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Original Article

The effect of short-term particular matter$_{2.5}$ exposure on asthma attacks in asthma children in Fukuoka, Japan

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Objectives: We investigated whether asthma attacks in asthmatic children were caused by short-term exposure to particulate matter(PM)$_{2.5}$.
Methods: Subjects were 411 patients who received inhalation therapy in National Fukuoka Hospital, from March to May 2013. All subjects were outpatients. We surveyed the air quality measurement results in the stations closest to the address of the patients. Data were used from the City of Fukuoka website data on air pollution. We carried out a case-crossover study and compared $PM_{2.5}$ concentration between 7 days after asthma attack occurred and the day asthma attack occurred and 1, 2 and 3 days before asthma attack occurred.
Results: Highest hourly concentration of the day (OR 1.013, 95%CI 1.000-1.025) showed a significant association with 1 day before $PM_{2.5}$ concentration statistically. And 0-1 year-old infants were more vulnerable to the highest concentration of 1 day before $PM_{2.5}$ concentration($P < 0.05$). Average concentration of NO_2 and O_3 and asthma attack also showed a significant association.
Conclusions: Maximal daily $PM_{2.5}$ concentrations within 24 hours prior to the attack affect asthma exacerbation. 0-1 year-old infants are particularly vulnerable to $PM_{2.5}$ concentration. Asthma exacerbation is aggravated by NO_2 and O_3 concentration on the day of the asthma attack.

Key Words: Air pollution, Asthma, Asthma attack, Japan

$PM_{2.5}$ (ultrafine dust) refers to dust having particles smaller than 2.5 ㎛ in diameter. It can be directly released into the atmosphere or produced through secondary changes. As human nasal hair or cilia are unable to filter $PM_{2.5}$, it can cause various respiratory diseases.[1]

In particular, children are relatively vulnerable to $PM_{2.5}$, as they have immature lungs and a less developed immune system than adults. In addition, their respiration rate is high relative to their weight, which means they contact a greater amount of air. Their activity level is higher and they have a relatively narrower airway. For these reasons, they can be more easily exposed to lung damage.[2]

The effects of $PM_{2.5}$ on children with asthma are widely known, and it increases emergency department (ED) visit and hospitalization rates due to

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asthma attacks.[3] It is also known that a rise in $PM_{2.5}$ concentration decreases peak expiratory flow in asthma patients.[4]

This study investigated the question of whether exposure to $PM_{2.5}$ caused asthma attacks in infants and children aged 0-18 years old in Fukuoka, Japan, and then divided the children studies into age groups for an analysis. It also looked into the effects of SPM (suspended particulate matter), NO_2, O_3, temperature and humidity, which are known as risk factors for asthma attacks.[5]

METRIALS AND METHODS

Selection Criteria

The subjects were selected from infants and children aged 0 to 18 years diagnosed with asthma who had come to the outpatient clinic of the Department of Pediatrics of the Fukuoka National Hospital due to asthma attacks from March 1 to May 31, 2013. The diagnoses of asthma attacks were based on the Japanese Allergy Guideline 2011 (JAGL 2011) and were made by pediatricians through physical examinations and based on symptoms such as dyspnea, stridor, decrease in respiratory sounds, chest retraction, orthopnea, cyanosis, rapid respiration and so on.[6] To investigate the effects of age, the subjects were divided into five groups according to their age.

Data on air pollution

During the survey period, data on $PM_{2.5}$, SPM, NO_2 and O_3 in Fukuoka were collected from the city's official webpage for air pollution monitoring (http://www.fihes.pref.fukuoka.jp/taiki-new/Nipo/OyWbNpKm0151.htm).[1] The concentrations of all substances other than O_3 were measured at all monitoring stations by time and the concentration of ozone was measured at several monitoring stations. Data from the measuring stations closest to the patients' addresses were used as the base data; when these were incomplete, the data from other nearest stations in the surrounding areas were used. The concentration of $PM_{2.5}$ was measured from March to May, 2013 and measurement of SPM, NO_2 and O_3 concentrations was conducted from March to April, 2013. 24-hour average concentrations were calculated based on the values obtained from 0:00 am on the day of measurement to 0:00 am on the following day. The temperature and relative humidity were taken from the data of the Japan Meteorological Agency. There were ten monitoring stations located in the areas where more than two patients were reported to have had asthma attacks.

