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ORIGINAL ARTICLE

Correlation between Asian Dust Storms and Worsening Asthma in Western Japan

Masanari Watanabe[1], Akira Yamasaki[1], Naoto Burioka[1], Jun Kurai[1], Kazuhiko Yoneda[1], Atsushi Yoshida[4], Tadashi Igishi[1], Yasushi Fukuoka[1], Masaki Nakamoto[1], Hiromi Takeuchi[2], Hisashi Suyama[1], Toshiyuki Tatsukawa[1], Hiroki Chikumi[1], Shingo Matsumoto[1], Takanori Sako[3], Yasuyuki Hasegawa[1], Ryota Okazaki[1], Kazunori Horasaki[4] and Eiji Shimizu[1]

ABSTRACT

Background: Severe wind storms during spring in East Asia, called Asian dust storms (ADS), have been assessed in the past for their effect on health in Asian countries. Our objective was to study the ADS association with asthma symptoms in adult patients in Japan.

Methods: We designed a telephone survey to assess ADS influence on upper and lower respiratory, ocular and cutaneous symptoms in 98 patients with adult asthma from April to May 2007. Peak expiratory flow (PEF) was also measured from February to May.

Results: Worsening lower respiratory symptoms were noted by 22 of 98 patients during ADS in April, when Japanese cedar pollen levels also increased. During ADS in May, however, Japanese cedar and cypress pollen levels were not elevated, 11 patients had worsening of lower respiratory symptoms. None required emergency treatment for the exacerbation. Lower respiratory symptoms worsening most were cough and sputum; this was more common in patients with allergic rhinitis or atopy than in those without ($P < 0.05$). Min%Max differed significantly at 88.7 ± 6.6% during dust dispersion period, defined as the ADS day plus the next 6 days, versus 92.0 ± 5.3% during the 7-day period before a dust storm.

Conclusions: We found that ADS aggravated lower respiratory symptoms in adult patients with asthma, but this influence was mild.

KEY WORDS

Asian dust storms, asthma, lower respiratory symptom, peak expiratory flow, telephone survey

INTRODUCTION

Asian dust storms (ADS) originating in East Asia deserts during the spring affect much of East Asia, including Japan.[1] Asian dust occasionally even reaches the North American east coast.[2] Recently, ADS have become a serious problem due to heavy pollution and an increase of frequency and duration.[3] Asian dust has been reported to contain pollutants such as SO_2 and NO_2.[4,5] Therefore, the health problems caused by ADS have attracted attention.

Numerous epidemiologic studies suggest an association between atmospheric particulate-matter levels, and respiratory, cardiovascular morbidity, and mortality.[6] McCreanor *et al.*[7] reported that patients with asthma had asymptomatic reduction of pulmonary function and an inflammatory response after walking for only 2 hours along a roadside, although the actual changes were small. ADS health effects have been studied little, compared to those of other air pollution. Studies mostly in Taiwan have assessed the possible ADS association with hospital visits and admission, cardiovascular onset and mortality, cerebrovascular, and pulmonary disease, and conjunctivi-

[1]Department of Respirology and Rheumatology, [2]Department of Otolaryngology, Head and Neck Surgery, Faculty of Medicine, Tottori University, [4]Tottori Prefectural Institute of Health and Environment, Tottori and [3]Department of Respiratory Medicine, Obase Hospital, Fukuoka, Japan.
Correspondence: Masanari Watanabe, MD, PhD, Department of Respirology and Rheumatology, Faculty of Medicine, Tottori University, 36–1 Nishi-machi, Yonago, Tottori 683–8504, Japan.
Email: watanabm@grape.med.tottori–u.ac.jp
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tis and rhinitis occurence.[8-20] Some studies showed increased mortality, emergency cardiovascular-related hospital visits, and ADS-associated hospitalization for pneumonia.[18-20] Most studies have however indicated that ADS association with such factors is not statistically significant.[8-17] Reports from Korea have associated ADS with mortality, pulmonary function, and respiratory symptoms in patients with asthma.[21-25] In children with mild asthma, ADS are associated with increase of acute respiratory symptoms and changes in peak expiratory flow (PEF).[23] Kwon *et al*.[21] reported increased mortality after two days of ADS. In China, Meng *et al*. reported increasingly frequent hospitalization for pneumonia during ADS.[26] Kanatani *et al*.[27] reported from Japan that ADS was associated with increased risk of hospitalization in child asthma.

