Environmental Pollution 224 (2017) 698–705

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Positive association between short-term ambient air pollution exposure and children blood pressure in China–Result from the Seven Northeast Cities (SNEC) study☆

Xiao-Wen Zeng [a], Zhengmin (Min) Qian [b], Michael G. Vaughn [c], Erik J. Nelson [d], Shyamali C. Dharmage [e], Gayan Bowatte [e], Jennifer Perret [e], Duo-Hong Chen [f], Huimin Ma [g], Shao Lin [h], Benjamin de Foy [i], Li-Wen Hu [a], Bo-Yi Yang [a], Shu-Li Xu [a], Chuan Zhang [a], Yan-Peng Tian [a], Min Nian [a], Jia Wang [a], Xiang Xiao [a], Wen-Wen Bao [a], Ya-Zhi Zhang [a], Guang-Hui Dong [a, *]

[a] Guangzhou Key Laboratory of Environmental Pollution and Health Risk Assessment, Department of Preventive Medicine, School of Public Health, Sun Yat-sen University, Guangzhou 510080, China
[b] Department of Epidemiology, College for Public Health and Social Justice, Saint Louis University, Saint Louis 63104, USA
[c] School of Social Work, College for Public Health and Social Justice, Saint Louis University, Saint Louis 63104, USA
[d] Department of Epidemiology and Biostatistics, School of Public Health, Indiana University Bloomington, Bloomington, IN 47405, USA
[e] Allergy and Lung Health Unit, Melbourne School of Population and Global Health, University of Melbourne, Melbourne, Vic 3052, Australia
[f] Guangdong Environmental Monitoring Center, State Environmental Protection Key Laboratory of Regional Air Quality Monitoring, Guangdong Environmental Protection Key Laboratory of Atmospheric Secondary Pollution, Guangzhou 510308, China
[g] State Key Laboratory of Organic Geochemistry and Guangdong Key Laboratory of Environmental Protection and Resources Utilization, Guangzhou Institute of Geochemistry, Chinese Academy of Sciences, Guangzhou 510640, China
[h] Department of Epidemiology and Biostatistics, School of Public Health, State University of New York, Albany, NY 12144-3445, USA
[i] Department of Earth and Atmospheric Sciences, Saint Louis University, Saint Louis 63108, USA

ARTICLE INFO

Article history:
Received 21 October 2016
Received in revised form
21 January 2017
Accepted 21 February 2017
Available online 2 March 2017

Keywords:
Ambient air pollution
Blood pressure
Short-term exposure
Children
China

ABSTRACT

The impact of ambient air pollution on health causes concerns in China. However, little is known about the association of short-term air pollution exposure with blood pressure (BP) in children. The goal of present study was to assess the association between short-term air pollution and BP in children from a highly polluted area in China. This study enrolled 9354 children in 24 elementary and middle schools (aged 5–17 years) from the Seven Northeast Cities (SNEC) study, respectively, during the period of 2012–2013. Ambient air pollutants, including particulate matter with an aerodynamic diameter of ≤10 μm (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2) and ozone (O_3) on the days (1–5 days) preceding BP examination were collected from local air monitoring stations. Generalized additive models and two-level regression analyses were used to evaluate the relationship between air pollution and BP after adjusting for other covariates. Results showed that with an interquartile range (IQR) increase in PM_{10} (50.0 μg/m^3) and O_3 (53.0 μg/m^3) level during the 5-day mean exposure, positive associations with elevated BP were observed, with an odds ratio of 2.17 (95% CI, 1.61–2.93) for PM_{10} and 2.77 (95% CI, 1.94–3.95) for O_3. Both systolic BP and diastolic BP levels were positively associated with an IQR increase of four air pollutants at different lag times. Specifically, an IQR increase in the 5-day mean of PM_{10} and O_3 was associated with elevation of 2.07 mmHg (95% CI, 1.71–2.44) and 3.29 mmHg (95% CI, 2.86–3.72) in systolic BP, respectively. When stratified by sex, positive relationships were observed for elevated BP with NO_2 exposure only in males. This is the first report on the relationship between ambient short-term

☆ This paper has been recommended for acceptance by David Carpenter.

* Corresponding author. Guangzhou Key Laboratory of Environmental Pollution and Health Risk Assessment, Department of Preventive Medicine, School of Public Health, Sun Yat-sen University, 74 Zhongshan 2nd Road, Yuexiu District, Guangzhou 510080, China.
E-mail addresses: donggh5@mail.sysu.edu.cn, donggh512@hotmail.com (G.-H. Dong).

http://dx.doi.org/10.1016/j.envpol.2017.02.054

air pollution exposure and children BP in China. Findings indicate a need to control air pollutants and protect children from heavy air pollution exposure in China.

1. Introduction

Having an elevated blood pressure (BP) as a child is a risk factor for hypertension and CVD as an adult, therefore understanding the possible causes is imperative (Liang and Mi, 2011). Previous studies conducted concerning short-term or long-term exposure to air pollution have shown acute increases in BP among subjects, especially with regard to particulate matter [(PM) $\leq$ 2.5/10 μm in aerodynamic diameter ($PM_{2.5}$/PM_{10})] (Chan et al., 2015; Dong et al., 2013; Hoffmann et al., 2012; van Rossem et al., 2015). High blood pressure is a known risk factor for cardiovascular disease (CVD) in adults, however, little research has investigated the relationship between air pollution and blood pressure in children. There are varied results among the limited studies conducted to evaluate the effect of air pollution on BP in children. A cross-sectional study in Germany showed that long-term air pollution and BP among 2368 children (mean age of 10) are not consistently linked (Liu et al., 2014). On the other hand, long-term exposure to traffic-related air pollution, specifically NO_2 and $PM_{2.5}$, was shown to increase diastolic blood pressure among subjects of a birth cohort study conducted in the Netherlands (Bilenko et al., 2015). In another cohort study of 6–13 year olds living in high air pollution areas, they found significant links between short-term exposure (7 days exposure) to $PM_{2.5}$ and mean arterial pressure (Calderón-Garcidueñas et al., 2007). In addition, results from a different study in Pakistan found that children had higher systolic and diastolic BP (115.9/70.9 mm Hg) when exposed to short-term traffic pollution than children from lower air pollution areas (108.3/66.4 mm Hg) (Sughis et al., 2012).

