Acta Cardiol Sin 2017;33:66–73

Original Article doi: 10.6515/ACS20160118B

General Cardiology

A Case-Crossover Study between Fine Particulate Matter Elemental Composition and Emergency Admission with Cardiovascular Disease

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Background: It is generally understood that Fine Particulate Matter ($PM_{2.5}$) can cause high blood pressure. However, it remains unclear whether there is a relationship between the elemental composition of $PM_{2.5}$ and cardiovascular disease in emergency department patients.

Methods: Crossover design for time stratified cases and conditional logistic regression were used to analyze the correlation between emergency admissions for cerebral hemorrhage, cerebral infarction, TIA (Transient ischemic attack), coronary heart disease and $PM_{2.5}$, concentrations of chemical element compositions, and Particulate Matter 10 (PM_{10}) in Changsha city.

Results: When the temperature, atmosphere pressure, maximum wind speed, NO_2 and SO_2 were adjusted, the OR (Odd Ratio) of cerebral hemorrhage was 1.177 [95% confidence interval (CI): 1.006-1.376, p = 0.04] with every10 $\mu g/m^3$ increase of $PM_{2.5}$. PM_{10} was unrelated to cardiovascular emergencies ($p > 0.05$). In addition, with each additional IQR (Interquartile Range) increase of Ni, Zn and Pb concentrations in $PM_{2.5}$, the values of OR were 1.826 (95% CI: 1.031-3.233), 1.568 (95% CI: 1.015-2.423) and 1.682 (95% CI: 1.010-2.800), respectively.

Conclusions: Concentration rises of nickel, zinc and lead elements for $PM_{2.5}$ in Changsha city were related to the increase of emergency admissions with cerebral hemorrhage.

Key Words: Cerebral hemorrhage • Emergency admission • Fine particulate matter • Hypertension

INTRODUCTION

The latest survey data show that there are approximately 254 million patients with hypertension in China,[1] and hypertensive patients have a high incidence of stroke.[2,3] Studies have shown that fine particulate matter ($PM_{2.5}$) is an important underlying component for people suffering from high blood pressure and could induce and aggravate cardiovascular and cerebrovascular diseases, and even affect average life expectancy.[4-6] Clinical observation have found that short-term exposure to high concentrations of $PM_{2.5}$ would elevate blood pressure, increase heart rate variability (HRV), induce arrhythmia, aggravate congestive heart failure and stimulate complications such as atherosclerosis, ischemic heart disease and stroke, leading to increased morbidity and mortality of cardiovascular diseases.[7-10] $PM_{2.5}$ is a complex compound, and the biological effects and toxicity of $PM_{2.5}$ with different chemical compositions are significantly distinct.[11] Current evidence has shown that elevated levels of $PM_{2.5}$ are associated with an increase in emergency admissions for hypertension.[12] However, the impact of the concentration changes for major elemental composition of $PM_{2.5}$ on hypertension and the emergency admissions of the associated cardiovascular

Received: April 15, 2015 Accepted: January 18, 2016
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diseases require further investigation.

The purpose of this study was to investigate the correlation between $PM_{2.5}$ and its chemical elemental composition, and emergency admissions for cardiovascular diseases in Changsha, which may provide further evidence for targeted interventions.

MATERIAL AND METHODS

Data on emergency admission

Data obtained upon emergency admission were from medical records of the Third Xiangya Hospital of Central South University, including daily data of the emergency admissions for hypertensive patients with cardiovascular diseases from June 1, 2009 to October 31, 2009. Specific characteristics of these emergency cases included sex, age, treatment department, hospital department, diagnosis and home address of the patients. Classification of diseases was performed according to the International Classification of Diseases, 10th edition coding (ICD-10), and cerebrovascular diseases (ICD-10: I60-70) were collected and classified. Cerebral hemorrhage and cerebral infarction cases were diagnosed by CT or MRI. The Third Xiangya Hospital of Central South University is located in the Yuelu District of Changsha city, which was the area's largest 3A hospital. The information collected in this study was derived from the local residents as well as long-term foreign residents in this area, who comprised a certain representation for data analysis on emergency admission for cardiovascular diseases and $PM_{2.5}$ exposure in the area. This study was approved by the hospital's Ethics Committee.

