



A Case-Control Study: Exposure Assessment of VOCs and Formaldehyde for Asthma in Children

Gyuseok Hwang¹, Chungsik Yoon², Jaewook Choi^{3*}

¹ Institute of Health and Environment, School of Public Health, Seoul National University, Seoul, Korea

² Department of Environmental Health, School of Public Health, Seoul National University, Seoul, Korea

³ Department of Preventive Medicine, College of Medical School, Korea University, Seoul, Korea

ABSTRACT

Based on the results of an ISAAC questionnaire, an asthma case group (33) and a control group (40) were selected in an elementary school in Seongbuk, Seoul. To determine the VOCs and formaldehyde levels of exposure, we performed personal, indoor, and outdoor sampling using passive samplers for 3 days.

In comparing the results of the levels of VOCs and formaldehyde exposure between the case and control groups, it was shown that toluene and *o*-xylene were higher in the case group in personal sampling and the benzene concentration was higher in the case group in indoor measurements ($p < 0.1$). In outdoor measurements, benzene and methylcyclohexane were higher in the case group ($p < 0.05$). The VOCs concentration was the highest in the personal sampling. However, the concentration of formaldehyde was the highest in indoor sampling ($p < 0.05$). In the multiple logistic regression, after adjusting residential and socioeconomic factors, there was no significant factors.

In conclusion, it was shown that the childhood asthma case group was exposed to higher VOCs than the control group, and it was found by measurement methods that VOCs in personal sampling were higher than the values obtained in indoor and outdoor measurements, and the formaldehyde value was the highest in indoor measurements.

Keywords: Asthma; Case-control; Children; Formaldehyde; VOCs; ETS.

INTRODUCTION

The prevalence of childhood asthma has increased in developed countries for the past 40–50 years and this phenomenon has also been shown to exist in developing countries (Eder *et al.*, 2006; Lee *et al.*, 2008). In Korea, it has been reported that the prevalence of childhood asthma was 5.6% in 1983 and > 10% in the late 1980s (Cho *et al.*, 2006). Although asthma and respiratory diseases may develop in all ages, it is one of the major factors causing non-attendance and inhibiting regular physical activities (Austin *et al.*, 2005).

For several decades, air pollution has spread and environmental quality has deteriorated as a result of industrialization and urbanization in Korea. It has been suggested that the environment plays an important role in respiratory symptoms and it has been reported in traditional studies that chemicals, such as VOCs and formaldehyde generated in the environment and tobacco smoke, are potential

risk factors for respiratory diseases (Wieslander *et al.*, 1997; Norback *et al.*, 1995; Burr *et al.*, 1999). However, the influence of VOCs and formaldehyde on childhood asthma is controversial. In a study conducted as a part of the worldwide European community respiratory health survey, it was reported that chemicals, such as formaldehyde and VOCs, cause inflammation of the airway and increased the risk of asthma by 50% (Wieslander *et al.*, 1999). Additionally, in a population-based control study conducted against children from 6 months to 3 years of age in Australia, it was reported that formaldehyde increased childhood asthma (Rumchev *et al.*, 2002). In a review of 21 epidemiologic surveys involving indoor residential chemical emissions, emission-related materials or activities, and respiratory health or allergies in infants or children, some strong associations have been reported between a number of risk factors and respiratory or allergic effects (Mendell, 2007). However, in another study on the residential environment of children, it was reported that the total VOCs were not the major determinant (Venn *et al.*, 2003). In addition, a review on the residential exposure to VOCs and asthma reported that observational studies have consistently found a relationship between VOCs and indicators of asthma, but interventional studies have generally failed to find a relationship between exposure to residential levels of formaldehyde and other

* Corresponding author. Tel.: +82-2-926-4704;
Fax: +82-2-920-6442
E-mail address: shine@korea.ac.kr

volatile organic compounds and asthma (Robert and Mark, 2004).

Therefore, this study determined the association between childhood asthma and air pollution exposure through personal, indoor, and outdoor measurements with investigation of residential environmental factors.