Previous research showed that short-term elevated particulate matter is connected to increased risk of heart attack and stroke among adults, and our study in China revealed a higher risk of hypertension among children living in polluted cities (Dong et al., 2014). Nevertheless, there is still a knowledge gap regarding the relationship between short-term air pollution and BP in children (Peters et al., 2001; Dong et al., 2014). The aim of this investigation is to enhance the understanding of this association by studying an area with high pollution levels in China, which includes pollutants such as PM_{10}, ozone (O_3), sulfur dioxide (SO_2) and nitrogen dioxide (NO_2). The children in this study were recruited from the Seven Northeast Cities (SNEC) study (Dong et al., 2014).

2. Methods

2.1. Study population

This cross-sectional study investigates associations between ambient air pollution and a series of health outcomes in children. (see Dong et al., 2014 for additional description of the SNEC study). We studied the region of Liaoning province in Northeastern China starting from April 2012 to June 2013. Seven cities (Shenyang, Dalian, Anshan, Fushun, Benxi, Liaoyang, and Dandong) were selected based on their mean air pollution level data recorded between 2009 and 2011. These cities were selected to contrast the differences in inter- and intra-city ambient air pollution levels.

Two urban districts from Liaoyang, three from Anshan, Benxi, and Dandong, four from Fushun, four from Dalian, and five from Shenyang were selected for investigation. Each of the 24 districts had an elementary and middle school within 1 km of a municipal air monitoring station (48 schools in total). The final sample for this study (9354 children, n = 4771 males and n = 4583 females) included children who had lived in the district for more than 2 years prior to the study.

All study participants and parents of participants provided written informed consent. This research was conducted according to the World Medical Association Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects. The Human Studies Committee of Sun Yat-sen University has approved the study.

2.2. BP measurements

Trainees involved in the study were required to take a qualifying exam in order to obtain a BP observer certificate, and all investigators were trained based on the procedures of the American Academy of Pediatrics (National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, 2004). Study participants were encouraged not to drink coffee, or tea, and to abstain from exercise for at least 30 min prior to BP measurements. After resting for 5 min, participants should have seated with their back supported, feet on the floor and right arm supported, cubital fossa at heart level. The trainees measured the brachial artery BP on upper right arm of children using a standardized mercuric-column sphygmomanometer. This was done three times at 2 min intervals. We used the average of three measurements of BP as reported BP value. If average systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) was higher than the 95th percentile based on sex, age, and height, the child's blood pressure was considered elevated. This definition is based on guidelines from the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (2004).

2.3. Air pollution and meteorological data

Air monitoring stations, located away from major roads, industrial sources or residential sources of emissions, recorded hourly ambient concentrations of PM_{10}, SO_2, NO_2 and O_3 as well as daily mean temperature. Monitoring was performed according to standards set by the State Environmental Protection Administration of China (1992). PM_{10} was measured using beta-attenuation, SO_2 was measured using ultraviolet fluorescence, NO_2 was measured using chemiluminescence, and O_3 was measured using ultraviolet photometry. After excluding outliers, the data was composed of measurements from days where at least 75% of the 1-h values were available. We subsequently calculated each participant's exposure using 24-h average concentration of PM_{10}, SO_2 and NO_2, and 8-h daily mean O_3 (10:00 a.m. to 6:00 p.m.) at short-term exposure, 1–5 days preceding BP measurement in each district. Day 1 was set as the day BP was assessed.

2.4. Statistical analysis

After testing for normality using Shapiro-Wilks W-test and

testing for homogeneity using Bartlett's test for unequal variances, we utilized a generalized additive model to approximate the association of short-term air pollution exposure with BP. We a used a two-staged multiple regression model to determine the relationship between short-term air pollutants and the increase of elevated BP.

The model we used has been described elsewhere (Dong et al., 2014). Briefly, participants were the first-level units and districts were the second-level units. At the participant level, we modeled the logit of the prevalence of elevated BP as a function of k covariates ($X_1, \ldots, X_k$) as follows:

$$\text{logit}\left[\text{Probability}\left(Y_{ij}\right)\right] = \alpha_j + \beta_1 X_{1ij} + \ \ldots\ + \beta_k X_{kij} + e_{ij} \qquad (1)$$

where the outcome variable (Y) is elevated BP based on the BP diagnosis criteria described previously, the subscript i indicates the participant ($i = 1, \ldots, n_j$), the subscript j is for districts ($j = 1, \ldots, 24$), α_j is the intercept at the district level, $\beta_1 \ldots \beta_k$ are the regression coefficients of the covariates, and e_{ij} is the random error assumed to have means of zero and constant variance. In general, a district with a higher α_j predicts higher BP prevalence rate than a district with a lower α_j.

At the district level, we regressed the district-specific intercepts α_j on the district-specific pollutant level (Z_j) to explain the variations of α_j, as follows:

$$\alpha_j = \alpha + \gamma_j Z_j + u_j \qquad (2)$$

Equation (2) predicts the prevalence in a district by Z_j. If γ_j is positive, then adjusting for covariates, the prevalence of elevated BP is higher in districts with a higher pollutant levels. If γ_j is negative, then adjusting for covariates, the prevalence is lower in districts with a higher pollutant levels. The random error at the district level, u_j, is assumed to be independent and to follow a normal distribution with a mean of zero and constant variance. These random errors represent the between-district variation and are assumed independent from e_{ij} at the participant level. It should be noted that α, $\beta_1, \ldots, \beta_k$, and γ_j are not assumed to vary across districts. Therefore, they have no subscript j to indicate to which district they belong. They are therefore referred to as fixed effects as they apply to all districts.