Meteorological and air pollution data

Meteorological data were collected from routine monitoring by the Changsha Municipal Meteorological Bureau and Central South University. Daily average concentrations of sulfur dioxide (SO_2), nitrogen dioxide (NO_2) and PM_{10} in Changsha during the study period were obtained from the Public Weather Information Service website of Changsha City (http://www.csqx.com/). Meteorological data (average daily temperature, average daily relative humidity, daily average barometric pressure and daily maximum wind speed) were downloaded from the International Meteorological website (http://www.wunderground.com/, monitoring points: Huanghua Airport). The $PM_{2.5}$ concentration monitoring and main chemical element composition analysis method were consistent with a previous study.[13] The $PM_{2.5}$ monitoring location was 3 kilometers (KM) from the hospital environment monitoring points. The sample acquisition time was from June 1, 2009 to October 31, 2009, and $PM_{2.5}$ samples were collected by PQ200 Ambient Fine Particulate Sampler (BGI Incorporated, Waltham, MA, USA) during the study to establish mass and concentration database of the daily average of $PM_{2.5}$. Analysis of $PM_{2.5}$ elemental composition was performed by Energy Dispersive X-Ray Fluorescence (EDXRF) spectrometer ED 2000 (Oxford Instruments, UK). The contents of the chemical composition for the particulate matter in $PM_{2.5}$ sample were analyzed, in which 18 kinds of chemical elements were measured, including Sodium (Na), magnesium (Mg), aluminium (Al), silicon (Si), phosphorus (P), sulfur (S), potassium (K), calcium (Ca), titanium (Ti), manganese (Mn), iron (Fe), nickel (Ni), copper (Cu), zinc (Zn), lead (Pb), vanadium (V), arsenic (As) and chromium (Cr). These 18 kinds of elements were further used to establish the mass and concentration database of the chemical elements.

Cross study for cases

This study referred to the report of Guo et al.[12] in the literature. Case crossover design was used to compare the cardiovascular disease risk in the case period to that in the control period, and to examine the differences in air pollutant exposure that can be used to explain the differences in the daily number of cases. The controls and cases were matched by the day of the week, which could control any weekly patterns in emergency admission and air pollution levels.

Hysteresis effect

Due to the time lag effect of an atmospheric pollutant concentration increase on emergencies with hypertension and its related cardiovascular diseases, emergency situations of hypertension and other cardiovascular diseases on day 0, 2 and 4 after $PM_{2.5}$ and PM_{10} concentration alterations were observed in the study. The PM concentration on the day of the incident was considered as the pollutant concentration of lag 0d, while the

PM concentration on day 2 or day 4 before the incident was considered as the pollutant concentration of lag 2d or lag 4d. Generally, the optimal lag was determined according to the maximum effect value (OR).

Statistical analysis

Spearman's correlation analysis and conditional logistic regression model were used in this study, with the daily emergency visits of hypertension and its related cardiovascular diseases taken as a weight, and the Cox regression of SPSS 17.0 (SPSS Inc, Chicago, Illinois, USA) software used to fit. Furthermore, the exposure odds ratio (OR) of the total $PM_{2.5}$ concentration and its elemental composition concentration in the illness period and control period of emergency cases with hypertension and its related cardiovascular diseases each day were analyzed. The possible impact of the daily meteorological factors (temperature, pressure and maximum wind speed) for the selected $PM_{2.5}$ on cardiovascular diseases was taken into account as covariates. The air temperature, barometric pressure and maximum wind speed as well as $PM_{2.5}$ were introduced into regression to perform a single pollutant model study, while correcting NO_2 and SO_2 to study multiple pollution models.

RESULTS

Trends for time changes of atmospheric pollutants, meteorological factors and cardiovascular emergencies

The daily average concentration of $PM_{2.5}$ from June 1, 2009-October 31, 2009 was 87.79 $\mu g/m^3$ for $PM_{2.5}$, and 93.96 $\mu g/m^3$, 31.22 $\mu g/m^3$ and 35.42 $\mu g/m^3$ for PM_{10}, SO_2 and NO_2, respectively. The time sequence diagram of the daily average $PM_{2.5}$, PM_{10}, SO_2 and NO_2 were plotted. As shown in Figure 1A, $PM_{2.5}$ concentrations increased gradually and reached their peak in the area in early October. As shown in Figure 1B to 1D, the lowest values of PM_{10}, SO_2 and NO_2 concentrations appeared in July or August during the summer. All four kinds of major pollutants in the atmosphere had significantly increased in October.

