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Associations of short-term exposure to ambient air pollutants with emergency ambulance calls for the exacerbation of essential arterial hypertension

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ABSTRACT

We investigated the association between daily emergency ambulance calls (EAC) for elevated blood pressure that occurred during the time intervals of 8:00–13:59, 14:00–21:59, and 22:00–7:59, and exposure to CO, PM_{10}, and ozone. We used Poisson regression to explore the association between the risk of EAC and short-term variation of pollutants, adjusting for seasonality and weather variables. Before noon, the risk was associated with an interquartile range (IQR) (7.9 μg/m^3) increase in PM_{10} at lag 2–4 days below the median (RR = 1.08, p = 0.031) and with an IQR (0.146 mg/m^3) increase in CO at lag 6–7 below the median (RR = 1.05, p = 0.028). During 14:00–21:59, the risk was associated with an IQR (18.8 μg/m^3) increase in PM_{10} on the previous day below the median (RR = 1.04, p = 0.031). At night, EAC were negatively affected by lower O_3 (lag 0–2) below the median (per IQR decrease RR = 1.10, p = 0.018) and a higher PM_{10} at lag 0–1 above the median for the elderly (RR = 1.07, p = 0.030).

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Carbon monoxide; particulate matter; ozone; emergency ambulance calls; exacerbation of essential arterial hypertension

Introduction

In recent years, a number of papers have been published on the associations between emergency ambulance calls (EAC) for cardiovascular and respiratory diseases and such environmental factors as weather conditions and air pollution (Sajani et al. 2014; Michikawa et al. 2015; Vencloviene et al. 2015a, 2015b; Ichiki et al. 2016; Tasmin et al. 2016; Liu et al. 2017; Vencloviene et al. 2017). Most of these authors postulated a positive association between the concentration of particulate matter and the rate of EAC for the aforementioned diseases.

Arterial hypertension (AH) is one of the risk factors of cardiovascular disease (Mancia et al. 2014) and can lead to damage of target organs, e.g. heart (left ventricular hypertrophy, congestive heart failure, or coronary artery disease), blood vessels (peripheral artery disease, aortic aneurysm, or aortic dissection), nerves (a stroke or hypertensive encephalopathy), eyes (hypertensive retinopathy), and kidneys (chronic kidney disease) (Weir 2005, p. 203, 204; Wexler and Aukerman 2006). Over the last

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two decades, a number of studies have linked short-term changes in air pollution to increased emergency hospital visits for AH (Guo et al. 2010a, 2010b; Szyszkowicz et al. 2012; Brook and Kousha 2015) or an increased risk of hospital admission for AH (Arbex et al. 2010; Nascimento and Francisco 2013).

Many epidemiological studies presented possible negative effects of air pollution on the mechanisms of the cardiovascular system: increased air pollution was associated with endothelial dysfunction, elevated blood pressure, and poorer blood coagulability indices (Watkins et al. 2013). In addition, increased air pollution was associated with an imbalance in the autonomic nervous system, favoring sympathetic nervous system activity (Brook et al. 2004; Szyszkowicz et al. 2012). Circadian rhythm is a very important factor in the physiology of the cardiovascular system, as it induces diurnal variation of blood pressure, respiratory activity, heart rate, and other physiological parameters. It affects the balance of the activity of the sympathetic and parasympathetic nervous system. The sympathetic simulation usually occurs in the morning, and the increase in the parasympathetic nervous system activity begins later (Rudic 2009). The significant circadian variation in blood pressure usually includes a morning increase, a small postprandial decrease, and a wider lowering during nocturnal rest (Hermida et al. 2007). Several studies observed that the rise in systolic and diastolic blood pressure began early in the morning (from 4:00 to 8:00), reached the maximum in the afternoon (about at 14:00), and dropped in the evening (at 20:00–21:00) (Stanton et al. 2003; Koroboki et al. 2012). Studies also found that heart rate, plasma cortisol levels, vascular tone, blood viscosity, and platelet aggregation increased in the early morning, whereas vagus nerve activity decreased (White 2007). In response to the increased activation of the sympathetic nervous system, the blood pressure rises shortly (Furlan et al. 1990). The reaction to environmental triggers may vary during different periods of the day. Short-term exposure to high levels of PM_{10} has been found to have a visible impact on the circadian rhythms of blood pressure (high nighttime blood pressure and a blunted nocturnal systolic dipping profile) and sodium excretion (low sodium excretion during daytime) (Tsai et al. 2012). In their previous work, the authors (Vencloviene et al. 2017) found that the associations between air pollution and the risk of paroxysmal atrial fibrillation were dependent on the time of the day. It is probable that the same methodology as used in (Vencloviene et al. 2017) will allow for the evaluation of the associations of air pollutants with EAC for elevated arterial blood pressure (EABP) during different times of the day.