ADS tends to be shorter in duration in Japan than in Korea, Taiwan, and China, and the concentration of particular matter with a diameter less than 10 μm (PM_{10}) during ADS is lower.[28] To determine how ADS may effect on some patient's conditions in Japan, we conducted a telephone survey assessing ADS influence on upper and lower respiratory, ocular and cutaneous symptoms in adult patients with asthma. This is the first epidemiological study in Japan to study the lower respiratory effects of ADS in adult patients with asthma.

METHODS

PATIENTS

We enrolled 112 patients at least 18 years old with asthma managed by Tottori University Hospital from December 2006 to January 2007. All met Global Initiative for Asthma (GINA) guidelines[29] criteria for asthma. They had a history of intermittent wheezing and airway hyperresponsiveness to methacholine or >20% diurnal fluctuation of peak expiratory flow (PEF). None evidenced chronic obstructive pulmonary disease (COPD) or other disorders. Asthma severity was classified based on Asthma Prevention and Management Guideline 2009, Japan,[30] and patients with mild persistent and moderate disease were recruited. Patients were excluded if they needed to increase medication or their asthma/respiratory infections were exacerbated between registration and the first ADS event. All patients lived in Yonago City, Tottori Prefecture, Japan, and all gave informed consent to take part.

ADS AND PM_{10}, METAL AND ION MEASUREMENT

Yonago City, located in rural western Japan and having a population of 160,000, has no major air pollution sources except from a paper mill and motor vehicles.

ADS are defined in Japan based on a visibility of less than 10 km due to dust from East Asian deserts. The Japanese Ministry of the Environment has observed Asian dust in real time using a light detection and ranging (LIDAR) network and has measured atmospheric particulate matter (PM_{10}). The Japan Meteorological Agency and Ministry of the Environment define individual ADS events based on local data. In this study, we defined ADS events for Yonago City based on Japan Meteorological Agency and Ministry of the Environment announcements.

PM_{10} samples were collected and metal and ionic component concentrations in samples determined by the Tottori Prefectural Institute of Health and Environment from March to May 2007. Metals measured were iron (Fe), aluminum (Al), calcium (Ca), cadmium (Cd), manganese (Mn), nickel (Ni), copper (Cu), and chromium (Cr). Nitrate (NO_3^-), sulfate (SO_4^{2-}), calcium (Ca^{2+}), magnesium (Mg^{2+}), and ammonium (NH_4^+) were measured as ions.

AIRBORNE POLLEN

Airborne pollen in Yonago City was measured with a Durham sampler on the roof of a building 10 m above ground where free air movement was allowed on all sides. Slides covered with glycerine jelly containing fuchin were exposed to air 24 hours, then pollen grains on slides in an 18 × 18 mm area were identified and counted after staining with Calbela's solution. Total daily pollen counts were expressed as the number of pollen particles per cm^2 per day.

PEF MONITORING

All patients measured morning PEF daily using a peak flow meter (Mini-Wright, Clement Clarke International, Harlow, UK, American Thoracic Society scale) from January to May 2007 and recorded the best value from three attempts. PEF was measured within 30 minutes of when patients got up in the morning and before they inhaled corticosteroids or β_2-agonists or took oral drugs. The highest morning PEF from January to May was defined as the personal best value.

