Childhood Onset Adult Asthma: A Comparison of Asthma Development with Exposure to High and Reduced Levels of Air Pollution

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ABSTRACT
Background: In the 1960s when air pollution levels were high in Kanagawa prefecture as same as in other Japanese metropolises, the prevalence of asthma increased distinctly. Air pollution has been reduced rapidly from the 1970s, but asthma morbidity has not decreased and therefore air pollution has not been considered as an essential factor in asthma development. However, air pollution may be considered as a risk factor for infantile asthma. To clarify the influence of air pollution on infantile asthma development, we compared the background of adult asthmatics who were born in 1960s and in 1970s.

Methods: We studied 10,823 adult asthma patients who underwent examination at Sagamihara hospital from 1972 to 1995. We investigated the ratio of young onset (equal to or less than 19 years old, 3264 cases) asthma in adult asthma year by year. In order to ascertain the influence of air pollution on airway hypersensitivity, we compared the asthmatics born in 1960s (born in 1963~1970) when air pollution was severe with those born in 1970s (born in 1971~1978) when air pollution levels were reduced.

Results: Childhood onset (less than 15 years old) asthma held a constant ratio in adult asthma from 1972 to 1980. However, infancy onset (0~4 years old) asthma increased in 1980, peaked in 1988, and then decreased. From a viewpoint of the birth year, young onset asthma has increased since 1945. In particular, the ratio of infancy onset (0~4) asthma had become distinctly higher than the other onset groups since 1960, peaking in 1970 and then decreasing. The fluctuation of infancy onset asthma coincided with the indices of air pollution in Japan.

Lung function tests in the three groups (group I ; born in 1955~62, group II ; born in 1963~70, group III ; born in 1971~78) did not have a difference among each other. However, we were able to find a difference in threshold of non-specific airway hypersensitivity. The airway hypersensitivity of the infancy onset asthmatics born in 1960s was much more enhanced than that of the asthmatics born in 1970s.

Conclusions: The dramatic increase of infancy onset asthmatic born after 1960 coincided with the increases in levels of air pollution. The infancy onset adult asthmatics born in 1960s were more hypersensitive to non-specific bronchial stimuli than those born in 1970s. This strongly suggested that the air pollution of 1960s might have accelerated the development of infancy onset asthma and aggravated non-specific bronchial hyperreactivity.

KEY WORDS
adult asthma, ambient air pollution, infancy onset asthma, lung function tests, non-specific bronchial hyperreactivity
INTRODUCTION

The economy grew rapidly in Japan from 1955. In Kanagawa and a neighboring metropolis, Tokyo, the SO2 concentration in ambient air increased since 1962 and fell in 1970 (Fig. 1). The improvement of air pollution of 1970s was nationwide (Fig. 2). Increases in prevalence of asthma and other respiratory tract diseases coincided with the intensification of air pollution of the 1960s. These serial facts suggest that air pollution was a cause of asthma. However in many other countries, air pollution has improved despite continuing decreases in asthma morbidity. Therefore the ambient air pollution has not been regarded as an essential factor in asthma development.

Air pollution increases asthma symptoms and potentiate airway hypersensitivity, but does not directly cause asthma in itself. Air pollutants potentiate an allergen specific hypersensitivity so that asthma development is much more prominent in childhood-onset asthma than in adult-onset asthma. In order to ascertain the influence by air pollution on asthma development, we compared asthmatics that were born in 1960s, a period of severe air pollution and in 1970s, a period of reduced air pollution.

We investigated the following points in young (equal to or less than 19 years old) onset asthma.

1) According to the consultation age, is there annual fluctuation in the ratio of childhood onset asthma compared to adult asthma?

2) According to the birth year, does the fluctuation of the infancy onset asthma ratio coincide with the air pollution level?

3) Are there any differences in the following two points among the aforementioned groups of asthmatics?

i) Lung function tests (FEV1.0%, %VC), ii) Acetylcholine inhalation test (non-specific bronchial hyperreactivity, BHR)

METHODS

SUBJECTS

We examined 10,823 adult asthma patients who visited Sagamihara hospital from 1972 to 1995. We investigated the ratio of young onset asthma (3264 patients, and 30.2%) in all adult asthma patients each consultation year and from the viewpoint of the corresponding birth year.

In order to ascertain the influence of air pollution on lung function tests, we classified the 0–19 years-old onset asthmatics who underwent both BHR and spirometry into three groups by their birth year, group I (born in 1955–62, 20 cases), group II (born in 1963–70, 244 cases) and group III (born in 1971–78, 214 cases). In order to ascertain the influence of asthma onset age on BHR, we compared the BHR threshold of groups II and III. Because there were few patients in group I, we excluded them from this examination.