We used a single regression (3) to simplify the above description by substituting model (2) into model (1):

$$\text{logit}\left[P\left(Y_{ij}\right)\right] = \left(\alpha + \gamma_j Z_j + \beta_1 X_{1ij} + \ldots + \beta_k X_{kij}\right) + \left(u_j + e_{ij}\right) \qquad (3)$$

We conducted data analyses using GLIMMIX in SAS version 9.4 (SAS Institute, Cary, North Carolina). All estimates adjusted for temperature age, sex, BMI, breast feeding, birth weight, exercise time, personal area, passive smoking exposure, parental education, family income, family history of hypertension, and district. All statistical tests were two-sided and an *a priori* *P*-value of less than 0.05 demonstrated statistical significance.

3. Results

In current study, a total of 10,428 children were selected originally from 24 districts of the seven cities, with 9567 children completing survey and examination (response rate: 97%). After excluding 213 children for not living in their current district for at least 2 years prior to the study, a total of 9354 children were selected in this investigation. Table 1 displays the study subjects' characteristics. Among the 5762 elementary school students, the prevalence rate of elevated BP was 10.1% for males and 10.8% for females. The rate of elevated BP among the 3592 middle schoolers was 20.1% for males and 18.2% for females. During the study period, daily ambient PM_{10} concentrations were 108.8 $\mu g/m^3$, which exceeded the 50 $\mu g/m^3$ Grade I level set forth by the Chinese National Ambient Air Quality Standards (Table 2). Ambient air pollutants, including PM_{10}, SO_2 and O_3, and temperature were correlated with each other ($P < 0.05$), such as PM_{10} correlate with O_3 positively ($r = 0.75$), and correlated with temperature negatively ($r = -0.54$).

We evaluated the relationship between short-term exposure to ambient air pollution and increased of elevated BP in children with a two-level binary logistics regression model, results of which can be seen in Table 3. There was no significant association between SO_2 and NO_2 and elevated BP in children, however we observed an associated between elevated BP and an increased IQR for PM_{10} and O_3. For all participants there was an increased of elevated BP. Each IQR increase in PM_{10} (ranged from 42.7 to 50.0 $\mu g/m^3$) and O_3 (ranged from 48.3 to 53.0 $\mu g/m^3$) during day 1 through day 5 of exposure was associated with an increased of elevated BP in children, and associations were more significant for O_3 (odds ratios, OR ranged from 2.59 to 2.85 for 1–5 day mean). There was a positive relationship for elevated BP with NO_2 exposure in males, with mean OR that ranged from 1.32 (95% CI, 1.00–1.73) to 1.45 (95% CI, 1.04–2.02) with each IQR increase during 1–5 day mean exposure, which was apparent when the population was stratified by sex (see Table 3). However, when stratified by schools, there is no significant interation between air pollution exposure and school types on the elevated BP (Table 4).

In Fig. 1 we see the relationship between short-term ambient air pollutant exposures and SBP and DBP. Short-term air pollutant exposure was positively associated with the change of BP levels at different lag times for all participants (Fig. 1). Both SBP and DBP tended to increase consistently with the levels of PM_{10} averaged over the 1–5 days before examination. Elevated PM_{10} and O_3 were more clearly linked to increase SBP in the model (Fig. 1.A). For example, in the single pollutant model, an IQR increase in ambient PM_{10} (47.4 $\mu g/m^3$) and O_3 (51.4 $\mu g/m^3$) in the previous 5-day mean exposure predicted an increase in SBP of 2.07 mmHg (95% CI, 1.71–2.44) and 3.29 mmHg (95% CI, 2.86–3.72), respectively (Fig. 1. A).

4. Discussion

Little information exists regarding the link between short-term exposure to ambient air pollutants and measured BP in children, even though many studies have evaluated the relationship in adults (Giorgini et al., 2016). To help close this knowledge gap, we investigated the association between short-term ambient air pollution and childhood blood pressure in China, using participants from the SNEC study. Our results suggest a positive association between air pollutants and both systolic and diastolic blood pressure.

It is clear that pediatric hypertension is a risk factor for elevated BP in adults and impacts heart and blood vessel health (Dwyer et al., 2013). Therefore, it is important to identify possible causes of pediatric hypertension and take early intervention properly (Rao, 2016).

Based on a systematic Medline search, we believe this study is the first to report the association between short-term ambient air pollution and BP in children in China. For other countries, four previous studies reported on the association between short-term air pollution exposure and BP in children (Bilenko et al., 2015; Calderón-Garcidueñas et al., 2007; Pieters et al., 2015; Sughis et al., 2012). Our findings are consistent with two other studies. A cross-sectional study (n = 179) out of Pakistan found a higher SBP

Table 1
Characteristics of the children in the Chinese Seven Northeast Cities Study (SNEC), 2012–2013.

