia group	22.5 ± 3.6	1.9 ± 0.7	52.4 ± 13.2	10.7 ± 3.5
Control group	28.6 ± 3.7	2.2 ± 0.5	56.8 ± 14.6	3.5 ± 1.2
F	5.927	6.102	5.768	4.825
p	0.026	0.024	0.029	0.037

The Comparisons of Lung Ventilation Index

The FEV_1/predicted value, FEV_1/FVC and MMEF/predicted values in the cough asthma group and the typical asthma group were significantly lower than those of other groups ($p < 0.05$), but when comparing within the two groups respectively, the difference was not statistically significant ($p > 0.05$) (Table III).

Discussion

The ingredients of PM2.5 are very complicated, with differences in various areas. The key ingredient is black carbon aerosols, which plays an important role in various chemicals and photochemical reactions in the atmosphere, heterogeneous reaction as well as the conversion processes of gas and particle[8]. It makes important contributions to local and global climatic effects of aerosols[8]. Black carbon aerosols can aggravate oxidation of lung tissue and increase inflammatory injury. It also raised the level of eosinophils, specific IgE and IgG antibody expression and triggers asthma. By using carbon black particles to transfect RAW264.7 cells, Robert[9] reported that PM2.5 triggered the release of large quantities of inflammatory cell mediators such as IL-6 and TNF-α. However, the simple carbon could not create the same response. This finding suggested that contaminants adsorbed on PM2.5 are the main source of the problem. Although PM2.5 particles are very small, they have relatively large surface and are present in large quantities in the air. They have slow sedimentation rate and long propagation distance. Chemicals and microorganisms can be absorbed on the surface of PM2.5 and become allergens and trigger asthma and play an important role in the development process of asthma as well. Prior studies[10] showed that β-glucan and lipopolysaccharide absorbed on PM2.5 could promote effectively the gene expression in murine macrophage Toll-like receptor 2 and NLRP3 inflammation complex so as to release IL-1β and worsen inflammatory reaction.

Gary et al[11] established regression model through the relationship between PM2.5 and emergency rate of children with asthma in Seattle, Washington area and pointed out the concentration of PM2.5 increased every 11 μg/m^3, the OR value of the emergency rate of children with asthma was 1.15 (95% CI: 1.08 to 1.23). Lee et al[12] studied the hospitalization rate of children with asthma under 18 in Hong Kong, China. They found that after adjusting SO_2, O_3 and NO_3, PM2.5 was closely related to the admission rate of asthma, when the height of PM2.5 was 20.6 μg/m^3, the admission rate increased by 3.24% (95% CI: 0.93 to 5.60). Compositions of PM2.5 invade respiratory tract, a large number of particles enter into the lung and block partial tissues, which leads to the decrease of ventilation function of partial bronchus and weakened gas exchange function of bronchiole and alveolus. Particles adhering harmful gases also can stimulate and corrode alveolar wall and damage and reconstruct structures of lung tissues. Clinical symptoms include unsmooth breathing, chest oppression, dry cough, dry pharynx and throat itching. Long-term inhalation may cause rhinitis, pharyngolaryngitis and bronchitis. It may also cause acute asthma attacks, chronic bronchitis and other chronic diseases. The nosogenesis of chronic airway inflammation of asthma is relatively complex and may be related to anaphylaxis and abnormal autoimmunity regulation. The early symptom of children cough variant asthma is mainly coughing, which can be simply confused with bronchitis and can be a misdiagnosis. When miss diagnosis happens the treatment cannot be carried out and diseases cannot be cured in a timely manner, and it develops to typical asthma[13].

Not all experts are convinced that a link exists between PM2.5 and typical asthma[14]. There are few researches on whether children cough variant

Table III. The comparison of ventilation index.

Group	FEV_1/predicted value	FEV_1/FVC	MMEF/predicted value
Cough asthma group	88.7 ± 13.5	80.2 ± 7.8	78.6 ± 15.4
Typical asthma group	85.4 ± 14.6	76.3 ± 7.6	72.5 ± 16.3
Pneumonia group	92.3 ± 12.3	92.4 ± 9.2	86.9 ± 18.7
Control group	94.6 ± 13.7	95.3 ± 9.4	93.4 ± 15.5
F	5.624	5.758	5.329
p	0.037	0.035	0.041

asthma is related to PM2.5. Our work showed that the onset seasons of a cough variant asthma and typical asthma were different; the onset seasons could be spring and winter, and it had nothing to do with time. In China, pollens during the spring, suspended particle and smog in winter are the main causes of cough variant asthma. Both cough variant asthma and typical asthma are positively correlated with PM2.5 level. Changes in immunology and lung functions remained same, suggesting that physiopathologic mechanisms of cough variant asthma and typical asthma might be the same. This study set up the pneumonia group and the healthy control group at the same time and found that serum lymphocyte ratio, $CD^{4+}/CD^{8+}T$, IgE, pulmonary ventilation index and hs-CRP had significant differences. This suggested that cough variant asthma was different from biological changes of pneumonia and could be used as a differential point.

Conclusions

PM2.5 was related to the onset of children variant asthma, it could decrease immunoregulation and ventilation function, and it might be consistent with changes of typical asthma. We must pay attention that the protection of environment and prevention of cough variant asthma in the early stage have very important clinical and social significance.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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