Two-Year Follow-Up Study of the Effect of Acid Fog on Adult Asthma Patients

Hiroshi TANAKA, Shin-ichi HONMA, Motoi NISHI*,
Tomofumi IGARASHI**, Fumihiko NISHIO*** and Shosaku ABE

Acid fog is a complex mixture of atmospheric pollutants containing multiple stimuli that may be capable of inducing bronchoconstriction. To investigate the effect of ambient acid fog on bronchoconstriction, we examined the relation between the hospital visit for asthma symptoms of 102 patients and various meteorological conditions for over the two-year period from January 1992 to December 1993. Dense fog occurs frequently every summer in Kushiro, a city located in Hokkaido, northernmost island in Japan. The acidity of the fog ranged from pH 3.32 to 6.91 (mean pH=5.05) during this period. A significant increase ($p<0.05$) of hospital visits on a foggy day was found in 9 cases, and a tendency ($p<0.10$) was found in 10 cases. The odds ratio for a hospital visit on a high water vapor pressure day (>12 hPa) was significantly high ($p<0.01$) in 5 cases among the above 19 cases. To exclude the effect of high water vapor pressure, the data was restricted to the condition of a foggy day with low water vapor pressure (<12 hPa); 9 patients had a significant increase ($p<0.05$) in hospital visits on such a day. These results indicated that hospital visits for asthma symptoms was increased on acid fog days in 8.8% of adult asthma patients. Inhalation of naturally occurring acid fog may have adverse effects on the respiratory tract of the asthmatic patient.

(Internal Medicine 35: 100–104, 1996)

Key words: acid aerosol, air pollutant, bronchial asthma, weather factor

Introduction

Weather-related factors alone may induce a response in asthmatics. The response may be due to the changing the concentration of airborne pollutants. Naturally occurring fog has recently been shown to be quite acidic, with pH values as low as under 2.0 (1). The major ions present in acid fog are hydrogen, sulfate, nitrate, ammonium and chloride (1, 2), suggesting that the low pH is in large part due to the presence of sulfuric (H_2SO_4) and nitric (HNO_3) acid. However, the potential adverse health effects of breathing acid fog have not been adequately examined (3, 4).

Exposure to acidic aerosols and sulfates has been associated with increased respiratory mortality, morbidity and symptoms in a variety of settings (3, 5–8). Chamber exposure studies suggest that asthma patients are more sensitive to the acidic sulfates than normal volunteers (9–11). On the other hand, some reports (12, 13) revealed that healthy adults and asthmatic

subjects have shown little or no bronchoconstriction in methacholine reactivity after acute exposure to H_2SO_4 fog. Overall, the results of chamber exposure studies suggested that asthmatics might be an appropriate “sensitive population” to airborne acid aerosol (3, 8).

Kushiro is a city of 200,000 residents located on the Pacific coast in the northeastern Japan. It has little industry. Dense fog frequently occurs there every summer. Daily fog acidity in the Kushiro urban area was measured in 1992 by the group of Nishio, one of the author of this paper. The fog acidity is quite acidic there; the annual average fog pH was 4.94 and the minimum was 3.32 in 1992.

To investigate the effects of acid fog on adult asthmatics, we conducted a retrospective study of the correlation between the hospital visits for asthma symptoms and various meteorological conditions.

From the Third Department of Internal Medicine, *the Department of Public Health, Sapporo Medical University School of Medicine, Sapporo, **the Division of Respiratory Medicine, Kushiro City General Hospital, Kushiro and ***Hokkaido University of Education, Kushiro

Received for publication June 28, 1995; Accepted for publication October 27, 1995

Reprint requests should be addressed to Dr. Hiroshi Tanaka, the Third Department of Internal Medicine, Sapporo Medical University School of Medicine, South-1, West-16, Chuo-ku, Sapporo 060

Materials and Methods

A total of 102 physician diagnosed asthmatics (15–79 year-old, 45 males and 57 females) were eligible to participate in this study. All patients were Kushiro residents and were followed at Kushiro City General Hospital for two years from January 1992 to December 1993. The asthma severity (14) of the 102 patients was as follows; 9 severe, 53 moderate and 40 mild subjects. Forty patients were treated with theophylline and inhaled salbutamol, 62 patients received inhaled beclomethasone dipropionate (300–1,200 μ g/day) and 8 cases were administered oral prednisolone. When the patient had at least one of the following criteria they were defined as atopic; 1) one or more positive skin prick tests, 2) a total serum IgE level of more than 500 U/ml, 3) one or more positive specific serum IgE tested by the commercial kit (MAST systems, Hitachi Kasei, Tokyo, Japan). In the light of this criteria, 58 patients were considered as atopic and 44 patients were non-atopic.