Characteristics	Elementary school		Middle school	
	Males (n = 3006)	Females (n = 2756)	Males (n = 1765)	Females (n = 1827)
Age (years)[a]	9.4 ± 2.0	9.3 ± 1.9	13.5 ± 1.2	13.3 ± 1.1
Height (cm)[a]	141.7 ± 12.4*	140.7 ± 12.7	167.1 ± 8.6*	160.1 ± 5.8
BMI (kg/m^2)[b]	19.1 ± 4.2*	17.7 ± 3.4	21.9 ± 4.9*	20.7 ± 3.8
Low birth weight (%)	93 (3.1)*	113 (4.1)	56 (3.17)*	86 (4.7)
Premature birth (%)	169 (5.6)	151 (5.5)	86 (4.9)	88 (4.8)
Breast feeding (%)	2006 (66.7)*	1907 (69.2)	1194 (67.7)*	1365 (74.7)
Family history of hypertension (%)	1084 (36.1)*	1107 (40.1)	679 (38.5)	729 (39.9)
Parental education ≥ high school (%)	1985 (66.0)	1818 (66.0)	1101 (62.4)	1172 (64.2)
Income per year				
≤5000 RMB (%)[c]	318 (10.6)	319 (11.6)	206 (11.7)	189 (10.3)
5000–10,000 RMB (%)	400 (13.3)	368 (13.4)	208 (11.8)	235 (12.9)
10,000–30,000 RMB (%)	1039 (34.6)	945 (34.3)	614 (34.8)	632 (34.6)
30,000–100,000 RMB (%)	1105 (36.8)	979 (35.5)	659 (37.3)	698 (38.2)
>100,000 RMB (%)	144 (4.8)	145 (5.3)	78 (4.4)	73 (4.0)
Passive smoking exposure				
None (%)	1567 (52.1)	1388 (50.0)	942 (53.4)	971 (53.2)
Father smoking (%)	883 (29.4)	860 (31.2)	560 (31.7)	607 (33.2)
Mother smoking (%)	268 (8.9)	245 (8.9)	141 (8.0)	136 (7.4)
Others (%)	288 (9.6)	263 (9.5)	122 (6.9)	113 (6.2)
Home coal use (%)	292 (9.7)	249 (9.0)	170 (9.6)	177 (9.7)
Walking time from home to school (min)	14.5 ± 9.3*	13.9 ± 8.8	17.4 ± 10.3	16.8 ± 9.9
Personal area (m^2/person)	22.6 ± 9.7	22.1 ± 9.9	23.6 ± 12.5*	22.7 ± 8.9
Excise time (hour/week)	8.5 ± 8.3*	7.7 ± 8.0	7.0 ± 6.9	6.6 ± 7.0
Elevated BP (%)[d]	305 (10.1)	297 (10.8)	354 (20.1)	333 (18.2)

*indicates significance comparisons between males and females at $P < 0.05$, performed with *t*tests.
[a] Variables: Mean ± SD.
[b] BMI = Body mass index.
[c] RMB = Renminb: the official currency of the People's Republic of China; the baseline of poverty in China: 2300 RMB/person/year.
[d] BP = Blood pressure.

Table 2
Summary statistics and Spearman correlation of daily mean air pollutant levels and meteorological variable in the 24 districts of seven cities, China, 2012–2013.

Exposure	Summary statistics					*r*			
	Mean	Median	Max	Min	Interquartile range	SO_2	NO_2	O_3	Temperature
PM_{10} (μg/m^3)	108.8	108.6	189.0	45.2	47.4	0.35*	0.31*	0.75*	−0.54*
SO_2 (μg/m^3)	30.2	24.6	80.4	4.4	22.8	1.00	0.54*	0.30*	−0.34*
NO_2 (μg/m^3)	26.9	25.5	64.0	3.6	18.6		1.00	0.26	−0.14
O_3 (μg/m^3)	69.0	69.4	132.4	19.0	51.4			1.00	−0.57*
Temperature (°C)	14.2	15.3	24.0	1.5	10.0				1.00

*$P < 0.05$.

(115.9 mm Hg, 95% CI: 114.0–117.9 mmHg) and DBP (66.4 mm Hg, 95% CI: 64.4–68.4 mm Hg) in 10-year-old children (8–12 years old) living in areas with heavy traffic air pollution (mean daily value of $PM_{2.5}$: 183.0 μg/m^3) than in children living in areas with less traffic air pollution (mean daily value of $PM_{2.5}$: 28.5 μg/m^3) (Sughis et al., 2012). Additionally, a significant association between short-term (7-day) cumulative $PM_{2.5}$ levels and mean pulmonary arterial pressure and systolic pulmonary arterial pressure in 59 children (6–13 years old) living in Mexico City exposed to high air pollution levels was observed by Calderón-Garcidueñas et al. (2007). However, two studies came to conclusions that are inconsistent with what we found. In the PIMA study, a birth cohort consisting of 1432 children 12 years of age in the Netherlands evaluated different long-term exposure and short-term exposure to traffic-related air pollution conditions (Bilenko et al., 2015). While there was no relationship with short-term air pollution, long-term exposure to NO_2 and $PM_{2.5}$ may increase DBP (adjusted mean difference 0.83 mm Hg, 95% CI: 0.06 to 1.61 for NO_2 and 0.75 mm Hg, 95% CI: −0.08 to 1.58 for $PM_{2.5}$) (Bilenko et al., 2015). A Belgian study of 130 children (6–12 years old) showed that an IQR (860 particles/cm^3) increase in nano-sized ultra-fine PM fraction (20–30 nm) was associated with a 6.35 mm Hg (95% CI: 1.56, 11.14; P = 0.01) increase in SBP, but no effects on SBP or DBP were found for $PM_{2.5}$ (Pieters et al., 2015). The inconsistence findings from these four available published studies may likely due to different methodological design in investigation, including different geographical regions (North America, Europe and Asia), exposure concentration (low and high exposure levels), BP measurement devices (auto device and mercury sphygmomanometer) as well as population characteristics. For example, air pollutant levels in panel study conducted by Calderón-Garcidueñas et al. (2007) were collected from government atmospheric monitoring system (same as our study) while air pollutant concentrations in PIMA study reported by Bilenko et al. (2015) were estimated by Land-Use Regression models. In addition, the range of air pollutant exposure level may also contribute to the observed health outcome. Take PM_{10} for example, the ambient PM_{10} level in our study (mean:108.8 μg/m^3) and study from Sughis et al. (2012) (mean: 223.0 μg/m^3 for low pollution area and 728.6 μg/m^3 for high pollution area) were much higher than that reported by Bilenko et al. (2015) (mean: 24.7 μg/m^3) and Pieters et al. (2015).