Analysis method

This research was designed as a case-crossover study. A logistic regression analysis was carried out with ED or outpatient clinic visits due to asthma attacks as a dependent variable, and the hourly maximal concentrations of air pollutants ($PM_{2.5}$, SPM, NO_2 and O_3), daily average concentrations, temperatures and relative humidity as independent variables. Each air pollutant was ana-

lyzed to identify odds ratios, 95% confidence intervals and statistical significance. The exposure concentrations of pollutants were investigated for asthma attack days, one day, two days and three days prior to the asthma attack days. The days after seven days of the asthma attacks were set as control days with no influence of air pollutants. The data were analyzed using SPSS version 21.0 (IBM Co. Statistics, USA).

Purpose

The purpose of this study was to identify the effects of short-term exposure to $PM_{2.5}$, and other air pollutants on asthma attacks among infants and children with asthma.

RESULTS

Over the 3-month survey period, 411 children came to the ED or the outpatient clinic of the Fukuoka National Hospital due to asthma attacks, and these children were the subjects of this research. The sex ratio was 1.45 and the age range was from 0 to 18, with 5.58 as mean age (Table 1). The subjects were divided into five groups according to their age and classified into elementary schooler group (6-12 years old), middle schooler group (13-15 years old) and high schooler group (16-18 years old).

In the 28 monitoring stations over the city of Fukuoka, the levels of $PM_{2.5}$, SPM and NO_2 were measured on a daily basis. Of these stations, ten were located in areas where more than two patients with asthma attacks had been reported (Fig. 1). Of the ten areas, Oohasi, which is the area nearest to the hospital, had the most asthma attacks, at 161 (39.2%) patients (Fig. 1).

The maximal concentrations and average concentrations of air pollutants were measured for 24 hours on asthma attack days, one day, two days, and three days prior to the attack days. The results were compared with the concentrations of the days after seven days of asthma attacks, which were set as control group (Table 2). The maximal concentration of $PM_{2.5}$ measured a day prior to

Table 1. Characteristics of the study groups.

	Number	Percent
Total	411	
Sex ratio (M:F)	1.45	
Mean age(± SD)	5.58 ± 4.41	
Age		
0-1	97	23.6
2-5	142	34.5
6-12	136	33.1
13-15	30	7.3
Over 16	6	1.5

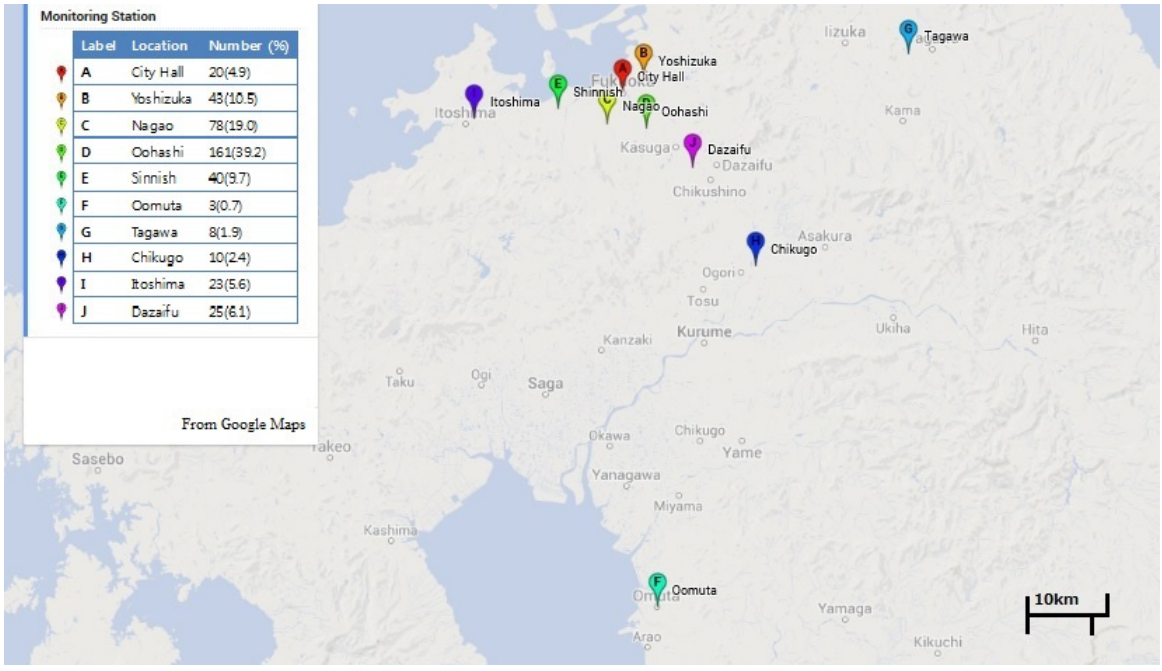

Fig. 1. Map of monitoring stations in Fukuoka. The table on the left shows the names of monitoring stations, the number of asthma patients, and percentage.

asthma attack days (35.44 ± 18.22 $\mu g/m^3$) was higher than the maximal concentration of the control group (32.84 ± 15.63 $\mu g/m^3$), and the difference was statistically significant (P = 0.029). The other days did not show statistically significant differences between the average concentration of $PM_{2.5}$ and that of the control group.