The total number of study subjects with hypertension and other cardiovascular diseases in this study was 1027, with 86 cases of simple hypertension, 99 cases of cerebral hemorrhage, 353 cases of cerebral infarction, 242 cases of transient ischemic attack (TIA), and 246 cases of coronary heart diseases. As shown in Figure 1 and Figure 2, there was no obvious time lag between daily air pollutant and daily emergency department visits relating to cardiovascular diseases.

Analysis of the main chemical element composition in $PM_{2.5}$ and the change trend

The average mass and concentration levels of Na and the other 17 kinds of chemical elements in $PM_{2.5}$ were shown in Table 1. During the course of our study, the descending order of the average concentration of elements in $PM_{2.5}$ in Changsha was S, Si, K, Al, Ca, Fe, Zn, Mg, Na, Mn, Pb, Ni, Ti, Cu, V, Cr, P, and As, of which the concentrations of S, Si and K reached more than 1000 ng/m^3, namely 3753.23 ng/m^3, 1702.69 ng/m^3 and 1546.74 ng/m^3.

Correlation analysis between atmospheric pollutants and meteorological factors

Considering the impact of air temperature, relative humidity, atmospheric pressure and the maximum wind speed, Spearman's correlation between the atmospheric pollutants ($PM_{2.5}$, PM_{10}, SO_2, NO_2) and the temperature, relative humidity, barometric pressure and maximum wind speed were analyzed. Our study found that $PM_{2.5}$ was positively correlated with PM_{10}, SO_2, NO_2, negatively correlated with temperature and maximum wind speed, and positively correlated with atmospheric pressure. PM_{10} was positively correlated with SO_2 and NO_2, and had positive correlation with barometric pressure.

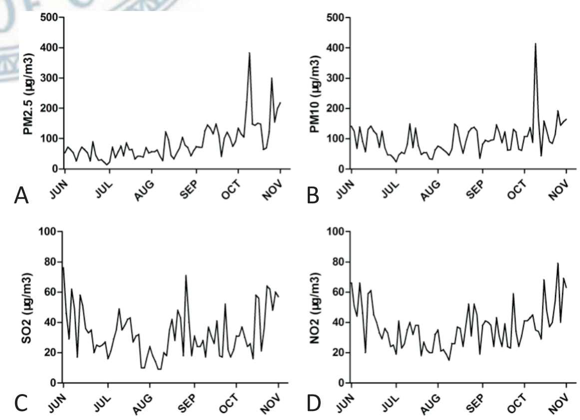

Figure 1. *Concentration change of daily air pollutant from June 1 through October 31, 2009. (A) Daily Fine Particulate Matter ($PM_{2.5}$) concentration change. (B) Daily Particulate Matter 10 (PM_{10}) concentration change. (C) Daily sulfur dioxide (SO_2) concentration change. (D) Daily nitrogen dioxide (NO_2) concentration change.*