MATERIALS AND METHODS

Subject

This study surveyed the prevalence of asthma of students and their residential environment, lifestyle habits, and socioeconomic features against all grades of an elementary school located in Seongbuk-gu, Seoul through a questionnaire in May 2008. For the prevalence of asthma, self-reported asthma (SA) and physician-diagnosed asthma (PDA) were determined by the standardized international study of asthma and allergies in childhood (ISAAC) questionnaire (Asher *et al.*, 1995; Tsai *et al.*, 2006). The questionnaire was answered by the parents. Children who had asthma symptoms or were diagnosed with asthma by a physician were designated as the case group. By matching gender and age, the control group, who had no asthma symptoms or an asthma diagnosis, was selected. For measurement of exposure to air pollution for the children in the asthma case group and the control group, written messages were sent to their parents and the environmental pollution exposure was measured against children who submitted written consents. We selected controls matched for age and gender to the cases who were diagnosed. This study was reviewed and approved by the Board of the Korea University Hospital for the Protection of Research Subjects.

Exposure Assessment for VOCs and Formaldehyde

In the houses of the case and control groups, VOCs and formaldehyde concentrations were measured. For these measurements, researchers visited each home to install personal, indoor, and outdoor measurement equipment and provided instructions for personal measurement, such as always attaching the equipment to his/her body and placing the front side of the sampler face out. For the measurement of VOCs, a charcoal-based passive sampler (3M 3500, 3M, Ontario, Canada) was used. The measurement was conducted at three points by subjects. In order to assess personal exposure, the passive sampler was attached to the respiratory area of each child and for indoor and outdoor measurements of VOCs and formaldehyde, passive samplers were installed in the living room and veranda. The equipment for indoor measurement was installed 1 m above the floor and at least 30 cm out from the wall. Each sampling was performed for 3 working days (approximately 72 hr), not including weekends and holidays. During sleeping, the equipment for indoor measurement was suspended in the air distant from the wall or the floor near their head. For measurement of formaldehyde, a passive sampler (3M 3721, 3M, Ontario, Canada) was also used and the measurement method was the same for the VOCs.

Analysis for Chemicals

Nine common solvents (benzene, toluene, ethylbenzene, styrene, *m,p*-xylene, *o*-xylene, *n*-hexane, cyclohexane and

methylcyclohexane) were identified and quantified by the external standard technique. These VOCs were selected from previous studies and Korea indoor air quality management act (Norback *et al.*, 1990; Mendell, 2007; Ministry of Environment, 2008). The extraction solvent was carbon disulfide and all extracts were analyzed by gas chromatography (Agilent-6890 Plus; USA) with a flame ionization detector (HP 7683 series autosampler) using a supelco fused silica capillary column (30.0 m/250 μm i.d./1 μm). Analytical and internal standards were prepared, and VOC concentrations were calculated (Chung *et al.*, 1999a; Chung *et al.*, 1999b). The collection media for formaldehyde were 3M Model 3721 formaldehyde diffusion monitors, designed to measure the time-weighted average concentration of formaldehyde gas. Formaldehyde samples were analyzed by UV spectrophotometer (UV mini 1240; Shimadzu, Japan) at 580 nm, in accordance with NIOSH method 3500 (NIOSH, 1994).

Statistical Analysis

Demographic, socioeconomic, and residential environmental conditions between the case group and the control group were performed using chi-square analysis and a t-test. Visual examination of frequency distribution graphs indicates that the data are log-normally distributed, therefore the analysis results were converted in logarithm and geometric mean (GM) and standard deviation (GSD) were used in the statistical summary. For comparison of VOCs and formaldehyde concentrations between the case and control groups, a Student's t-test was conducted and ANOVA analysis was used for concentration comparison by measurement points, such as personal, indoor, and outdoor measurements. In addition, in order to investigate the association of the level of benzene known for one of the carcinogens in VOCs and formaldehyde with asthma in children, multiple logistic regression analysis was performed after considering residential and socioeconomic factors (e.g., gender, age, and income, academic background of parents and passive smoking). For statistical analysis, SPSS 12.0 was used.