Individual extra hospital visits for asthma symptoms including emergency room visits at night were picked up retrospectively from the patient's medical record. Asthma symptoms were wheezing, shortness of breath, chest tightness or cough.

The following daily meteorological data were obtained from the Kushiro Meteorological Observatories; fog occurrence, barometric pressure, temperature, water vapor pressure, relative humidity, wind velocity, wind direction and precipitation. Fog was gathered with a large screen collector and the acidity of the fog water was measured with a pH meter. The levels of daily air pollutants in this area, for example suspended particulate matter of less than 10 μ m, SO₂, NO, NO₂, ozone, were all within the Ambient Air Quality Standards of the Environment Agency of Japan (15).

Statistical analysis

Each meteorological variable was divided into two categories (Table 1). Observed and expected individual hospital visits related to the above various meteorological factors for category "1" in Table 1 was using chi-square test. Odds ratio for each meteorological variable to category "1" in Table 1 was also calculated in each patient using the method of Mantel and Haenzel (16).

Results

Fog occurred 380 days during the study period from January 1992 to December 1993. The fog acidity could be measured 51 days; it ranged from pH 3.32 to 6.91. The mean pH was 5.05 and SD was 0.69.

Percent increase of hospital visit as related to each meteorological condition is shown in Table 2. The rate was the highest (9/102) on foggy days, the second rate (7/102) was observed on high vapor pressure (≥ 12 hPa) days and the third value (6/102) was observed on low barometric pressure (<1,000 hPa) days. Nine patients (2 severe, 5 moderate and 2 mild) visited the hospital in significant correlation ($p < 0.05$) with fog and 10 patients (3 severe, 2 moderate and 5 mild) had a tendency

Table 1. Categorization of Meteorological Parameters

Meteorological parameter	1	0
Fog	Yes	No
Barometric pressure	$\geq 1,000$ hPa	<1,000 hPa
Daily temperature difference (max minus min)	$\geq 10^\circ\text{C}$	<10 $^\circ\text{C}$
Day-to-day temperature difference (max of previous day minus min)	$\geq 10^\circ\text{C}$	<10 $^\circ\text{C}$
Water vapor pressure	≥ 12 hPa	<12 hPa
Relative humidity (mean)	$\geq 90\%$	<90%
Relative humidity (minimum)	>75%	<75%
Wind velocity (mean)	≥ 4 m	<4 m
Wind velocity (maximum)	≥ 9 m	<9 m
Wind direction at maximal velocity	South	North, East, West
Precipitation	≥ 1 mm	<1 mm

Table 2. Percent Increase of Hospital Visits in Various Meteorological Conditions

Meteorological parameter	Percent increase of hospital visit	
	1*	0*
Fog	8.8	3.9
Barometric pressure	0	5.9
Daily temperature difference (max minus min)	2.0	1.0
Day-to-day temperature difference (max of previous day minus min)	0	3.9
Water vapor pressure	6.9	3.9
Relative humidity (mean)	2.0	1.0
Relative humidity (minimum)	4.9	1.0
Wind velocity (mean)	1.0	2.0
Wind velocity (maximum)	1.0	2.0
Wind direction at maximal velocity	2.9	1.0
Precipitation	0	1.0

*Each category was shown in Table 1.

($p < 0.10$) to visit the hospital on a foggy day. The characteristics of these patients are shown in Table 3.

The odds ratios to various meteorological conditions in the above 19 patients are shown in Tables 4 and 5. Odds ratio to high vapor pressure equal to and higher than 12 hPa was significantly high ($p < 0.01$) in 5 cases in 19 cases respectively. The odds ratio of high mean relative humidity ($\geq 90\%$) was significantly high ($p < 0.01$) in 3 cases and that of high minimum relative humidity ($\geq 75\%$) was also significantly high ($p < 0.01$) in 5 cases. For the other meteorological conditions, three had significantly ($p < 0.01$) increased hospital visits on south wind days and another patient had significantly ($p < 0.01$) increased visits on high mean wind velocity (≥ 4 m) days.