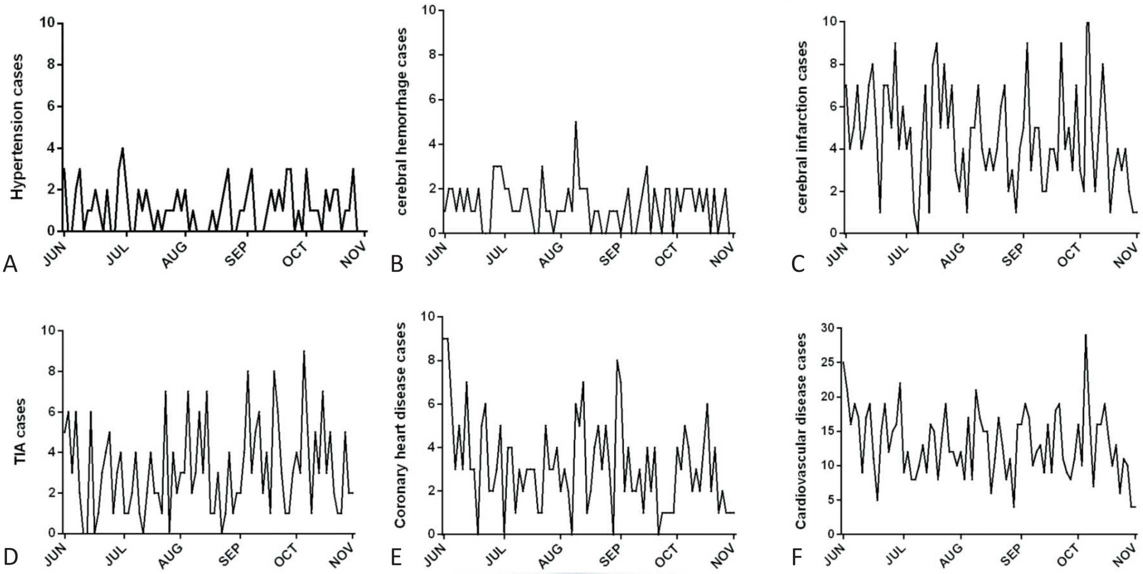

Figure 2. *Change of daily emergency admission with cardiovascular disease during June 1 and October 31, 2009. (A) Hypertension cases. (B) Cerebral hemorrhage cases. (C) Cerebral infarction. (D) Transient ischemic attack (TIA) cases. (E) Coronary heart disease cases. (F) Cardiovascular disease cases.*

Table 1. Average mass concentration levels of PM2.5 chemical elements in Changsha city (ng/m^3)

Indicators	Average value	Standard deviation	Minimum	Maximum	Percentiles (P)		
					25	50	75
Na	107.78	44.26	58.07	332.41	81.29	96.43	119.65
Mg	168.25	109.51	70.57	839.72	120.00	138.65	175.82
Al	833.55	380.31	425.83	2763.00	642.29	739.38	882.94
Si	1940.61	1158.14	759.44	9528.38	1430.57	1702.69	2095.75
P	12.19	5.78	1.80	45.55	9.08	11.20	13.27
S	3780.55	1525.23	966.14	9425.91	2763.43	3753.23	4415.92
K	1997.57	1695.27	296.39	11273.27	900.14	1546.74	2610.00
Ca	568.06	221.62	385.44	1638.62	438.02	483.09	612.40
Ti	34.53	18.73	13.05	145.10	23.49	30.84	38.83
Fe	462.51	222.12	181.63	1723.37	340.41	412.09	506.90
Mn	65.79	65.23	7.58	318.61	24.78	35.03	94.90
Ni	40.72	18.62	9.04	100.95	30.50	39.80	47.73
Cu	29.68	14.25	6.38	73.63	20.92	28.21	37.94
Zn	324.33	178.03	86.27	915.87	223.00	270.47	368.41
Pb	56.67	24.70	15.84	140.77	41.10	51.18	66.23
V	27.66	13.77	4.29	73.87	16.51	26.05	34.85
Cr	20.69	7.05	7.58	45.02	15.86	20.41	25.49
As	11.91	6.41	1.62	30.95	7.40	10.79	14.34

Al, aluminium; As, arsenic; Ca, calcium; Cr, chromium; Cu, copper; Fe, iron; K, potassium; Mg, magnesium; Mn, manganese; Na, Sodium; Ni, nickel; P, phosphorus; Pb, lead; S, sulfur; Si, silicon; Ti, titanium; V, vanadium; Zn, zinc.

SO_2 had a positive correlation with NO_2, and was negatively correlated with the relative humidity. NO_2 was negatively correlated with air temperature and relative humidity, but positively correlated with barometric pressure (Table 2).