Some evidence have suggested that higher risks occur in longer-term pollutants exposure than shorter-term exposure (Brook et al., 2010). We then compared this study with Dong et al. (2014) which

Table 3
Adjusted OR and 95% CI for the elevated BP related to short-term exposure to air pollutants stratified by sex.

Exposure	IQR of exposure	Males (n = 4771) OR (95% CI)[a]	Females (n = 4583) OR (95% CI)[a]	Total (n = 9354) OR (95% CI)[a]	Interaction *p*-value
PM_{10} (μg/m^3)					
1-day mean	50.0	1.88 (1.39–2.55)	1.73 (1.27–2.34)	1.80 (1.34–2.42)	0.311
2-day mean	43.5	1.79 (1.36–2.36)	1.72 (1.30–2.27)	1.76 (1.34–2.30)	0.589
3-day mean	42.7	2.05 (1.51–2.71)	1.89 (1.42–2.50)	1.97 (1.50–2.58)	0.284
4-day mean	45.0	2.08 (1.55–2.80)	1.99 (1.48–2.68)	2.03 (1.53–2.71)	0.560
5-day mean	47.4	2.22 (1.63–3.03)	2.11 (1.55–2.89)	2.17 (1.61–2.93)	0.558
SO_2 (μg/m^3)					
1-day mean	23.0	1.23 (0.96–1.58)	1.21 (0.95–1.55)	1.22 (0.96–1.55)	0.777
2-day mean	21.5	1.21 (0.97–1.51)	1.20 (0.96–1.49)	1.20 (0.97–1.49)	0.820
3-day mean	18.7	1.18 (0.96–1.44)	1.17 (0.96–1.43)	1.17 (0.97–1.43)	0.875
4-day mean	22.0	1.20 (0.94–1.55)	1.21 (0.94–1.55)	1.21 (0.94–1.54)	0.966
5-day mean	22.8	1.20 (0.92–1.57)	1.21 (0.93–1.58)	1.21 (0.93–1.56)	0.925
NO_2 (μg/m^3)					
1-day mean	18.0	1.33 (1.01–1.76)	1.17 (0.89–1.54)	1.25 (0.96–1.63)	0.055
2-day mean	18.5	1.32 (1.00–1.73)	1.15 (0.87–1.52)	1.23 (0.94–1.61)	0.065
3-day mean	20.0	1.40 (1.03–1.33)	1.16 (0.88–1.40)	1.28 (0.93–1.76)	**0.037**
4-day mean	19.8	1.45 (1.04–2.02)	1.19 (0.85–1.66)	1.32 (0.95–1.81)	**0.023**
5-day mean	18.6	1.38 (1.00–1.91)	1.15 (0.83–1.59)	1.26 (0.92–1.73)	**0.030**
O_3 (μg/m^3)					
1-day mean	53.0	2.57 (1.82–3.64)	2.61 (1.85–3.69)	2.59 (1.86–3.61)	0.882
2-day mean	52.0	2.84 (2.02–4.00)	2.75 (1.96–3.87)	2.80 (2.02–3.88)	0.7481
3-day mean	51.3	2.88 (1.99–4.18)	2.82 (1.94–4.08)	2.85 (1.99–4.08)	0.819
4-day mean	48.3	2.70 (1.91–3.81)	2.70 (1.91–3.81)	2.70 (1.94–3.76)	0.995
5-day mean	51.4	2.76 (1.91–4.00)	2.77 (1.92–4.01)	2.77 (1.94–3.95)	0.982

IQR, Interquartile range; OR, odds ratio; CI, confidence interval; BP, blood pressure.
All estimates adjusted for temperature age, sex, BMI, breast feeding, birth weight, exercise time, personal area, passive smoking exposure, parental education, family income, family history of hypertension, and district.
[a] OR was scaled to the IQR for each pollutant. The number in bold indicates the interaction of *p*-value < 0.05.

Table 4
Adjusted OR and 95% CI for the elevated BP related to short-term exposure to air pollutants stratified by school.

Exposure	IQR of exposure	Elementary school (n = 4771) OR (95% CI)[a]	Middle school (n = 4583) OR (95% CI)[a]	Interaction *p*-value
PM_{10} (μg/m^3)				
1-day mean	50.0	1.82 (1.22–2.73)	1.72 (1.12–2.64)	0.841
2-day mean	43.5	1.92 (1.31–2.81)	1.60 (1.13–2.27)	0.459
3-day mean	42.7	2.43 (1.61–3.67)	1.67 (1.19–2.34)	0.147
4-day mean	45.0	2.52 (1.65–3.84)	1.71 (1.20–2.44)	0.142
5-day mean	47.4	2.67 (1.75–4.08)	1.78 (1.22–2.61)	0.135
SO_2 (μg/m^3)				
1-day mean	23.0	1.01 (0.67–1.53)	1.33 (0.99–1.77)	0.289
2-day mean	21.5	1.07 (0.70–1.63)	1.23 (0.96–1.58)	0.574
3-day mean	18.7	1.06 (0.73–1.54)	1.21 (0.96–1.52)	0.568
4-day mean	22.0	1.06 (0.67–1.69)	1.25 (0.97–1.66)	0.555
5-day mean	22.8	1.05 (0.65–1.68)	1.26 (0.93–1.72)	0.506
NO_2 (μg/m^3)				
1-day mean	18.0	1.12 (0.67–1.87)	1.27 (0.93–1.75)	0.675
2-day mean	18.5	1.26 (0.75–2.12)	1.18 (0.86–1.64)	0.853
3-day mean	20.0	1.18 (0.67–2.10)	1.27 (0.85–1.91)	0.834
4-day mean	19.8	1.26 (0.70–2.28)	1.28 (0.86–1.91)	0.966
5-day mean	18.6	1.23 (0.70–2.16)	1.23 (0.83–1.82)	0.999
O_3 (μg/m^3)				
1-day mean	53.0	3.24 (2.03–5.18)	2.12 (1.40–3.23)	0.151
2-day mean	52.0	3.40 (2.18–5.31)	2.32 (1.54–3.50)	0.170
3-day mean	51.3	3.33 (2.10–5.28)	2.34 (1.46–3.75)	0.240
4-day mean	48.3	3.05 (2.01–4.65)	2.25 (1.43–3.55)	0.283
5-day mean	51.4	3.17 (2.00–5.04)	2.29 (1.41–3.71)	0.291