To exclude the effect of high vapor pressure, the data was restricted to conditions of vapor pressure under 12 hPa and

Table 3. Characteristics of Asthmatics with Fog-related Symptoms and the Results of Chi-square Test

Case	Age/Sex	Atopy	Total IgE (IU/ml)	WBC (mm ³)	Eosino (%)	Severity	Daily therapy	No. of visit on fog day observed /expected		pvalue of visit on fog & <12 hPa vapor pressure day
1 HS	37/M	+	460	6,250	4.3	Moderate	S,B	5/ 2.6	(p<0.05)	p<0.05
2 TH	61/M	+	280	6,200	7.1	Moderate	T,S,B	6/ 3.1	(p<0.05)	p<0.05
3 TW	15/M	+	910	7,880	11.1	Mild	T,S	13/ 7.8	(p<0.05)	NS
4 MT	28/F	+	1,000	7,040	6.1	Severe	S,B,P	24/16.6	(p<0.05)	NS
5 II	70/M	+	1,000	4,610	10.3	Mild	T,B	11/ 6.8	(p<0.05)	NS
6 IT	49/M	+	210	6,440	3.0	Moderate	S,B	12/ 7.8	(p<0.05)	p<0.10
7 KK	32/M	+	630	5,820	5.2	Mild	T,S	6/ 3.6	(p<0.10)	p<0.05
8 IM	16/F	+	510	7,060	3.4	Mild	T,S	4/ 2.1	(p<0.10)	p<0.10
9 EK	38/F	+	1,600	7,030	13.3	Mild	T	8/ 5.2	(p<0.10)	NS
10 KK	32/F	+	630	6,640	9.2	Mild	T,S	8/ 5.2	(p<0.10)	p<0.10
11 JS	30/M	+	120	8,800	1.2	Severe	S,B	4/ 2.1	(p<0.10)	p<0.05
12 SW	36/M	+	650	4,940	8.6	Moderate	S,B	41/33.8	(p<0.10)	p<0.05
13 AI	22/F	+	970	7,560	16.6	Mild	T,S	6/ 3.6	(p<0.10)	NS
14 TI	68/F	-	37	6,730	11.0	Severe	T,S,B	81/51.5	(p<0.05)	p<0.05
15 AN	79/F	-	99	6,950	16.9	Moderate	S,B	17/11.5	(p<0.05)	p<0.05
16 MS	70/M	-	32	9,640	14.5	Moderate	S,B	31/20.3	(p<0.05)	p<0.05
17 MT	55/F	-	56	8,930	7.0	Severe	T,S,B,P	3/ 1.6	(p<0.10)	p<0.10
18 MT	59/F	-	57	7,550	4.9	Severe	S,B,P	3/ 1.6	(p<0.10)	p<0.10
19 NS	50/F	-	55	8,090	3.2	Severe	S,B	6/ 3.8	(p<0.10)	p<0.10

T: theophylline, S: inhaled salbutamol as required, B: inhaled beclomethasone dipropionate, P: oral prednisolone, NS: p>0.10.

foggy days; 9 cases (30–79 year-old, 2 severe, 6 moderate and 1 mild) showed significantly increased ($p<0.05$) visits and 5 cases (2 severe, 1 moderate and 2 mild) had a tendency of increased ($p<0.10$) visits (Table 3). Overall, 19 out of 102 patients (18.6%) had a tendency toward increased hospital visits. When the data was restricted to the day of fog occurrence and low water vapor pressure, the hospital visits were significantly ($p<0.05$) increased in nine patients (8.8%) in this study population.

Discussion

The present results suggest that inhalation of acid fog might increase asthma symptoms; 8.8% of adult asthma patients had an increase of hospital visits for asthma symptoms in our study population. And the percent increase of hospital visits on a foggy day was the highest among other meteorological parameters. There have been no studies on the prevalence of the effect of naturally occurring acid fog in asthmatics or residents. In this study, all of the participants were carrying out typical daily life and thus some patients may not have been outdoors and they did not inhale acid fog equally. If all the patients had inhaled an equal amount of fog, the number might have been increased. Hospital visits based on the asthma symptoms, as a parameter of the fog effect is a relatively crude measure of the actual response to the fog and may reflect events only in minor subjects. If we calculate the number of symptoms from the patient's diary or daily peak expiratory flow rate (17), the percentage of the effect of acid fog might also increase.

In our study, the hospital visits on a foggy day with low water vapor pressure was significantly increased ($p<0.05$) in 9 cases. There was no significant difference in age, treatment or disease severity between these 9 patients and the other 93 patients. We hypothesized that the number of hospital visit in non-atopic patients might be more increased than that of atopic patients, because atopic patients exacerbate by inhalation of causative antigen, the trend of the effect of acid fog is more clearly apparent in non-atopic subjects than in atopic subjects. However, there was no difference between these two types.