Correlation analysis between $PM_{2.5}$, PM_{10} and emergencies with cardiovascular diseases

After the impact of everyday air temperature, air pressure and maximum wind speed were adjusted for the selected $PM_{2.5}$, the OR value for the impact of lag 0d

Table 2. Spearman's correlation analysis between atmospheric pollutants and meteorological factors

Items	$PM_{2.5}$	PM_{10}	SO_2	NO_2	Air temperature	Relative humidity	Atmospheric pressure	Maximum wind velocity
$PM_{2.5}$	1.000	0.546#	0.281*	0.463#	-0.471#	0.011	0.645#	-0.262*
PM_{10}		1.000	0.591#	0.728#	-0.111	-0.210	0.398#	-0.115
SO_2			1.000	0.775#	0.114	-0.456#	0.160	-0.095
NO_2				1.000	-0.063	-0.361#	0.355#	-0.233*
Air temperature					1.000	-0.597#	-0.683#	-0.027
Relative humidity						1.000	0.070	0.135
Atmospheric pressure							1.000	-0.148
Maximum wind velocity								1.000

* $p < 0.05$; # $p < 0.01$.

$PM_{2.5}$ pollution on emergency admissions with hypertension, cerebral hemorrhage and TIAs reached the maximum. And the OR value for the impact of lag 2d $PM_{2.5}$ pollution on emergency admissions with cerebral infarction, coronary heart disease and the overall cardiovascular diseases was the largest, but the differences were not statistically significant ($p > 0.05$). The concentration of $PM_{2.5}$ and chemical elements on the day of the emergency, which is lag 0d, were chosen in subsequent study to analyze its effects on emergencies with cardiovascular diseases, and lag 0d was chosen in PM_{10} analysis as well.

Taking into account that $PM_{2.5}$ and PM_{10} were positively correlated with SO_2 and NO_2, SO_2 and NO_2 were further corrected to perform multi-pollutant model analysis. As shown in Figure 3, after NO_2, SO_2 and meteorological factors were corrected simultaneously, the OR value of the emergency admissions with cerebral hemorrhage was 1.177 [95% confidence interval (CI): 1.006-1.376] when the $PM_{2.5}$ increased by 10 $\mu g/m^3$, and the correlation was statistically significant ($p = 0.04$). While the OR values of the emergency admissions with simple hypertension, cerebral infarction, TIA, coronary heart disease and total emergency hospital admissions were 1.080 (95% CI: 0.960-1.215), 1.040 (95% CI: 0.953-1.135), 1.028 (95% CI: 0.901-1.172), 1.021 (95% CI: 0.901-1.156) and 1.014 (95% CI: 0.896-1.148), respectively, these association had no statistical significance ($p > 0.05$). Figure 4 showed that the difference of the OR value between PM_{10} and emergency admissions with cardiovascular diseases was not statistically significant.

Correlation analysis between concentrations of chemical elements in $PM_{2.5}$ and emergency admission with cardiovascular diseases

The correlation analysis between concentrations of elemental composition in $PM_{2.5}$ and the emergency admission with cardiovascular disease was shown in Table 3. Therein, the concentration of Ni, Zn and Pb elements

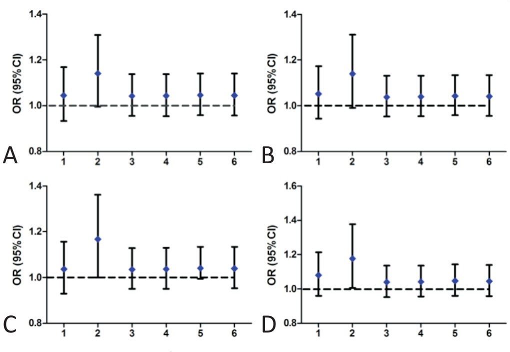

Figure 3. *Correlation of $PM_{2.5}$ concentrations and cardiovascular disease risk. (A) $PM_{2.5}$. (B) $PM_{2.5}$ corrected SO_2. (C) $PM_{2.5}$ corrected NO_2. (D) $PM_{2.5}$ corrected SO_2 and NO_2. 1, hypertension. 2, cerebral hemorrhage. 3, cerebral infarction. 4, TIA. 5, coronary heart diseases. 6, cardiovascular diseases.*