RESULTS

Demographic Characteristics

A total of 1,005 (86.4%) of 1,163 students answered this residential environment and asthma prevalence survey; the SA was 129 (12.8%) and the PDA was 68 (6.8%). In the case group, the number of students who agreed to home visits and environmental measurements was 33. A total of 40 normal students agreed to the measurement and they were selected as the control group. The demographic data are shown in Table 1. Between the case and control groups, demographic factors (age, gender, and BMI) and socioeconomic factors (home income, parent's academic background, family history, and residential format) were compared and it was found that there was no significant difference between the two groups (Table 1).

In the survey on activity patterns of the subjects, it was found that they were indoors 88.0% of the time, and outdoors and in traffic 7.2% and 4.9% of the time, respectively. The

Table 1. Demographic characteristics of participants.

Variables		Case (%)	Control (%)	<i>p</i>
	N	33 (45.2)	40 (54.8)	-
Age (yr)	8–9	20 (60.6)	30 (75.0)	0.214
	10–13	13 (39.4)	10 (25.0)	
Sex	Male	22 (66.7)	20 (50.0)	0.164
	Female	11 (33.3)	20 (50.0)	
Parents' income (million KRW)	≤ 20	4 (19.0)	4 (17.4)	1.000
	>20	17 (81.0)	19 (82.6)	
Parents' academic background	High school	5 (22.7)	6 (23.1)	1.000
	College	17 (77.3)	20 (76.9)	
Family asthma history	Yes	18 (85.7)	26 (96.3)	0.306
	No	3 (14.3)	1 (3.7)	
Home ownership	Rented	14 (60.9)	19 (65.5)	0.778
	Own	9 (39.1)	10 (34.5)	
Type of house	Single family	2 (8.7)	4 (13.8)	0.682
	Multifamily	21 (91.3)	25 (86.2)	
House repair during last 12 months	Yes	12 (54.5)	14 (48.3)	0.779
	No	10 (45.5)	15 (51.7)	
Amount of house sunlight	Little	14 (60.9)	12 (41.4)	0.264
	Much	9 (39.1)	17 (58.6)	
Humidity of house	Much	13 (56.5)	20 (69.0)	0.397
	Little	10 (43.5)	9 (31.0)	
Distance from bus within 100 m	Yes	12 (54.5)	17 (58.6)	0.784
	No	10 (45.5)	12 (41.4)	
Passive smoking	Yes	12 (36.4)	7 (17.5)	0.107
	No	21 (63.6)	33 (82.5)	
	§BMI	18.2 (3.0)*	16.9 (3.0)*	0.110

§Student t-test, the others: chi-square test. * Mean (Standard Deviation)

time the subjects spent indoors in private homes was 60.6%, followed by school (19.7%) and other indoor places (7.5%) (Table 2).

VOCs and Formaldehyde Levels of Case and Control Groups

In a comparison of personal sampling results between the case and control groups, it was found that the concentrations of toluene and *o*-xylene in the case group were higher than the control group. The concentration of toluene in the case group (76.6 $\mu\text{g}/\text{m}^3$) was higher than the control group (49.6

$\mu\text{g}/\text{m}^3$) ($p = 0.07$), and the concentration of *o*-xylene in the case group (4.1 $\mu\text{g}/\text{m}^3$) was higher than the control group (2.6 $\mu\text{g}/\text{m}^3$) ($p = 0.06$).

In a comparison of indoor sampling results between the case and control groups, it was found that the benzene concentration of the case group was higher than that of the control group. Specifically, the concentration of benzene in the case and control groups was 2.8 $\mu\text{g}/\text{m}^3$ and 1.7 $\mu\text{g}/\text{m}^3$, respectively ($p = 0.08$).