We could not analyze all types of fog; diffuse or short-lived fogs did not provide enough condensate to examine pH and ions. In a few samples we measured the anions of the fog; for example the condensate on September 3, 1992 contained 30 ppm of SO_4^{2-} , 15 ppm of NO_3^- and 10 ppm of NO_2^- . The proportion of these anions showed daily variation but the trend of the content of these ions did not change in several types of fog water. The major ions reported to be present in acid fog are hydrogen, sulfate, nitrate, ammonium and chloride (1, 2) and the low pH is due to the presence of sulfuric and nitric acid. Glotfelty et al (18) reported a variety of pesticides and their toxic alteration products in fog. Hydroxymethanesulfonic acid, the bisulfite (HSO_3^-) adduct of formaldehyde (CH_2O) was a common constituent of California acid fogs (19). No tests were conducted specifically for pesticides or their products in Kushiro. Since not only ions but also other acidic materials that have an adverse effect, it is of interest to elucidate the unknown materials that lower fog pH.

The odds ratio to variable meteorological factors revealed

Effect of Acid Fog on Asthmatics

Table 4. Odds Ratio of Hospital Visits for Meteorological Variables on Atopic Asthmatics

Meteorological parameter	1. HS	2. TH	Patient 3. TW	4. MT	5. II	6. IT
1. Fog	>50 (p<0.05)	>50 (p<0.01)	6.18 (p<0.01)	2.89 (p<0.01)	5.20 (p<0.01)	3.78 (p<0.05)
2. Barometric pressure	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
3. Daily temperature difference (max minus min)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
4. Day-to-day temperature difference (max of previous day minus min)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
5. Water vapor pressure	(NS)	(NS)	11.3 (p<0.01)	2.84 (p<0.01)	38.3 (p<0.01)	5.61 (p<0.01)
6. Relative humidity (mean)	(NS)	6.68 (p<0.01)	(NS)	(NS)	(NS)	3.87 (p<0.01)
7. Relative humidity (minimum)	(NS)	5.79 (p<0.01)	(NS)	(NS)	(NS)	(NS)
8. Wind velocity (mean)	(NS)	(NS)	(NS)	(NS)	6.67 (p<0.01)	(NS)
9. Wind velocity (maximum)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
10. Wind direction at max velocity	(NS)	(NS)	(NS)	(NS)	(NS)	4.70 (p<0.01)
11. Precipitation	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)

Meteorological parameter	7. KK	8. IM	9. EK	Patient 10. KK	11. JS	12. SW	13. AI
1.	5.61 (p<0.10)	>50 (p<0.10)	3.75 (p<0.10)	>50 (p<0.10)	>50 (p<0.10)	1.64 (p<0.10)	5.61 (p<0.10)
2.	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
3.	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
4.	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
5.	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
6.	(NS)	(NS)	(NS)	>50 (p<0.10)	(NS)	(NS)	(NS)
7.	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
8.	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
9.	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
10.	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
11.	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)

Odds ratio for "1" of each category in Table 1.

NS: $p \geq 0.10$

Table 5. Odds Ratio of Hospital Visits for Meteorological Variables in Non-atopic Asthmatics

Meteorological parameter	14. TI	15. AN	Patient 16. MS	17. MT	18. MT	19. NS
Fog	6.57 (p<0.01)	3.65 (p<0.01)	4.62 (p<0.01)	>50 (p<0.10)	>50 (p<0.10)	5.04 (p<0.10)
Barometric pressure	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
Daily temperature difference (max minus min)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
Day-to-day temperature difference (max of previous day minus min)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
Water vapor pressure	(NS)	(NS)	19.0 (p<0.01)	(NS)	(NS)	(NS)
Relative humidity (mean)	3.04 (p<0.01)	(NS)	(NS)	(NS)	(NS)	(NS)
Relative humidity (minimum)	3.68 (p<0.01)	2.91 (p<0.01)	2.56 (p<0.01)	>50 (p<0.01)	(NS)	(NS)
Wind velocity (mean)	(NS)	(NS)	(NS)	>50 (p<0.01)	(NS)	(NS)
Wind velocity (maximum)	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)
Wind direction at maximal velocity	2.24 (p<0.01)	(NS)	3.13 (p<0.01)	(NS)	(NS)	(NS)
Precipitation	(NS)	(NS)	(NS)	(NS)	(NS)	(NS)

Odds ratio to "1" of each category in Table 1.