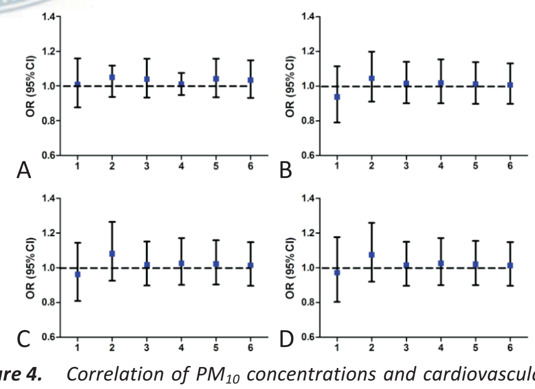

Figure 4. *Correlation of PM_{10} concentrations and cardiovascular disease risk. (A) PM_{10}. (B) PM_{10} corrected SO_2. (C) PM_{10} corrected NO_2. (D) PM_{10} corrected SO_2 and NO_2. 1, hypertension. 2, cerebral hemorrhage. 3, cerebral infarction. 4, TIA. 5, coronary heart diseases. 6, cardiovascular diseases.*

Table 3. PM 2.5 element concentrations and emergency treatment OR values of hypertension associated with cardiovascular disease (for each additional one IQR)

	Hypertension	Cerebral hemorrhage	Cerebral infarction	TIA	Coronary heart disease	Total cardiovascular diseases
Na	0.704 (0.259-1.916)	1.157 (0.407-3.294)	0.918 (0.439-1.921)	0.959 (0.450-2.042)	1.022 (0.489-2.139)	0.944 (0.454-1.963)
Mg	1.131 (0.641-1.995)	0.984 (0.697-1.390)	1.049 (0.784-1.402)	1.042 (0.780-1.392)	1.040 (0.779-1.390)	1.044 (0.782-1.393)
Al	1.241 (0.702-2.196)	1.163 (0.759-1.783)	1.066 (0.742-1.532)	1.066 (0.740-1.534)	1.065 (0.742-1.529)	1.066 (0.743-1.529)
Si	1.103 (0.610-1.991)	0.985 (0.692-1.402)	0.975 (0.708-1.344)	0.964 (0.700-1.326)	0.966 (0.703-1.328)	0.968 (0.704-1.332)
P	1.027 (0.596-1.769)	1.048 (0.630-1.744)	1.076 (0.699-1.656)	1.098 (0.706-1.707)	1.079 (0.700-1.661)	1.059 (0.690-1.625)
S	1.420 (0.468-4.307)	2.022 (0.865-4.724)	1.291 (0.683-2.439)	1.365 (0.723-2.580)	1.272 (0.679-2.385)	1.367 (0.724-2.579)
K	0.836 (0.472-1.480)	1.318 (0.686-2.532)	0.860 (0.564-1.308)	0.889 (0.593-1.334)	0.934 (0.626-1.392)	0.920 (0.617-1.317)
Ca	0.892 (0.570-1.395)	1.437 (0.734-2.813)	0.899 (0.603-1.342)	0.929 (0.623-1.386)	0.960 (0.649-1.420)	0.941 (0.636-1.392)
TI	0.879 (0.452-1.707)	1.079 (0.626-1.859)	0.936 (0.596-1.471)	0.933 (0.595-1.463)	0.924 (0.519-1.443)	0.942 (0.602-1.473)
V	1.922 (0.822-4.493)	1.622 (0.858-3.066)	1.759 (0.958-3.228)	1.644 (0.897-3.015)	1.665 (0.904-3.067)	1.736 (0.951-3.167)
Cr	0.448 (0.130-1.545)	1.269 (0.542-2.971)	1.241 (0.640-2.408)	1.159 (0.598-2.248)	1.157 (0.608-2.201)	1.165 (0.608-2.233)
Mn	1.042 (0.557-1.948)	0.987 (0.919-1.061)	0.878 (0.546-1.413)	0.869 (0.537-1.406)	0.981 (0.614-1.568)	0.933 (0.587-1.482)
Fe	1.084 (0.518-2.269)	1.054 (0.653-1.700)	1.034 (0.679-1.575)	1.030 (0.677-1.566)	1.038 (0.682-1.578)	1.029 (0.678-1.563)
Ni	1.016 (0.551-1.876)	1.826 (1.031-3.233)*	1.169 (0.723-1.890)	1.277 (0.777-2.097)	1.184 (0.725-1.933)	1.204 (0.747-1.941)
Cu	0.999 (0.449-2.225)	1.201 (0.623-2.317)	1.008 (0.569-1.786)	1.087 (0.617-1.916)	1.032 (0.586-1.819)	1.064 (0.609-1.861)
Zn	0.810 (0.474-1.384)	1.568 (1.015-2.423)*	1.059 (0.720-1.559)	1.054 (0.714-1.556)	1.084 (0.733-1.603)	1.063 (0.724-1.561)
As	0.998 (0.605-1.646)	1.155 (0.748-1.785)	1.019 (0.684-1.518)	1.116 (0.729-1.707)	1.066 (0.717-1.583)	1.046 (0.705-1.552)
Pb	0.838 (0.473-1.485)	1.682 (1.010-2.800)*	0.988 (0.657-1.485)	0.974 (0.646-1.468)	1.008 (0.675-1.505)	0.988 (0.660-1.478)