To assess PEF data, we defined a one-week "dust dispersion" period as the ADS event day plus the 6 days after the event, and the "control" period was the 7 days preceding the event. The lowest PEF during the dust dispersion period was expressed as a percentage of the highest PEF to calculate Min%Max PEF.[31] The lowest PEF during the one-week period before the event was expressed as a percentage of the highest PEF. The mean morning PEF was compared to Min%Max for the dust dispersion and control periods. "Control days" were defined as the period from February 1 to May 31, except for ADS event days, to compare mean morning PEF/personal best ratio between control and ADS event days.

TELEPHONE SURVEY

The survey was done by telephone within three days of the ADS event. We inquired whether patients had

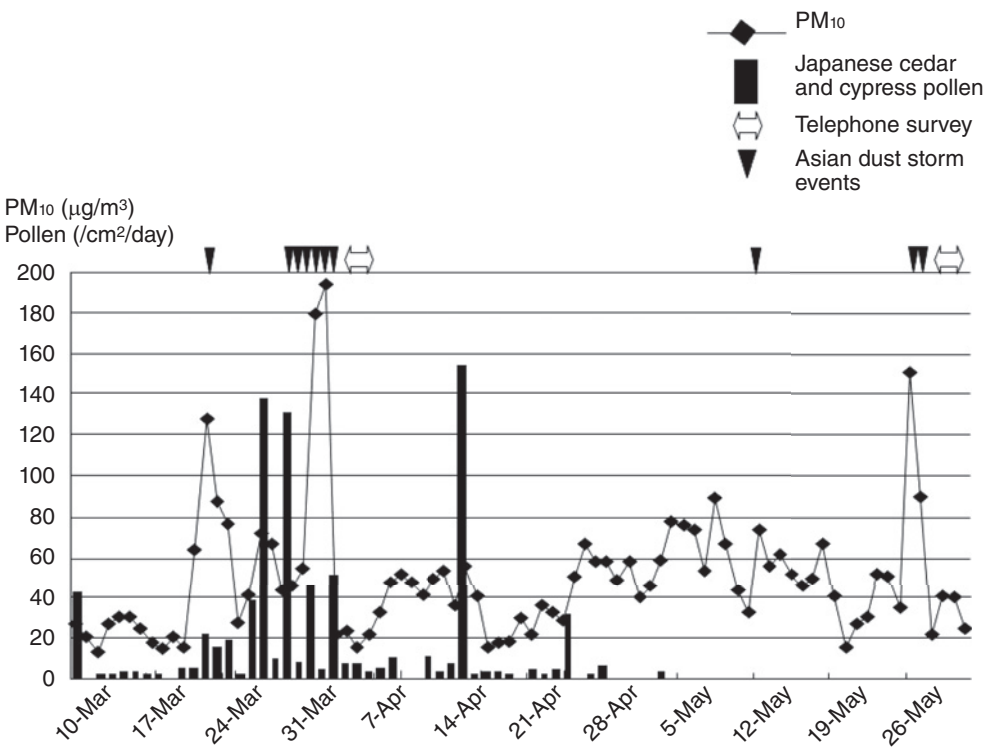

Fig. 1 The dispersion of pollen, Asian dust storm events, and PM_{10}. A large amount of Japanese cedar pollen was detected on March 28 - April 2, but Japanese cedar and cypress pollen was not identified on May 12 and May 27 - 28.

exacerbation of upper and lower respiratory, ocular, or cutaneous symptoms during the ADS event. We asked the following questions: (1) worsening cough, sputum, wheezing, and dyspnea, use of short-acting β_2-agonists and hospital visits for lower respiratory symptoms; (2) tearing, itching, mucus, and pain among ocular symptoms; (3) stuffiness, sneezing, pharyngalgia and itching among upper respiratory symptoms; and (4) itching, redness, and pain among cutaneous symptoms. We judged worsening to occur if a patient mentioned worsening of even one symptom, but excluded patients who had respiratory tract infection or suspected infection.

DATA ANALYSIS

Results are shown as mean ± standard error (SE). SPSS software (Japanese version 16.0 for Windows; SPSS Japan Inc., Tokyo, Japan) was used for statistical analysis. Group comparisons were done with the Mann-Whitney nonparametric test. The χ^2 test was used for categorical data. Multivariate logistic regression analysis was also done. Significance was defined as $p < 0.05$ for all analysis.