A logistic regression analysis was carried out on the results of the case-crossover study (Table 3, 4). This revealed that SPM is not related to asthma attacks. When one air pollutant was considered as a single variable, it was found that there was a significant correlation between the maximal concentration of $PM_{2.5}$ on a day prior to asthma attacks (odds ratio 1.009, 95% interval 1.001-1.017) and asthma attacks (Table 3). It also was found that there was a correlation between asthma attacks and the daily average concentrations of NO_2 (odds ratio 1.034, 95% confidence interval 1.002-1.068) and O_3, (odds ratio 1.031, 95% confidence interval 1.012-1.050) on asthma attack days (Table 4).

When $PM_{2.5}$, SPM, NO_2, O_3, temperature and humidity were considered as multi-variables, the following correlations between air pollutants and asthma attacks were found. The maximal concentration of SPM three days prior to asthma attack days (odds ratio 1.160, 95% confidence interval 1.037-1.297) and that of NO_2 two days prior to asthma attack days (odds ratio 1.101, 95% confidence interval 1.012-1.197) were statistically significant (Table 3). Also, the average concentration of NO_2 two days prior to asthma attack days (odds ratio 1.271, 95% confidence interval 1.027-1.572), that of O_3 three days prior to asthma attack days (odds ratio 1.475, 95% confidence interval 1.179-1.846) and that of O_3 two days prior to asth-

Table 2. Comparison of maximal, average concentration of $PM_{2.5}$ ($\mu g/m^3$).

	D-3†	Control day		D-2§	Control day	
Average(maximal)	35.65	36.50		35.52	33.91	
Standard deviation	18.53	19.34		18.73	16.81	
P			0.522			0.196
	D-1‖	Control day		D0¶	Control day	
Average(maximal)	35.44	32.84		35.71	34.53	
Standard deviation	18.22	15.63		18.19	18.23	
P			0.029			0.352
	D-3†	Control day		D-2§	Control day	
Average(average)	22.21	22.92		21.81	21.47	
Standard deviation	12.33	13.98		11.54	12.64	
P			0.439			0.684
	D-1‖	Control day		D0¶	Control day	
Average(average)	21.34	19.81		21.95	21.17	
Standard deviation	11.89	11.00		13.06	12.43	
P			0.057			0.382

* $P < 0.01$, † $P < 0.05$ by t-test
†D-3 : 3 days prior to day of attack
§D-2 : 2 days prior to day of attack
‖D-1 : 1 day prior to day of attack
¶D0 : day of asthma attack

ma attack days (odds ratio 1.128, 95% confidence interval 1.031-1.234) were found to be statistically significant as well (Table 4).

The maximal concentration of $PM_{2.5}$ one day prior to asthma attack days was positively correlated with asthma attacks (odds ratio 1.009, 95% confidence interval 1.001-1.017) (Table 3). This tendency was more pronounced in infants aged 0 to 1 year old, and the risk was higher (odds ratio 1.018, 95% confidence interval 1.001-1.035) (Table 5).

DISCUSSION

The correlation between air pollution and asthma attacks has been widely reported. However, it is difficult to assess the exact levels of exposure to pollutants among individuals, and inconsistent results have been produced due to reasons such as differences in genetic susceptibility.

This study showed that cases of asthma attacks increased among infants aged 0 to 1 year old when the maximal concentration of $PM_{2.5}$ was high one day prior to the asthma attack day (Table 1). The average concentrations of NO_2 and O_3 on the days of asthma attacks were also associated with asthma attacks (Table 4). It was confirmed that the risk of asthma attacks increased by 9% when the concentration of $PM_{2.5}$ on a day prior to asthma attack days rose by 10 $\mu g/m^3$ (Table 3). Particularly, when the concentration of $PM_{2.5}$ increased by 10

Table 3. Odds ratios and 95% confidence intervals of asthma attack by maximal 1-hour concentration of each air pollutant.