IQR, Interquartile range; OR, odds ratio; CI, confidence interval; BP, blood pressure.
All estimates adjusted for temperature, age, sex, BMI, breast feeding, birth weight, exercise time, personal area, passive smoking exposure, parental education, family income, family history of hypertension, and district.
[a] OR was scaled to the IQR for each pollutant.

investigate the association between long-term exposure of air pollutant and BP in the same population. For PM_{10}, both of us revealed that exposure to PM_{10} was associated with elevated BP in the SNEC study. Higher increasing of elevated BP in association with IQR increment to PM_{10} was found in males (OR: 1.79–2.22 for 1-d to 5-d mean) in our study compared to that in long-term exposure (OR: 1.55) (Dong et al., 2014). For O_3, our result also found stronger positive association with elevated BP (OR: 2.59–2.85 for 1-d to 5-d mean) than that reported in long-term exposure study (OR: 1.12 for males and 1.11 for females) by Dong et al. (2014). For SO_2,

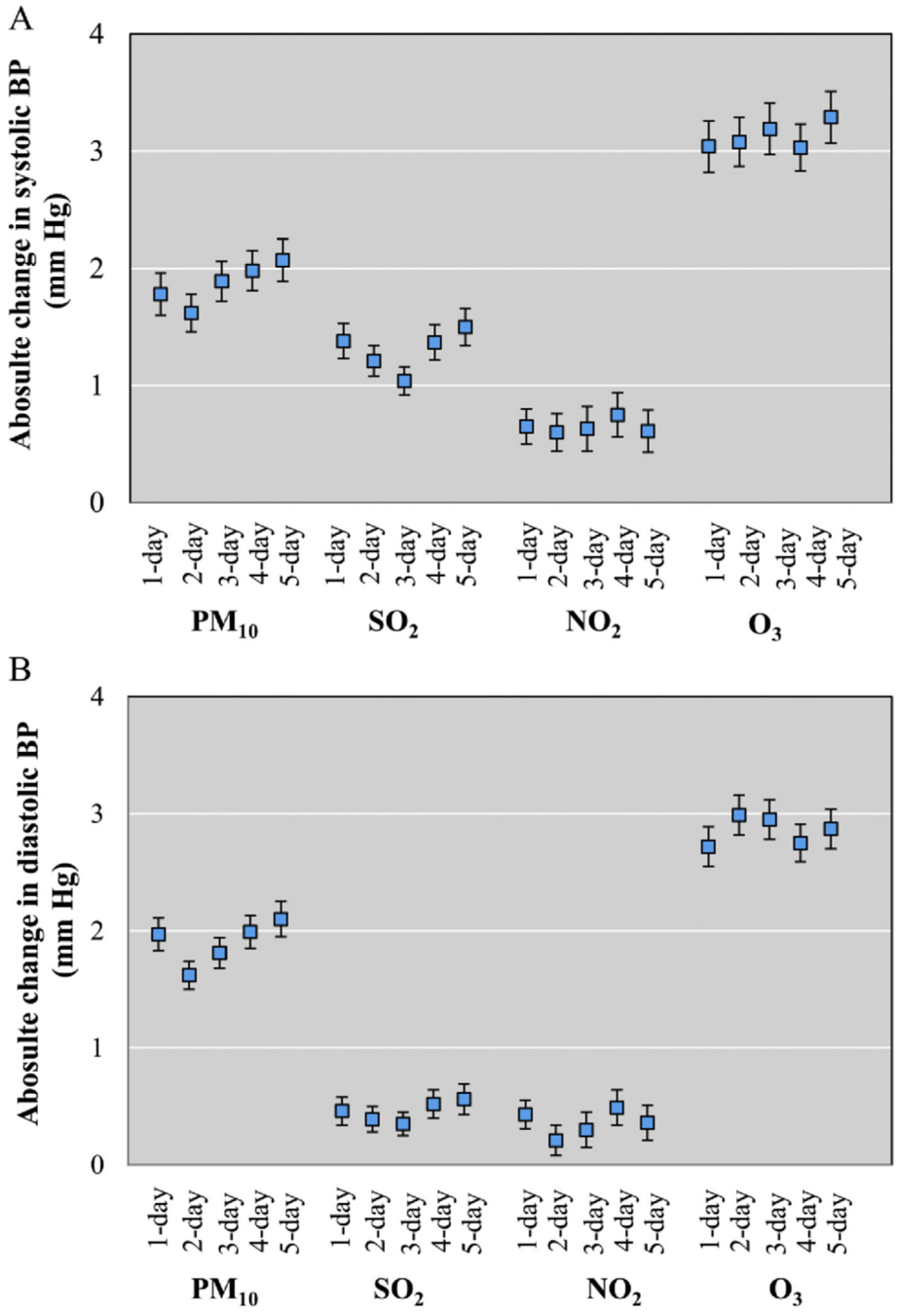

Fig. 1. Estimated absolute increase of (A) SBP (mm Hg) and (B) DBP (mm Hg) related to short-term increase of air pollutants, per IQR of the exposure metric. All estimates adjusted for temperature, age, sex, BMI, breast feeding, birth weight, exercise time, passive smoking exposure, parental education, family income, family history of hypertension, and district. Error bars indicate the standard errors.