RESULTS

RELATIONSHIP AMONG ADS EVENTS, AIRBORNE POLLEN, AND PM_{10}

Ten ADS event days were identified, i.e., March 22, March 28 - April 2, May 12, and May 26 - 27 (Fig. 1). During ADS events, Japanese cedar pollen, but not cypress pollen, was identified, although the Japanese cedar pollen level was not high during ADS events, except on March 28. In fact, no Japanese cedar pollen was identified on May 12 and May 26 - 27. No differences were seen in airborne pollen levels between ADS event and control days in March and April (Table 1).

PM_{10} COMPONENTS

Table 1 shows PM_{10} metal and ionic component concentrations. The average PM_{10} level on ADS days was significantly higher than the average on comparison days (101.2 μg/m^3 on ADS days versus 40.5 μg/m^3 on comparison days). Levels of natural metals such as Fe, Al, Ca, and ionic components were similar, although mean Cd, Mn, and Ni levels were significantly higher on ADS days than on comparison days.

RESULTS OF THE TELEPHONE SURVEY

We conducted telephone surveys twice, on April 3 - 5 and May 28 - 29, with the results shown in Figure 2. A total of 112 asthma patients were enrolled and 98 patients participated in the first telephone survey, while 12 patients could not be contacted and 2 patients met exclusion criteria. Table 2 shows patient summaries. The 22 patients with worsening lower respiratory

Table 1 Concentration of component in PM_{10}

		ADS event days	Comparison days	*P* Value
	PM_{10} (μg/m³)	101.2 ± 29.5	40.5 ± 4.5	*P = 0.03*
Metal component	Fe (μg/m³)	3.37 ± 1.45	1.34 ± 0.38	NS
	Al	2.99 ± 1.21	0.94 ± 0.21	NS
	Ca	1.73 ± 0.60	0.65 ± 0.19	NS
	Cd	0.01 ± 0.002	0.001 ± 0.001	*P = 0.009*
	Mn	0.087 ± 0.032	0.026 ± 0.005	*P = 0.04*
	Ni	0.018 ± 0.003	0.008 ± 0.002	*P = 0.006*
	Cu	0.022 ± 0.008	0.012 ± 0.003	NS
	Cr	0.012 ± 0.003	0.007 ± 0.001	NS
Ionic component	NO_3^- (μg/m³)	2.65 ± 0.65	1.61 ± 0.27	NS
	SO_4^{2-}	6.22 ± 1.02	5.75 ± 0.80	NS
	Ca^{2+}	1.73 ± 0.60	0.65 ± 0.19	NS
	Mg^{2+}	0.37 ± 0.06	0.32 ± 0.05	NS
	NH_4^+	1.04 ± 0.19	1.33 ± 0.23	NS
Organic constituent	Japanese cedar pollen and/or crypress pollon (/cm²/day)	35.9 ± 47.0	12.0 ± 31.2	NS

NS, not significant.