In a comparison of outdoor sampling results between the case and control groups, the benzene and methylcyclohexane

Table 2. Daily time activity pattern for case and control groups (hour)

Variables	Total (N = 61) [Mean (SD) (%)]	Case (N = 28) [Mean (SD)]	Control (N = 33) [Mean (SD)]	<i>p</i>
Indoor Sum	66.1 (3.9) (87.8)	65.8 (4.3)	66.3 (3.5)	0.579
<i>Residential indoors</i>	45.6 (4.2) (60.6)	45.2 (4.2)	46.0 (4.3)	0.427
<i>School indoors</i>	14.8 (3.1) (19.7)	14.5 (2.8)	15.1 (3.4)	0.430
<i>Others indoors</i>	5.6 (3.6) (7.5)	6.1 (4.0)	5.2 (3.1)	0.306
Outdoor Sum	5.5 (3.8) (7.3)	6.1 (4.3)	5.0 (3.4)	0.264
<i>Residential outdoors</i>	2.4 (2.3) (3.2)	2.7 (2.6)	2.2 (2.0)	0.451
<i>School outdoors</i>	2.0 (2.5) (2.7)	2.3 (3.1)	1.8 (1.8)	0.422
<i>Others outdoors</i>	1.0 (1.4) (1.4)	1.1 (1.5)	1.0 (1.4)	0.699
Trans Sum	3.7 (2.3) (4.9)	4.1 (2.2)	3.4 (2.3)	0.225
<i>walk</i>	2.5 (2.1) (3.3)	2.8 (2.1)	2.2 (2.0)	0.197
<i>bicycle</i>	0.0 (0.1) (0.0)	0.0 (0.1)	0.0 (0.2)	0.736
<i>car & bus</i>	1.2 (1.3) (1.6)	1.3 (1.5)	1.2 (1.1)	0.911

concentrations in the case group were significantly higher than in the control group. The concentration of benzene in the case and control groups was 2.7 $\mu\text{g}/\text{m}^3$ and 1.6 $\mu\text{g}/\text{m}^3$, respectively ($p < 0.05$), and the concentration of methylcyclohexane in the case and control groups was 5.3 $\mu\text{g}/\text{m}^3$ and 3.4 $\mu\text{g}/\text{m}^3$, respectively ($p < 0.05$) (Table 3).

VOCs and Formaldehyde Levels by Personal, Indoor and Outdoor Samplings

In pollution measurements by measurement points (personal, indoors, and outdoors), it was shown that the measurement values of toluene, *o*-xylene, *n*-hexane, cyclohexane, and methylcyclohexane were higher (in order) in the personal, indoors, and outdoors measurements ($p < 0.05$). The analysis results of personal versus indoor (P/I), personal versus outdoor (P/O), and indoor and outdoor (I/O) ratios were as follows: toluene, 1.5, 2.2, and 1.5; *o*-xylene, 1.2, 1.6, and 1.4; *n*-hexane, 1.4, 1.5, and 1.1; cyclohexane, 1.5, 2.2, and 1.4; and methylcyclohexane, 1.2, 1.6, and 1.3, respectively. However, the concentration of formaldehyde showed different trends from the above-mentioned VOCs. It was found that the P/I, P/O, and I/O ratios of the formaldehyde measurement data were 0.8, 5.6, and 6.7, respectively, and it was shown that the value was highest in the indoor measurement, followed by personal and outdoor measurements in order (Table 4).

Predictors of Childhood Asthma

Associations between asthma and exposures to VOCs were examined using multiple logistic regression models. Potential confounding factors such as child's age, gender, family income, parents' academic background, and passive smoking were considered in the analysis. Having controlled for these potential confounding variables, there was no significant variable (Table 5).

DISCUSSION

This study was a survey on VOCs and formaldehyde exposure in childhood asthma case and control groups. For selection of the case and control groups, we used ISAAC questionnaire which was verified and could be compared internationally (Asher *et al.*, 1995), and residential environment, lifestyle habits, and socioeconomic factors associated with asthma in children were surveyed in reference to existing studies (Tsai *et al.*, 2006; Lin *et al.*, 2008). The selection of the case and control groups could be biased if case and control subjects came from different geographical locations. This bias was minimized in this study as both cases and controls were chosen from the Seongbuk, Seoul.