NS: $p \geq 0.10$

individual variations as shown in Tables 4 and 5. Weather factors may induce a direct physiological response or a psychologically mediated response. Cold, damp, or windy/dusty weather conditions are often thought to exacerbate asthma, but epidemiologic evidence relating asthma attacks to short-time weather changes is equivocal (20). Temperature and relative humidity are the weather factors most easily isolated and studied in the laboratory. The short-term effects of relative humidity have been elucidated in studies of exercise-induced bronchoconstriction (21). Among the 19 patients with an increase of hospital visits on foggy days, no cases had a high odds ratio for the change of temperature, and 6 patients had a significantly high ($p < 0.01$) odds ratio for high relative humidity. Not all patients with fog-related symptoms grew more serious on a high relative humidity day. These findings suggested that inhalation of naturally occurring fog itself might be an adverse factor exacerbating asthma symptoms.

References

- 1) Jacob DJ, Waldman JW, Munger JW, Hoffman MR. Chemical composition of fog water collected along the California coast. *Environ Sci Technol* **18**: 827, 1985.
- 2) Waldman JM, Munger JW, Jacob DJ, Flagan RC, Morgan JJ, Hoffman MR. Chemical composition of acid fog. *Science* **218**: 677, 1982.
- 3) Balmes JR, Fine JM, Gordon T, Sheppard D. Potential bronchoconstrictor stimuli in acid fog. *Environ Health Perspect* **79**: 163, 1989.
- 4) Ostro BD, Lipset MJ, Wiener MB, Selner JC. Asthmatic response to airborne acid aerosols. *Am J Public Health* **81**: 694, 1991.
- 5) Thurston GD, Ito K, Lippmann M, Hayes C. Reexamination of London, England, mortality in relation to exposure to acidic aerosols during 1963–1971 winters. *Environ Health Perspect* **79**: 73, 1988.
- 6) Ware JH, Ferris BG, Dockery DW, Spengler JD, Stram DO, Speizer FE. Effects of ambient sulfur oxides and suspended particles on respiratory health of preadolescent children. *Am Rev Respir Dis* **133**: 834, 1986.
- 7) Bates DV, Sizto R. The Ontario air pollution study: Identification of the causative agent. *Environ Health Perspect* **79**: 69, 1989.
- 8) Fine JM, Gordon T, Sheppard D. The role of titrate acidity in acid aerosol-induced bronchoconstriction. *Am Rev Respir Dis* **135**: 826, 1987.
- 9) Koening JQ, Pierson WE, Horike M. The effect of inhaled sulfuric acid on pulmonary function in adolescent asthmatics. *Am Rev Respir Dis* **128**: 221, 1983.
- 10) Utell MJ. Effect of inhaled acid aerosols on lung mechanics: Analysis of human exposure studies. *Environ Health Perspect* **63**: 39, 1985.
- 11) Avol EL, Linn WS, Wightman LH, Whynot JD, Anderson KR, Hackney JD. Short term respiratory effects of sulfuric acid in fog: a laboratory study of healthy and asthmatic volunteers. *J Air Pollut Control Assoc* **38**: 258, 1988.
- 12) Linn WS, Avol EL, Anderson KR, Shamo DA, Peng RC, Hackney JD. Effect of droplet size on respiratory responses to inhaled sulfuric acid in normal and asthmatic volunteers. *Am Rev Respir Dis* **140**: 161, 1989.
- 13) Aris R, Christian D, Sheppard D, Balmes JR. Lack of bronchoconstrictor response to sulfuric acid aerosols and fogs. *Am Rev Respir Dis* **143**: 744, 1991.
- 14) Lenfant C. Global Initiative for Asthma. in: *Global Strategy for Asthma Management and Prevention* NHLBI/WHO Workshop Report. NIH Publication, 1995, p.59.
- 15) Ambient Air Quality Standards. in: *Quality of the Environment in Japan 1990*. Environment Agency, Government of Japan, Tokyo, 1990, p.480.
- 16) Mantel N, Haenzel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* **22**: 719, 1959.
- 17) Higgins BG, Francis HC, Yates CJ, Warburton CJ, Fletcher AM. Effects of air pollution on symptoms and peak expiratory flow measurements in subjects with obstructive airways disease. *Thorax* **50**: 149, 1995.
- 18) Glotfelty DE, Seiber JN, Liljedahl LA. Pesticides in fog. *Nature* **325**: 602, 1987.
- 19) Aris R, Christian D, Sheppard D, Balmes JR. Acid fog-induced bronchoconstriction. The role of hydroxymethanesulfonic acid. *Am Rev Respir Dis* **141**: 546, 1990.
- 20) Barbee RA. The epidemiology of asthma. *Monogr Allergy* **21**: 21, 1987.
- 21) Freed AN, Omori C, Hubbard WC, Adkinson NF Jr. Dry air- and hypertonic aerosol-induced bronchoconstriction and cellular responses in the canine lung periphery. *Eur Respir J* **7**: 1308, 1994.