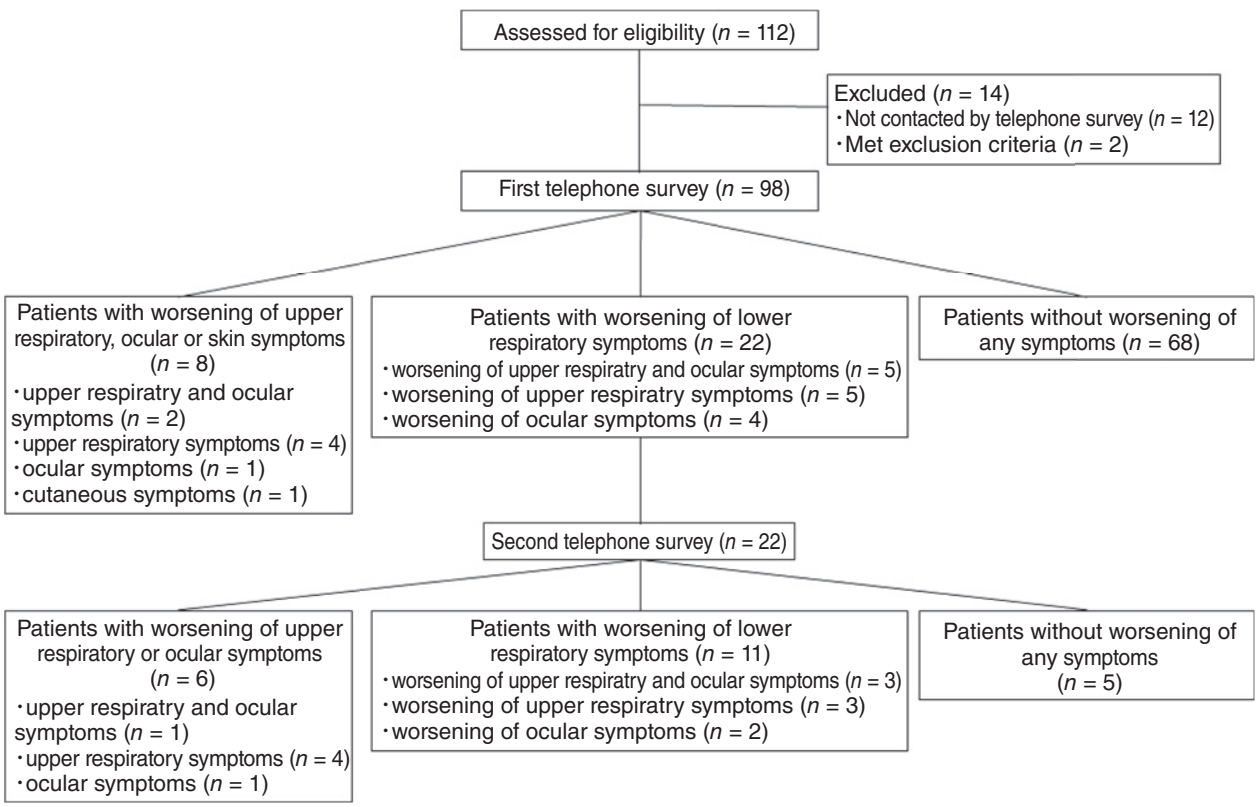

Fig. 2 Consort diagram showing the flow of patients through the study.

Table 2 Patient characteristics

Number	98
Age (years)	57 ± 17.2
Gender (male/female)	42/56
Disease duration (months)	109.3 ± 102.4
Smoking status	
Never	77 (78.6%)
Former	20 (20.4%)
Current	1 (1.0%)
Stage of asthma	
Mild persistent	39 (39.8%)
Moderate	59 (60.2%)

Data are presented as the mean ± S.E.

symptoms in the first survey were reviewed during the second.

Among these 22 patients, 5 had worsening upper respiratory and ocular symptoms, 5 only worsening upper respiratory symptoms, and 4 only worsening ocular symptoms. On the other hand, 8 of the 98 patients had worsening upper respiratory, ocular, and/or cutaneous symptoms without worsening lower respiratory symptoms.

When 22 patients took part in the second telephone survey on May 28 - 29, 11 patients had worsening of lower respiratory symptoms. Among the 6 patients without worsening lower respiratory symptoms, 1 patient had both worsening upper respiratory and ocular symptoms, 4 patients only worsening upper respiratory symptoms, and 1 patient only worsening ocular symptoms.

Lower respiratory symptoms becoming worse during ADS events included coughing in 14 (63.0%), sputum in 12 (55.6%), dyspnea in 6 (29.6%), and wheezing in 1 (7.4%) (Fig. 3). Eight patients used short-acting β_2-agonist for symptoms and noted improvement. None required emergency treatment for exacerbation, but 2 patients with wheezing had to increase their inhaled corticosteroid dose.