ACETYLCHELONE INHALATION TEST

The patients underwent the BHR test in stable condition within at most one month after from their first visit. Any asthma treatment was asked to be stopped at least twelve hours before the bronchoprovocation test. Baseline FEV1.0 was recorded and then sterile diluents (phosphate-buffered saline solution) followed by increasing concentrations of acetylcholine (0.78, 0.156, 0.313, 0.625, 1.25, 2.5, 5, 10 and 20 mg/mL) were administered for 2 minutes with nebulizer.
Fig. 2 Fluctuation of air pollution indices at all the measurement stations in Japan since 1970. Levels of air pollutants (NO₂, SO₂ and Suspended particulate Matter, SPM) from 1970 to 2002 have been improved since 1970 nationwide. Both data of motor exhaust and general environmental ambient air measurement reflects an average value of all the measurement stations in Japan.

at an air flow rate of 5 L/min. The acetylcholine inhalation was stopped when over a 20% decrease in FEV₁ from the baseline value was obtained. The provocative concentration of acetylcholine causing over 20% fall in FEV₁ was defined as the threshold value.

**LUNG FUNCTION TESTS**
Spirometry was performed in a stable condition with-
Fig. 3  Ratio of subjects who developed asthma before 19 years old (young onset asthma) in the total adult asthma population. According to the initial consultation age, ratio of young onset asthma in the total adult asthma was unchanged from 1970 to 1980. The ratio of each onset age group (0–4, 5–9, 10–14, 15–19 years old) was approximately 6%. However, the infancy onset (0–4 years old) asthma group increased remarkably from 1980 to 1990. On the other hand, during this period the ratio of the 10–19 years old onset asthma group did not increase.

Fig. 4  Ratio of young onset asthma in the total adult asthma in birth year. All young onset asthma increased since 1950. The ratio of infancy onset (0–4 years old) asthma had increased more remarkably than the other young onset groups. The infancy onset asthma peaked at 1970 and then decreased. Patients who were born before 1909 and after 1976 were few, less than 40 cases, consequently we did not include them in this figure.

out the presence of an asthma attack. FEV1% was defined as FEV1.0/FVC.

STATISTICS
All statistics were calculated using a Statmate II program (Nanzando Co. Ltd.). T-test (lung function
Mean FEV1.0% was 76.1% in group I (born in 1955–62), 68.9% in group II (born in 1963–70) and 73.1% in group III (born in 1971–78). There were no significant differences in lung function parameters between any two groups.

Table 1 Case number of infancy and older onset asthma according to their birth year

<table>
<thead>
<tr>
<th>Group</th>
<th>Birth year</th>
<th>Onset age</th>
<th>Total case</th>
<th>BHR case+</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>1963–70</td>
<td>0–4 y.o.</td>
<td>412</td>
<td>100</td>
</tr>
<tr>
<td>II</td>
<td>1963–70</td>
<td>10–19 y.o.</td>
<td>333</td>
<td>88</td>
</tr>
<tr>
<td>III</td>
<td>1971–78</td>
<td>0–4 y.o.</td>
<td>159</td>
<td>87</td>
</tr>
<tr>
<td>III</td>
<td>1971–78</td>
<td>10–19 y.o.</td>
<td>161</td>
<td>77</td>
</tr>
</tbody>
</table>

+ number of patients who underwent non-specific BHR (acetylcholine). Total number of Group I were few, so that not showed in this table.

tests) and chi square test (AHR) between the two groups and $p < 0.05$ was judged to be significant.

RESULTS

The ratio of young onset asthma for the adult asthma did not change from 1970 to 1980 (Fig. 3). The ratio of each onset age group (0–4, 5–9, 10–14, 15–19 years old) was approximately 6%. However, the infancy onset (0–4 years old) asthma group increased remarkably from 1980 to 1990. The 5–9 years old onset group increased slightly. The ratio of the 10–19 years old onset asthma group did not increase at all. According to the birth year, the young onset asthma increased since after 1950 (Fig. 4). In particular, the ratio of infancy onset asthma became distinctly higher than the other onset groups since 1960, peaked at 1970 and then decreased (Fig. 4). Because the patients who were born before 1909 or after 1976 were few (less than 40 patients), we did not show them in this figure.

This fluctuation coincided with the pollution levels of ambient air. The air pollution investigation began in 1970 nationwide, therefore available data in 1960s were limited. The SO2 concentration of the ambient air of the Kanagawa agency (Sagamihara city locates in the prefecture) and neighboring area worsened in the 1960s and improved rapidly in 1970. All indices of air pollution decreased since 1970. The fluctuation in infancy onset asthma seemed to coincide with the air pollution levels.