* $p < 0.05$.

were related to hypertensive cerebral hemorrhage in emergency admissions. For each additional increase IQR (17.23 ng/m^3) of Ni element concentration, the OR value was 1.826 (95% CI: 1.031-3.233, $p = 0.04$). For each additional increase IQR (145.41 ng/m^3) of Zn element, the OR value was 1.568 (95% CI: 1.015-2.423, $p = 0.04$), and for each additional increase IQR (25.13 ng/m^3) of Pb element, the OR value was 1.682 (95% CI: 1.010-2.800, $p = 0.05$). The concentration of other elements had no statistically significant association with emergencies involving hypertension cardiovascular diseases ($p > 0.05$).

DISCUSSION

To date, this is the first correlation study between chemical element compositions in $PM_{2.5}$ and hospital emergency admission associated with cardiovascular diseases in hypertensive population in Changsha, China. Time-stratified case-crossover design and conditional logistic regression models were used to analyze the correlation between emergency admission of cerebral hemorrhage, cerebral infarction, TIA, and coronary heart disease in hypertensive patients, and the concentrations of $PM_{2.5}$ and its chemical elemental composition.

Arising from the daily average concentration change analysis of 18 kinds of chemical elements in $PM_{2.5}$, we found that the increased concentration of three elements in $PM_{2.5}$, including Ni, Zn and Pb, would increase the number of emergency admissions with hypertensive cerebral hemorrhage. Zanobetti et al.[14] analyzed emergency admission data of the elders in 26 communities of the United States from 2000-2003, and found that Ni, As, Cr, Br and organic carbon (OC) component in $PM_{2.5}$ were closely related to hospitalization caused by coronary heart disease, myocardial infarction, heart failure, diabetes and respiratory diseases. The elemental analysis in this study showed that Na, K and other elements were derived from waste biomass fuel combustion and the secondary particles, that Ni element was from characteristic elements of diesel combustion, and that Zn and Pb were mainly from automobile tires, brake pads wear and vehicle fuel emissions. These elements were consistent with the main source (soil dust, traffic emissions, coal combustion, waste incineration, secondary particulate matter and diesel exhaust) of air pollution in

Changsha shown in a previous study.[13] Therefore, this study suggested that controlling the air pollution caused by transport emissions and biomass burning may reduce the occurrence of emergencies with hypertensive cerebral hemorrhage.