PEF CHANGES

In patients with worsening lower respiratory symptoms during ADS events, the mean morning PEF/personal best ratio was 87.2 ± 6.7% on ADS days versus 89.2 ± 5.6% on control days (Fig. 4a), with no significant statistical difference seen between periods. Min%Max was 88.7 ± 6.6% during dust dispersion versus 92.0 ± 5.3% during the control period (Fig. 4b), a statistically significant difference between the two periods ($p < 0.05$). In contrast, no significant change was seen in the mean morning PEF/personal best ratio or Min%Max in patients without worsening lower respiratory symptoms during ADS events (data not shown).

COMPARISON OF PATIENTS WITH OR WITHOUT WORSENING LOWER RESPIRATORY SYMPTOMS DURING ADS EVENTS

A significant difference was seen in the prevalence of allergic disease, allergic rhinitis, and atopy between patients with and without worsening lower respiratory symptoms during ADS events (Table 3). No significant difference was seen in age, gender, asthma severity, or asthma duration. Leukotriene antagonists and antihistamines were used as maintenance treatment significantly more commonly by patients with worsening lower respiratory symptoms than among those without. Multiple logistic regression analysis showed no statistically significant parameters.

DISCUSSION

Epidemiological studies have already examined the association of ADS with health, and several studies found an association,[18-21,23,26] but only one report have be made on ADS influence on patients with asthma in Japan.[27] We studied ADS influence on Japanese adult patients with asthma by conducting a telephone survey, finding that 11% - 22% of our patients noted worsening lower respiratory symptoms during ADS events. Those with worsening lower respiratory symptoms during ADS events increased when Japanese cedar pollen was present simultaneously in the atmosphere, and Min%Max was lower during dust dispersion than the control period among those with worsening lower respiratory symptoms during ADS events. None, however, required emergency treatment for exacerbated symptoms because changes were mild and improved in treatment using short-acting β_2-agonists.

Some previous epidemiological studies detected significant associations between ADS, mortality, and hospital admission, but the majority have not demonstrated an association between ADS and conditions such as cerebrovascular disease, COPD, asthma, conjunctivitis, or rhinitis. It may be common for patients with asthma to report mildly exacerbated respiratory symptoms during or after ADS events. We suspect that exacerbate symptoms due to ADS was mild, so few patients had to visit hospitals, which would make it difficult to find an association between ADS and hospital visits, admission frequency, disease onset, or mortality in Japan because the PM_{10} level during ADS is low in Japan compared to levels in China, Taiwan, and Korea. The telephone survey we conducted to assess the association of ADS with symptoms of adult patients with asthma was to study symptom exacerbation in patients who did not visit hospitals.

Our telephone survey showed that 30% of asthma patients had worsening upper and/or lower respiratory, ocular, or cutaneous symptoms during ADS events, with worsening being higher during a simultaneous increase in Japanese cedar pollen dispersion. The frequency of worsening lower respiratory symp-

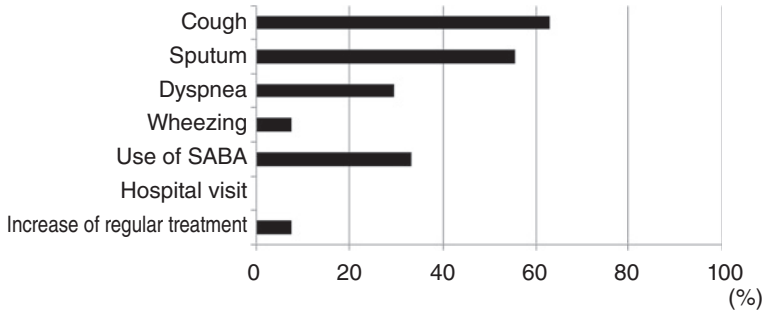

Fig. 3 Lower respiratory symptoms showing exacerbated during ADS events in the patients with worsening. The frequency was higher for cough and sputum compared with other lower respiratory symptoms. One patients with wheezing and dyspnea had asthma attacks. SABA, short acting β_2-agonists.