In comparison of VOCs and formaldehyde measurements between the case and control groups, it was found that the exposure concentration of benzene and methylcyclohexane of the case group in outdoor measurements were significantly higher than the results of the control group at the 5%

Table 3. The level of VOCs and formaldehyde for case and control groups ($\mu\text{g}/\text{m}^3$, GM (GSD)).

Variables	Personal		Indoor		Outdoor	
	Case (n = 33)	Control (n=40)	Case (n = 29)	Control (n=28)	Case (n = 26)	Control (n = 27)
Benzene	2.5 (2.6)	2.3 (3.2)	2.8 (2.6)*	1.7 (2.7)*	2.7 (2.1)**	1.6 (2.9)**
Toluene	76.6 (2.9)*	49.6 (2.6)*	46.1 (2.3)	37.0 (2.1)	32.1 (2.1)	24.1 (1.8)
Ethylbenzene	11.2 (2.4)	9.5 (2.0)	9.2 (2.4)	9.2 (1.8)	8.6 (2.4)	7.5 (2.0)
Stylene	4.9 (1.8)	5.1 (1.9)	4.7 (1.8)	3.8 (2.3)	4.3 (1.3)	4.1 (1.2)
<i>m,p</i> -xylene	17.3 (2.5)	14.4 (2.3)	13.8 (3.9)	13.3 (2.2)	13.3 (3.5)	12.1 (2.1)
<i>o</i> -xylene	4.1 (2.9)*	2.6 (2.7)*	3.1 (2.3)	2.4 (2.3)	2.3 (2.8)	1.7 (2.7)
<i>n</i> -hexane	6.7 (2.7)	5.9 (3.3)	5.1 (2.3)	3.9 (3.3)	4.7 (2.2)	3.7 (2.3)
Cyclohexane	8.9 (3.0)	7.4 (3.6)	5.3 (3.0)	5.2 (1.8)	4.1 (2.5)	3.3 (2.1)
Methylcyclohexane	6.7 (1.8)	6.6 (2.6)	5.4 (2.0)	5.1 (1.7)	5.3 (1.7)**	3.4 (2.4)**
Formaldehyde	26.8 (2.1)	28.6 (1.7)	30.9 (2.0)	36.1 (2.0)	5.7 (2.2)	4.4 (2.9)

* $p < 0.1$, ** $p < 0.05$, GM: Geometric Mean, GSD: Geometric Standard Deviation

Table 4. VOCs and formaldehyde level following sites ($\mu\text{g}/\text{m}^3$, GM (GSD)).

Variables	Personal	Indoor	Outdoor	P/I*	P/O**	I/O***
Benzene	2.4	2.2	2.1	1.1	1.1	1.1
Toluene	60.3	41.4	27.7	1.5	2.2	1.5
Ethylbenzene	10.3	9.2	8	1.1	1.3	1.2
Stylene	5	4.2	4.2	1.2	1.2	1.0
<i>m,p</i> -xylene	15.6	13.6	12.7	1.1	1.2	1.1
<i>o</i> -xylene	3.2	2.7	2	1.2	1.6	1.4
<i>n</i> -hexane	6.3	4.5	4.1	1.4	1.5	1.1
Cyclohexane	8.1	5.3	3.7	1.5	2.2	1.4
Methylcyclohexane	6.6	5.3	4.2	1.2	1.6	1.3
Formaldehyde	27.8	33.3	5.0	0.8	5.6	6.7

*P/I = Personal / Indoor, **P/O = Personal / Outdoor, ***I/O=Indoor/Outdoor

Table 5. Predictors of childhood asthma.