		D-3†			D-2§		
		OR*	95%CI†	*P*	OR*	95%CI†	*P*
$PM_{2.5}$	Single-variant	0.998	0.990-1.005	0.522	1.005	0.997-1.013	0.196
	Multi-variant	0.841	0.719-0.983	0.030	0.932	0.844-1.029	0.165
SPM	Single-variant	0.993	0.986-1.000	0.067	0.998	0.990-1.006	0.579
	Multi-variant	1.160	1.037-1.297	0.009	1.060	0.981-1.146	0.142
NO_2	Single-variant	1.004	0.988-1.021	0.615	1.013	0.997-1.029	0.105
	Multi-variant	0.973	0.885-1.069	0.564	1.101	1.012-1.197	0.026
O_3	Single-variant	0.984	0.971-0.997	0.197	0.986	0.972-0.999	0.042
	Multi-variant	1.174	1.089-1.264	0.000	1.043	0.995-1.094	0.081
		D-1‖			D0¶		
		OR*	95%CI†	*P*	OR*	95%CI†	*P*
$PM_{2.5}$	Single-variant	1.009	1.001-1.017	0.030	1.004	0.996-1.011	0.352
	Multi-variant	1.063	0.944-1.195	0.313	0.954	0.874-1.040	0.286
SPM	Single-variant	1.004	0.996-1.012	0.318	1.002	0.995-1.009	0.598
	Multi-variant	0.992	0.903-1.090	0.874	1.027	0.968-1.090	0.380
NO_2	Single-variant	1.016	1.000-1.033	0.052	1.010	0.995-1.026	0.197
	Multi-variant	1.001	0.922-1.086	0.984	1.111	0.944-1.308	0.207
O_3	Single-variant	1.003	0.988-1.019	0.661	1.015	0.999-1.030	0.065
	Multi-variant	0.920	0.860-0.985	0.016	1.011	0.965-1.056	0.646

*OR : odds ratio
†CI : confidence interval
‡D-3 : 3 days prior to day of attack
§D-2 : 2 days prior to day of attack
‖D-1 : 1 day prior to day of attack
¶D0 : day of asthma attack

Multi-variant variables contains $PM_{2.5}$, SPM, NO_2, O_3,

$\mu g/m^3$, the risk of asthma attacks grew by 18% among infants aged 0 to 1 year old, which shows a higher susceptibility in infants.

Previous studies by Odajima et al. reported that the fluidity of temperature, SPM and the concentration of NO_2 increase the hospitalization rate due to asthma attacks. The rises in SPM and NO_2 were related to the rate of hospitalization due to asthma, and the odds ratios were found to be 1.051 (95% confidence interval 1.013-1.070) and 1.112 (95% confidence interval 1.022-1.209), respectively. NO_2 (sulfur dioxide) and O_3 were less associated with the rate of hospitalization due to asthma.[7] The effects of $PM_{2.5}$ were not included in this study. In other studies by Odajima et al., there was also a report that the peak expiratory flow decreases when the concentration of SPM increases.[8]

In this study, it was confirmed that an increase in the concentration of $PM_{2.5}$ causes asthma attacks. These results are similar to those of the study by Iskandar. Exposure to $PM_{2.5}$ for a short period (four days or less) in Denmark increased the rate of hospitalization due to asthma. The risk was greater for infants, but the concentrations of

Table 4. Odds ratios and 95% confidence intervals of asthma attack by average daily concentration of each air pollutant.

		D-3†			D-2§		
		OR*	95%CI†	*P*	OR*	95%CI†	*P*
$PM_{2.5}$	Single-variant	0.996	0.986-1.006	0.439	1.002	0.991-1.014	0.683
	Multi-variant	0.777	0.564-1.072	0.124	1.052	0.880-1.257	0.581
SPM	Single-variant	0.992	0.981-1.002	0.133	0.994	0.983-1.005	0.304
	Multi-variant	1.299	0.963-1.752	0.086	0.977	0.854-1.117	0.729
NO_2	Single-variant	0.993	0.961-1.027	0.692	1.013	0.978-1.049	0.467
	Multi-variant	0.815	0.601-1.103	0.185	1.271	1.027-1.572	0.027
O_3	Single-variant	1.006	0.989-1.024	0.481	0.994	0.975-1.013	0.513
	Multi-variant	1.475	1.179-1.846	0.001	1.128	1.031-1.234	0.009
		D-1‖			D0¶		
		OR*	95%CI†	*P*	OR*	95%CI†	*P*
$PM_{2.5}$	Single-variant	1.012	1.000-1.024	0.057	1.005	0.994-1.016	0.382
	Multi-variant	1.068	0.907-1.259	0.430	1.004	0.893-1.129	0.941
SPM	Single-variant	1.009	0.997-1.020	0.133	1.004	0.993-1.014	0.506
	Multi-variant	0.952	0.835-1.085	0.456	0.974	0.894-1.063	0.558
NO_2	Single-variant	1.018	0.985-1.052	0.299	1.034	1.002-1.068	0.040
	Multi-variant	1.078	0.926-1.255	0.331	1.103	0.942-1.292	0.224
O_3	Single-variant	1.016	0.997-1.035	0.097	1.031	1.012-1.050	0.001
	Multi-variant	1.037	0.960-1.120	0.359	1.058	0.990-1.131	0.098