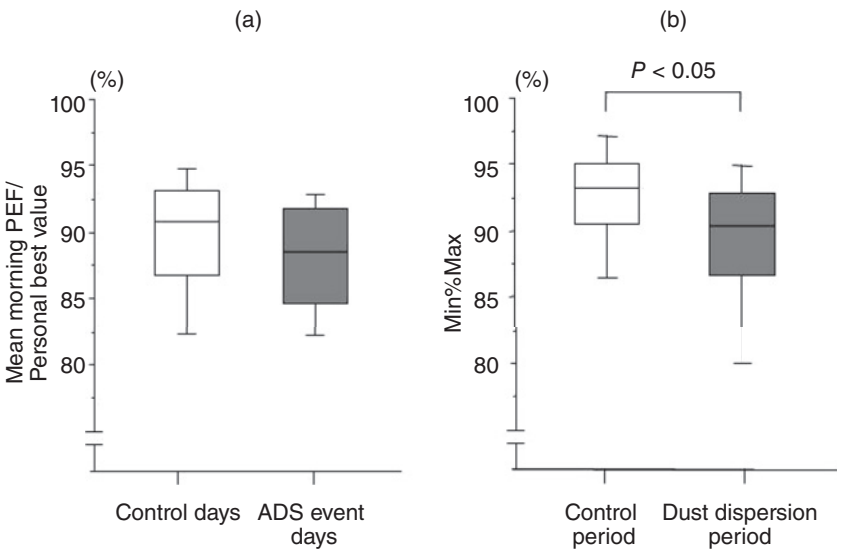

Fig. 4 Results of monitoring PEF in patients with worsening lower respiratory symptoms during ADS events. (**a**) The mean morning PEF to personal best ratio was 87.2 ± 6.7% in the ADS days versus 89.2 ± 5.6% in the control days. (**b**) Min%Max was 88.7 ± 6.6% in the dust dispersion period versus 92.0 ± 5.3% in the control period. A significant difference between the dust dispersion and control periods was detected ($p = 0.04$).

toms, but not upper respiratory or ocular symptoms, was highest (22%) when cedar pollen was dispersed. Only slightly worsening lower respiratory symptoms caused by ADS were seen because none of the patients required emergency treatment and improvement was achieved using short-acting β_2-agonists in our study. Our results are similar to those from other countries in that ADS aggravated the symptoms of asthma and decreased PEF, but did not increase the frequency of hospitalization, hospital attendance, or mortality in patients with asthma.[15,23,25] However, Kanatani *et al*.[27] reported to increase a risk of hospitalization caused by ADS in child asthma. The influence of ADS may be different between adult asthma and child asthma in Japan. It is necessary to perform the large number of study, and verify the difference of adult asthma and child asthma in the influence of ADS.

PEF monitoring showed a significant difference between dust dispersion and control periods for Min%Max, but not for best mean morning PEF/personal best ratio. There are two possible reasons for this result. First, the PEF decrease was not prolonged, because lower respiratory symptom exacerbation was mild and patients improved using short-acting β_2-agonists. Second, Min%Max decreases if a