Variables	B	aOR	95% CI	<i>p</i>
Benzene	0.031	1.0	0.9–1.2	0.712
Formaldehyde	0.018	1.0	1.0–1.1	0.492
Age	–0.395	0.7	0.1–3.4	0.634
Gender	1.775	5.9	1.0–36.1	0.055
Family income	–1.422	0.2	0.0–3.1	0.275
Parents' academic background	1.998	7.4	0.7–79.8	0.100
Passive smoking	2.080	8.0	1.3–51.4	0.028

significance level. Viewing study for the case-control group performed in Australia, in a study on VOC measurements at a hospital involving toddlers (0.5–3 years of age) with asthma, it was found that the VOC concentration in the case group was significantly higher and there was a clear difference between the case and control groups (Rumchev *et al.*, 2004). One limitation of this study is short-term sampling. We used 3-day sampling values for assessment of exposure to chemicals. It is not likely that just a 3-day measurement represents the past exposure to the chemicals. The reason why we failed to find the association of asthma with VOCs and formaldehyde could have arisen from the representativeness of this short-term sampling for the past exposure. However in the current study, there was a tendency for a higher exposure concentration in the case group, but only some substances were significant at the 0.05 level. This means that there is an additional cause, other than VOC exposure, in the development of childhood asthma (Crain *et al.*, 1994; Wang *et al.*, 1999; Second international workshop, 1992).

The ratios of P/I, P/O, and I/O were different between VOCs and formaldehyde because they had different sources. In analysis results by measurement points, it was found that the measurement values of toluene, *o*-xylene, *n*-hexane, cyclohexane, and methylenecyclohexane were the highest in personal measurement and there were significant differences in order of indoor and outdoor concentrations. Other VOCs showed the highest values in personal measurement and higher values in order of indoor and outdoor measurements, although they were not statistically significant. These results agree well with the results of existing studies (Laia *et al.*, 2004). From these results showing the highest exposure values in personal measurement and personal activity pattern results, it is considered that the personal measurement is more important in exposure assessment of children than indoor or outdoor measurements. In other words, vehicular exhaust and industrial emissions are the major sources of ambient VOCs (Mayrsohn and Crabtree, 1976; Brocco *et al.*, 1997; Guo *et al.*, 2006), while the sources of VOCs are quite numerous within any indoor environment. Many studies demonstrate these sources, including combustion by-products, cooking, construction materials, furnishings, paints, varnishes and solvents, adhesives, office equipment, and consumer products (Guo *et al.*, 2000; Jarnstrom *et al.*, 2008; Tian *et al.*, 2008;). However, it was found that the concentration of formaldehyde was the highest in indoor and there was significant differences in order of personal and outdoor measurement. It seems that major sources of formaldehyde exist indoors (Garrett *et al.*, 1999).

Based on survey results of activity patterns by times for the subjects, it was found that the subjects spent 88.0% of the total time indoors, 7.2% of the time outdoors, and 4.9% of the time in traffic. Among the time spent indoors, the time in a private home was the greatest (60.6%), followed by school (19.7%), and other indoor places (7.5%). In a study involving students participating in the United States School Health Initiative: Environment, Learning, and Disease (SHIELD) study, it was found that the students spent 93.6% of the time indoors, with 65.3% of the time at home and 25.1% of the time in school (Adgate *et al.*, 2004). The indoor time was longer than the results of the current study, perhaps because the SHIELD study included the winter season in its survey period. The differences in climate between Korea and the US could influence the results of time activity patterns. According to a study involving adults in the United Kingdom for 48 hours, it was found that they spent 89.5% of the time indoors, 3.8% of the time outdoors, and 6.7% of the time in traffic, and among the time spent indoors, 68.6% of the time was spent at home and 17.5% of the time was in business settings (Laia *et al.*, 2004). Thus, the time the subjects in the current study spent indoors was similar and with respect to the children who attended a school nearby, they spent relatively little time in traffic.

CONCLUSION

In conclusion, it was shown that the child asthma case group was exposed to higher VOCs than the control group but there was no significant effects from VOCs and formaldehyde after adjusting confounding factors. It was found that VOCs in personal sampling was higher than the values obtained in indoor and outdoor measurements, and formaldehyde values were the highest in indoor measurements. Therefore, it seems that personal measurement should be considered for a proper evaluation.

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