*OR : odds ratio
†CI : confidence interval
‡D-3 : 3 days prior to day of attack
§D-2 : 2 days prior to day of attack
‖D-1 : 1 day prior to day of attack
¶D0 : day of asthma attack

Multi-variant variables contains $PM_{2.5}$, SPM, NO_2, O3, temperature, and humidity.

pollutants were not classified by date.[9] In the present study, the time differences between air pollution concentrations and asthma attacks were investigated.

Studies have also reported that O_3 causes asthma attacks. According to Strickland et al., $PM_{2.5}$ and O_3 generated from vehicles increase ED visits due to asthma among children.[3] Other studies have also shown that exposure to O_3 increases hospitalization rate due to asthma, exacerbates asthma symptoms, makes it necessary to take rescue medication, causes an asthma attack and reduces peak expiratory flow.[10,11] It was confirmed that the O_3 concentration increased on the days of asthma attacks when the number of hospital visits rose. It was reported that a 1-ppb increase in the O_3 concentration led to a rise in hospitalization rate by 3.1%.

In addition, there have been also some reports on NO_2. According to these, exposure to NO_2 increased ED visits due to asthma, stridor and the need of rescue medication.[9,12,13] A 1-ppb increase in the average concentration of NO_2 increased the risk of asthma attacks by 3.4%.

Table 5. Odds ratios and 95% confidence intervals of asthma attack by maximal 1-hour concentration of $PM_{2.5}$ divided by age group.

Age group (years)	Odds ratio	95% Confidence interval	*P*-value
0-1	1.018	1.001-1.035	0.042
2-5	1.002	0.988-1.017	0.757
6-12	1.007	0.993-1.021	0.345
13-15	1.022	0.993-1.052	0.139
Over 16	0.987	0.879-1.108	0.822

It has been reported that the effects of air pollution are greater on infants than on older people, as their immune systems and lungs are immature, they have a higher respiratory rate per weight, and they are more active than adults. Moreover, since their airway is narrower than that of adults, airway inflammation brings about more severe airway obstruction.[2,14,15]

Gaudeman et al. reported that exposure to air pollution has serious and long-term effects on the growth of the respiratory system at the age of eight, and leads to defects in lung functions which are clinically significant at the age of 18. Major pollutants include NO_2, acid vapors, fine dusts and carbon oxides.[16] Thus, exposure to such pollutants during infancy should be avoided.

Air pollutants affect not only asthma but also other allergic diseases such as rhinitis and atopy.[17] It has also been reported that $PM_{2.5}$ exacerbates the skin symptoms of atopic dermatitis.[18] As there have been few studies on this so far, it is necessary to conduct more research on the correlation between allergic diseases and air pollution.

There were some limitations to the present study. First, other factors causing asthma attacks were not considered. Asthma attacks can also be caused by various factors including infection, antigens and air pollution; and infection and antigens such as dust mites will be considered in our next study.

Second, the data on pollutants other than $PM_{2.5}$ for May 2013 could not be obtained. This reduced the sample size and the statistical significance. As such, it is necessary to collect data in a more precise way and for a longer period of time.

Third, the differences between indoor $PM_{2.5}$ and outdoor $PM_{2.5}$ were not considered. Lim et al. reported that $PM_{2.5}$ may be higher indoors than outdoors due to smoking or cooking.[19] Indeed, indoor $PM_{2.5}$ (47.6 ± 16.5l g/㎥) was higher than outdoor $PM_{2.5}$ (37.7 ± 17.2l g/㎥), and the ratio was 1.37 ± 0.33 (correlation coefficient (r) = 0.89, $P < 0.001$). Basically, the indoor $PM_{2.5}$ comes from the outside, but the differences between indoor and outdoor $PM_{2.5}$ were not considered in the present study.

In conclusion, an increase in the maximal concentration of $PM_{2.5}$ within 24 hours causes asthma attacks. In particular, the risk increases among in-

fants under one year of age. In addition, an increase in the average concentration of NO_2 or O_3 also increases the risk of asthma attacks.

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