Mean FEV1.0% was 76.1% in group I, 68.9% in group II and 73.1% in group III. Mean %VC was 96.9% in group I, 94.2 in group II and 102.4% in group III (Fig. 5). There were no significant differences in the parameters of lung function between any two groups. However, the acetylcholine threshold was different between group II and III. The acetylcholine threshold value of group III was higher than that of group I (not showed, because there were few cases) and II.

Because of no increase in older (10–19 years old) onset asthma was found in the 1980s, we thought that the subjects developing asthma younger than 4 years old had a diathesis influenced by air pollution and were different from the older onset asthma. In order to study the influence of air pollution on non-specific BHR, we compared BHR thresholds among these groups. Table 1 shows the number of total cases and the number of cases taking BHR test in group II and III. In group III, the BHR threshold of the old onset asthma group was higher than that of the infancy onset asthma group (Fig. 6). However, in group II, subjects born in 1960s, the older onset asthmatics had the same BHR as the infancy onset asthmatics. This suggested that the air pollution might enhance the airway hypersensitivity not only in the infancy onset asthma but also in older onset asthma as well.

DISCUSSION

Because many epidemiological studies have shown that asthma increases in countries which become industrialized and developed, it is suggested that the degree of air pollution and asthmatic crisis are related. However in developed countries, the air pollu-
tion has been decreasing but the asthma prevalence continues to increase.\(^1\) This shows that in addition to air pollution, there might be the other causes of asthma development.\(^2\) Parental smoking,\(^3\) the increase of allergen exposure\(^7\) and the decrease of bacterial and tuberculosis infection in infancy\(^8\)\(^-\)\(^10\) are thought to be the causes for asthma increase. Air pollution has not been considered to be an essential risk factor for asthma development.

However, in most industrialized countries, it is a fact that asthmatic crisis increases as air pollution is aggravated. Our data showed that the infancy onset asthma increased remarkably from 1980, peaked at 1990 then decreased. This decrease indicates that the factor which causes asthma was transient and attenuated after 1990.

The economy has grown rapidly in Japan since 1955. Asthma and other respiratory tract diseases have increased resulting in the establishment of a law for air pollution prevention. Air pollution in all metropolitan areas has been decreasing rapidly since 1970. According to the birth year, an increase in the ratio of infancy onset asthma had been more prominent than the other young onset asthma since 1960, peaking in 1970 and then decreasing. These changes in the infancy onset asthma prevalence coincided well with the change of the air pollution level. This suggests that air pollution may be an important factor in asthma development in infancy.

Numerous epidemiological surveys and animal experiments on the influence of air pollution have been done. However we have not been able to identify specific air pollution material which conclusively contributes to asthma development. SO2, NO2 themselves enhance BHR to an inhaled mite allergen\(^11\)\(^,\)\(^12\) but never result in the development of asthma. A similar phenomenon occurs with ozone exposure.\(^13\)\(^,\)\(^14\) Air pollutants cannot cause asthma development by themselves, but may cause asthma when they act in synergy with allergens. Because most of the infancy onset asthma is atopic, the air pollution might influence a child with atopic diathesis and explain the infancy onset asthma increase in the 1960s.

In this study, we were not able to identify a specific cause but showed that air pollution is definitely important in developing asthma in infancy. Polluted ambient air does not directly develop asthma in itself but enhances BHR.\(^2\)\(^,\)\(^15\) Our results showed that the bronchial reactivates of both infancy onset and older onset asthmatics born during the period of the high levels of air pollution were highly sensitive to non-specific stimuli. However, in the subjects who were born during the period of reduced levels of air pollution, the older onset asthmatics had a higher threshold value in BHR than the infancy onset asthmatics. This suggests that if the degree of air pollution becomes severe, it worsens non-specific BHR not only in the infancy onset but also the older onset asthmatics without atopic diathesis.

Inhaled corticosteroid (ICS) improves BHR. How-
ever, the ICS had not been used by practitioners widely before 1990 in Japan. If the BHR improvement of group III had been caused by the use of ICS, the improvement should be found in not only the older onset asthmatic but also in the infancy onset asthmatics as well.

Even if air pollution is improved, the prevalence of asthma does not decrease. Therefore, besides air pollution, there must be many factors which cause of asthma increase. However, we think that the coincidence of the decrease of infancy onset asthma and the decrease in air pollution levels in the 1970s strongly suggests that air pollution in Sagamihara and neighboring areas hastened asthma development in infants and was one of the potent factors which contribute to BHR.

REFERENCES