Dong et al. (2014) found a significant association between long-term SO_2 exposure and elevated BP (OR: 1.32 for males and 1.35 for females), whereas our current study did not see the relationship between SO_2 with elevated BP. Findings in long-term and short-term pollutants exposure in the SENC study concordantly suggest harmful sequences on BP level after PM_{10} exposure. The positive association between O_3 exposure and elevated BP seems more obvious in children for short-term exposure in the SNEC study.

A pro-hypertensive response mediated by air pollution is a hypothesized pathway that links air pollution and hypertension (Brook et al., 2009). Mechanistic evidence supports that air pollutants can mediate increase of BP driven by increased arterial vasoconstrictor responsiveness due to endothelial dysfunction, oxidative stress, and inflammation (Giorgini et al., 2016). Endothelial dysfunction may contribute to increased systemic vascular resistance, thus leading to the development of hypertension, probably due to impaired endothelium-dependent vasodilation (Dinh et al., 2014). In addition, oxidative and inflammation play central role in the pathogenesis of endothelial dysfunction, therefore, affect hemodynamic responses (Giorgini et al., 2016). Experimental studies have demonstrated that exposure to PM and O_3 promote vascular dysfunction and oxidative stress, producing significant inflammation and injury to epithelial cells and inducing elevated atherogenesis (Brook et al., 2010; Chuang et al., 2009).

Besides, Breton et al. (2016) demonstrated the relationship between childhood O_3 exposure and elevated subclinical atherosclerosis in 861 college students averaging 20-years old from the University of Southern California. We recommend additional research to understand the mechanisms by which key molecular evens air pollution leads to hypertension.

We observed that males were more vulnerable to NO_2 exposure than females, which is in line with epidemiological evidence that associations between air pollution and health effects for males and females are different (Clougherty, 2010). Children may have different reactions to air pollution due to differences in lung function and the stage of lung development (Keitt et al., 2004), thus sex effects may be more complex. In a prospective cohort study in Poland, stronger associations were seen in males compared to females between SO_2 and total suspended particle (TSP) (Jedrychowski et al., 1999). Further exhibiting this difference, respiratory hospitalizations were associated with PM_{10} among males and with NO_2 among females in a Canadian case-crossover study (Lin et al., 2005). Greater airway resistance and lower respiratory volumes found in male children may affect this association (Bjornson and Mitchell, 2000). Smooth muscle function, vascular function, and hormonal levels may also influence sex-related susceptibility to air pollution effects on respiratory infections (Lin et al., 2005). In addition, gendered activities may also shape pollution response as demonstrated by a study in which males had longer outdoor physical activity time compared with females, especially for elementary school males (8.5 ± 8.3 h, Table 1). Different responses to air pollution may be due to societal factors.

The large sample size, which covered 24 districts in Northeastern China, is a strength of this study. The sample size of 9354 children, is one of the largest published studies evaluating the association between children's blood pressure and ambient air pollution. Furthermore air pollution concentrations were monitored across seven cities. For these reasons, our results may provide more robust conclusions on the health effects of ambient air pollution exposure even though we cannot establish causation that air pollution exposure increases BP levels due to the cross-sectional design of the study. Several possible exposure misclassification have to be noted. There is the possibility of inaccuracies in the exposure estimates due to the use of data from the existing municipal air monitoring stations. The lack of residential exposure assessments, including indoor air pollution measurement, traffic-related air pollution together with traffic noise which could have affected the observed outcome were the major limitations in this study. In addition, the mercury sphygmomanometer devices used in current study is prone to errors induced by the observer's bias toward particular digits. However, our BP observers were well trained nurses so that the possible bias could be minimized. Finally, we observed inter-correlation between PM_{10}, SO_2, NO_2 and O_3 level in current study. Therefore, we could only get the single-pollutant model analysis since it would be inappropriate to fit these four air pollutants in multi-pollutants model.

5. Conclusion

Little is known about the effect of short-term air pollution on BP in children compared to adults, especially in highly polluted areas. Our aim was to examine the association between short-term effects of air pollution, including PM_{10}, O_3, SO_2 and NO_2 and BP in school-aged children from the Seven Northeast Cities (SNEC) study. To our knowledge, this is the first study to report evidence that short-term ambient air pollution is positively associated with elevated BP in Chinese children. These findings suggest that control of air pollutants and initiation of efforts to protect children from heavy air pollution exposure in China should be a priority.

Source of funding

This research was supported by grants from the National Key Research and Development Program of China (2016YFC0207000), the Fundamental Research Funds for the Central Universities (No. 16ykzd02), and the Guangdong Province Natural Science Foundation (2014A050503027, 2016A030313342). The views expressed in this article are those of the authors and do not necessarily represent those of the funding source. The funding source had no role in the design or analysis of the study publication.

Acknowledgement

We thank the school principals, teachers, and students and their parents in the seven cities for their cooperation.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.envpol.2017.02.054.