We also confirmed that the $PM_{2.5}$ concentration increase was closely related to the emergencies of cerebral hemorrhage in hypertensive patients. After simultaneously correcting meteorological factors, including NO_2 and SO_2, as the daily average $PM_{2.5}$ increased by 10 ug/m^3, the OR value of cerebral hemorrhage was 1.177 (95% CI: 1.006-1.376). However, no association between the PM_{10} concentrations and emergency admissions with hypertension cardiovascular diseases was seen in this study. We speculated that the incidence of hypertension-related cerebral hemorrhage was mainly influenced by the concentration of $PM_{2.5}$ in Changsha, but not by PM_{10}. Guo[12] found that with every 10 ug/m^3 increase in $PM_{2.5}$ and PM_{10}, the hypertensive emergency admission risk in Beijing was 1.084 (95% confidence interval (CI: 1.028, 1.139) and 1.060% (95% CI: 1.020, 1.101). Nascimento[15] found that with 10 ug/m^3 for each additional PM_{10}, the hospitalization rate of hypertension increased by 13%. The pathogenesis and environmental data of the 63,724 death cases were analyzed in Japan, and it was found that death caused by brain hemorrhage was clearly correlated with the concentration of particulate matter (PM_7) within 2 hours before death. When the average concentration of PM_7 per hour reached above 200 ug/m^3 in this period, the OR value of the death caused by cerebral hemorrhage was 2.40 (95% CI: 1.480-3.890).[9] Nonetheless, the relationship between PM_{10} and hemorrhagic death in different areas remains controversial, while the researchers found that the correlation was negative in Chicago, but positive in Minneapolis.[9]

In order to investigate whether there was a time lag effect on the impact of $PM_{2.5}$ on emergencies with hypertensive cardiovascular diseases, the lag situation on day 0, 2, or 4 was analyzed. The results showed that when NO_2, SO_2 and meteorological factors were corrected, as $PM_{2.5}$ increased by 10 μg/m^3, the OR value of emergency admissions with hypertensive cerebral hemorrhage was 1.177 (95% CI: 1.006-1.376), and the correlation was statistically significant (p = 0.042). However, no association was found in the data of lag 2d or 4d, which was similar to Guo et al.'s findings.[16] The results of an association between $PM_{2.5}$ and death caused by cerebral hemorrhage suggested that the blood pressure increase caused by long-term and short-term $PM_{2.5}$ exposure was associated with the activation of the body's inflammatory response,[17,18] and Brook et al.[19] found that $PM_{2.5}$ had a delayed effect on the vascular injury. Even if a direct attack of $PM_{2.5}$ disappeared, the blood pressure would fall, but the damage to the vessels could last for 24 hours.

The temperature is generally negatively correlated with $PM_{2.5}$, which was confirmed by our data (Table 2). In the single pollutant models and multiple pollution models analysis, we took the air temperature as covariate to minimize the bias of temperature. Interestingly, we found the highest $PM_{2.5}$ concentration in October as Figure 1A showed. The environmental pollution problems in China have some special characteristics based on the complicated emission sources. Changsha is famous for fireworks manufacturing in China, and there were several large fireworks shows in October. In our monitoring data, the maximum concentration of $PM_{2.5}$ can even reach 382.14 μg/m^3 in October. Therefore, a large number of emissions lead to a higher concentration of $PM_{2.5}$ in October, and this phenomenon is repeated every year, which could well support our findings.

There were some limitations in this study. For example, the cases came from a single center, although they were all residents near the hospital. Since we cannot get the patient's socio-economic data, the study did not take the socio-economic factors into account, which may affect the patients' choice for hospital. As a pilot study, certain patients' characteristics (e.g. body mass index, smoking, comorbidity) were not analyzed in this study. Secondly, in our study, $PM_{2.5}$ was monitored for only five months, which is a comparatively short period. This is mainly because China mainland has just begun to monitor $PM_{2.5}$ concentration from 2013, yet the database is still not open to public and the elements of $PM_{2.5}$ have not been monitored regularly. Furthermore, the environmental concentrations and individual exposure concentrations had some differences. Because elemental concentrations of particulate matter were often lower, and obviously affected by various meteorological factors, no more elements and results associated with the disease were found. Hence, longer and prospective clinical studies are needed to further confirm this association.

CONCLUSIONS

In the present study, we found that concentration rises of nickel, zinc and lead elements for PM2.5 were related to the increase of emergency admissions with cerebral hemorrhage. This result aids to further understand the hazards mechanism of air pollution on the cerebrovascular diseases, and might provide a reference for the local environmental governance.

ACKNOWLEDGEMENTS

This study was supported by the National Natural Science Foundation of China (81673520, 81202166), the National Science and Technology Benefiting Funds (2012GS430101), and the Scientific and Technological Project of Hunan (2011SK3240).

COMPETING INTERESTS

None of the authors have any competing interests.

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