Table 3 Comparison of patients with or without worsening of respiratory symptoms

	Patients without worsening lower respiratory symptoms	Patients with worsening lower respiratory symptoms	*P* value
Number	76	22	
Age (years)	56.3 ± 14.2	54.7 ± 18.7	NS
Gender (male/female)	34/42	8/14	NS
Disease duration (months)	102.8 ± 75.6	106.3 ± 115.9	NS
Smoking status			NS
Never	59 (77.6%)	18 (81.8%)	
Former	17 (22.4%)	3 (13.6%)	
Current	0 (0%)	1 (4.5%)	
Asthma severity			NS
Mild persistent	30 (39.5%)	9 (40.9%)	
Moderate	46 (60.5%)	13 (59.1%)	
Existence of atopy	14 (18.4%)	16 (72.7%)	*P* < 0.05
Presence of other allergic diseases	15 (19.7%)	10 (45.5%)	*P* < 0.05
Allergic rhinitis	17 (22.4%)	9 (40.9%)	*P* < 0.05
Cedar pollen and cypress pollen allergy	5 (6.6%)	3 (13.6%)	NS
Perennial allergic rhinitis	12 (15.8%)	6 (27.2%)	NS
Allergic conjunctivitis	1 (1.3%)	1 (4.5%)	NS
Atopic dermatitis	2 (2.6%)	1 (4.5%)	NS
Non-allergic rhinitis	3 (3.9%)	0 (0%)	NS
Usual maintenance treatment			
Inhaled corticosteroid	74 (97.4%)	22 (100%)	NS
Oral corticosteroid	0 (0%)	0 (0%)	NS
Inhaled long-acting β_2-agonists	41 (53.9%)	14 (63.6%)	NS
Leukotriene antagonist	21 (27.6%)	12 (54.5%)	*P* < 0.05
Tephylline	8 (10.5%)	3 (13.6%)	NS
Antihistamines	5 (6.6%)	4 (18.2%)	*P* < 0.05

Data are presented as the mean ± SE, NS = not significant

single marked decrease in PEF occurs, suggesting that Min%Max may be useful in studying ADS-induced airflow obstruction.

The role of pollen in asthma has not been clearly demonstrated epidemiologically,[32,33] perhaps because the diameter of most pollen is 20 - 40 μm and unable to reach the human distal airway. Abundant sources in the literature, however, suggest that pollen precipitates asthma.[34] In this study, we monitored daily airborne pollen levels to assess the effect on patients with asthma. Both Asian dust and Japanese cedar pollen increased at the same time from March 28 to April 2. In contrast, no Japanese cedar or cypress pollen was detected on May 12 or May 26 - 27 during ADS events, so the influence of Japanese cedar and cypress pollen was excluded from the second telephone survey. Asthmatic patients without rhinitis also had worsening lower respiratory symptoms during ADS, so we must consider factors other than pollen aggravating lower respiratory symptoms in our asthma patients during ADS.

The ADS exacerbation mechanism in lower respiratory symptoms remains unclear. Asian dust particle diameter is 3 - 5 μm in Japan, so dust particles could reach the human distal airway, including small airway passages and alveoli. Lei *et al*.[35] reported that exposure to particulate matter due to ADS increased lung inflammation and injury in rats. Ichinose *et al*.[36] reported that Asian dust enhanced eosinophil infiltration and cytokine/chemokine expression induced by mite allergens in the murine airway. Hiyoshi *et al*.[37] reported an adjuvant effect of Asian dust on ovalbumin-induced eosinophil recruitment in the alveoli and airways of mice, so Asian dust may increase airway inflammation and exacerbate lower respiratory symptoms in patients with asthma.

Asian dust has been reported to contain chemicals and microorganisms.[4,5,38] PM_{10} during ADS days contained more industrial metals such as Cd, Mn and Ni than on comparison days, but actual Cd, Mn, and Ni levels were very low, so these would not likely worsen asthma symptoms in our patients.

Allergic rhinitis had been suggested an important determinant of worsening lower respiratory symptoms during ADS events, but worsening of symptoms did not depend on asthma severity, or asthma duration in our study. It had been reported that patients with pollen allergy develop coughing and wheezing

during pollen season,[39] while a challenge with nasal allergens can induce bronchial inflammation.[40] Patients with asthma may thus suffer worsening lower respiratory symptoms due to inflammatory factors in Asian dust affecting the nose.

In conclusion, we found that 30% of adult asthma patients showed worsening upper and/or lower respiratory, ocular, or cutaneous symptoms during ADS events, with worsening lower respiratory symptoms having the highest frequency, although no patients needed emergency treatment. ADS may possibly increase airway inflammation, but further studies are needed to define the association between ADS and health. It is also necessary to identify the Asian dust components influencing health and how the susceptible patient population shows symptom exacerbation on exposure to this dust.

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