References

Bilenko, N., Rossem, Lv, Brunekreef, B., Beelen, R., Eeftens, M., Hoek, G., et al., 2015. Traffic-related air pollution and noise and children's blood pressure: results from the piama birth cohort study. Eur. J. Prev. Cardiol. 22, 4–12.
Bjornson, C., Mitchell, I., 2000. Gender differences in asthma in childhood and adolescence. J. Gend. Specif. Med. 3, 57–61.
Breton, C.V., Mack, W.J., Yao, J., Berhane, K., Amadeus, M., Lurmann, F., et al., 2016. Prenatal air pollution exposure and early cardiovascular phenotypes in young adults. PloS One 11, e0150825.
Brook, R.D., Urch, B., Dvonch, J.T., Bard, R.L., Speck, M., Keeler, G., et al., 2009. Insights into the mechanisms and mediators of the effects of air pollution exposure on blood pressure and vascular function in healthy humans. Hypertension 54, 659–667.
Brook, R.D., Rajagopalan, S., Pope, C.A., Brook, J.R., Bhatnagar, A., Diez-Roux, A.V., et al., 2010. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the american heart association. Circulation 121, 2331–2378.
Calderón-Garcidueñas, L., Vincent, R., Mora-Tiscareño, A., Franco-Lira, M., Henríquez-Roldán, C., Barragán-Mejía, G., et al., 2007. Elevated plasma endothelin-1 and pulmonary arterial pressure in children exposed to air pollution. Environ. Health Perspect. 115, 1248–1253.
Chan, S.H., Van Hee, V.C., Bergen, S., Szpiro, A.A., DeRoo, L.A., London, S.J., et al., 2015. Long-term air pollution exposure and blood pressure in the sister study. Environ. Health Perspect. 123, 951–958.
Chuang, G.C., Yang, Z., Westbrook, D.G., Pompilius, M., Ballinger, C.A., White, C.R., et al., 2009. Pulmonary ozone exposure induces vascular dysfunction, mitochondrial damage, and atherogenesis. Am. J. Physiol. - Lung Cell. Mol. Physiol. 297, L209–L216.
Clougherty, J.E., 2010. A growing role for gender analysis in air pollution epidemiology. Environ. Health Perspect. 118, 167–176.
Dinh, Q.N., Drummond, G.R., Sobey, C.G., Chrissobolis, S., 2014. Roles of inflammation, oxidative stress, and vascular dysfunction in hypertension. BioMed Res. Int. 2014 (2014), 406960.
Dong, G.-H., Qian, Z., Xaverius, P.K., Trevathan, E., Maalouf, S., Parker, J., et al., 2013. Association between long-term air pollution and increased blood pressure and hypertension in China. Hypertension 61, 578–584.
Dong, G.-H., Qian, Z., Trevathan, E., Zeng, X.-W., Vaughn, M.G., Wang, J., et al., 2014. Air pollution associated hypertension and increased blood pressure may be reduced by breastfeeding in chinese children: the seven northeastern cities Chinese children's study. Int. J. Cardiol. 176, 956–961.
Dwyer, T., Sun, C., Magnussen, C.G., Raitakari, O.T., Schork, N.J., Venn, A., et al., 2013. Cohort profile: the international childhood cardiovascular cohort (i3c) consortium. Int. J. Epidemiol. 42, 86–96.
Giorgini, P., Di Giosia, P., Grassi, D., Rubenfire, M., Brook, R.D., Ferri, C., 2016. Air pollution exposure and blood pressure: an updated review of the literature. Curr. Pharm. Des. 22, 28–51.
Hoffmann, B., Luttmann-Gibson, H., Cohen, A., Zanobetti, A., de Souza, C., Foley, C., et al., 2012. Opposing effects of particle pollution, ozone, and ambient temperature on arterial blood pressure. Environ. Health Perspect. 120, 241–246.
Jedrychowski, W., Flak, E., Mróz, E., 1999. The adverse effect of low levels of ambient air pollutants on lung function growth in preadolescent children. Environ. Health Perspect. 107, 669–674.
Keitt, S.K., Fagan, T.F., Marts, S.A., 2004. Understanding sex differences in environmental health: a thought leaders' roundtable. Environ. Health Perspect. 112, 604–609.
Liang, Y., Mi, J., 2011. Pubertal hypertension is a strong predictor for the risk of adult

hypertension. Biomed. Environ. Sci. 24, 459–466.
Lin, M., Stieb, D.M., Chen, Y., 2005. Coarse particulate matter and hospitalization for respiratory infections in children younger than 15 years in toronto: a case-crossover analysis. Pediatrics 116, e235–e240.
Liu, C., Fuertes, E., Tiesler, C.M.T., Birk, M., Babisch, W., Bauer, C.-P., et al., 2014. The associations between traffic-related air pollution and noise with blood pressure in children: results from the giniplus and lisaplus studies. Int. J. Hyg. Environ. Health 217, 499–505.
National high blood pressure education program working group on high blood pressure in children and adolescents, 2004. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents Pediatrics, 114 (2 Suppl. 4th Report), 555–576.
Peters, A., Dockery, D.W., Muller, J.E., Mittleman, M.A., 2001. Increased particulate air pollution and the triggering of myocardial infarction. Circulation 103, 2810–2815.
Pieters, N., Koppen, G., Van Poppel, M., De Prins, S., Cox, B., Dons, E., et al., 2015. Blood pressure and same-day exposure to air pollution at school: associations with nano-sized to coarse pm in children. Environ. Health Perspect. 123, 737–742.
Rao, G., 2016. Diagnosis, epidemiology, and management of hypertension in children. Pediatrics 138. http://dx.doi.org/10.1542/peds.2015-3616.
State Environmental Protection Administration of China (SEPA), 1992. Standardized Environmental Monitoring and Analysis Methods (Beijing, China).
Sughis, M., Nawrot, T.S., Ihsan-ul-Haque, S., Amjad, A., Nemery, B., 2012. Blood pressure and particulate air pollution in schoolchildren of lahore, Pakistan. BMC Public Health 12, 1–8.
van Rossem, L., Rifas-Shiman, S.L., Melly, S.J., Kloog, I., Luttmann-Gibson, H., Zanobetti, A., Coull, B.A., et al., 2015. Prenatal air pollution exposure and newborn blood pressure. Environ. Health Perspect. 123, 353–359.