The aim of the study was to detect the complex association of daily EAC for EABP occurring in the morning – before noon (8:00–13:59), in the afternoon – in the evening (14:00–21:59), and at night and early in the morning (22:00–7:59) with short-term exposure to carbon monoxide (CO), ozone (O_3), and particulate matter with an aerodynamic diameter less than or equal to 10 μm (PM_{10}), controlling for seasonality, day length, weather, and space weather data. A significant association between the aforementioned confounding variables and daily EAC for EABP was presented before (Vencloviene et al. 2015a). The cut points of split of the day were designated according to the information on the fluctuation in the indicators of vascular and parasympathetic tone (respectively, low frequency and high frequency power in electrocardiograms).

Methods

The time-series study was conducted from 1 January 2009 to 30 June 2011 in Kaunas city, Lithuania with a population of 306,000 inhabitants. The study was based on the cohort of individuals that were selected from all residents of Kaunas city using the emergency calls database. Ambulance calls were received from patients who in the background of their usual antihypertensive pharmacological treatment suddenly experienced a rise in arterial blood pressure by more than 20 mm Hg and additional clinical symptoms such as chest pain, headache, dizziness, or other unusual symptoms. Upon arrival, an ambulance crew member filled out a special clinical evaluation form where he or she recorded the chief complaint, the anamnesis, the findings of the clinical examination (heart rate, blood pressure, clinical signs of heart failure, and ECG parameters), the prescribed home treatment, and the coding of the diagnosis according to the international classification of diseases (ICD-10). We reviewed these forms and selected patients whose clinical situation was evaluated by the ambulance crew as an exacerbation of essential hypertension accompanied by a significant elevation of arterial blood pressure (code I.10 – I.15). During 911 days of the study period, we analyzed 17,114 cards of emergency calls at Kaunas city ambulance service. We analyzed the associations between daily environmental conditions and the daily number of EAC for EABP during the time period of 8:00–13:59, 14:00–21:59, and 22:00–7:59 for all patients and separately for older (>65 years) and younger patients.

We used the mean daily concentrations of PM_{10} and the highest 8-h moving average of CO concentration calculated as the mean values from three air quality monitoring stations. We used daily data from the air monitoring stations of the National Environmental Department in Petrasiunai (a neighborhood in Kaunas city) and Noreikiskes (a town in Kaunas district) and from the Municipal Air Quality Monitoring System in Dainava station (in Kaunas city). The mean daily concentrations of ozone were obtained from the Municipal Air Quality Monitoring System in Dainava station. Two stations are located within the residential part of the studied region, and one – in the suburban region of Kaunas city. In these stations, the concentrations of the pollutants were measured automatically on an hourly basis.

Kaunas meteorological station (Air Force Datsav3 station number: 266290; coordinates +54.883N; +23.833E) located 6 km to the west of Kaunas city centre provided daily records of minimal, maximal, and mean daily air temperature (T, °C), wind speed (WS, knots), and barometric pressure (BP, hPA) for the studied period (http://www.geodata.us/weather/). Information on the mean daily relative humidity (RH, %) was obtained from Kaunas International Airport weather station (Force Datsav3 station number: 266295; coordinates +54.964N; +24.085E) located 14 km northeast of Kaunas city center. Both weather stations are located in the outskirts of Kaunas city.

The space weather variable was used as categorical predictor. Daily *Ap* indexes were used as a measure of the level of geomagnetic activity (GMA). We assessed the impact of low GMA – $Ap < 4$ (4 being the median of *Ap* during the studied period), active-stormy GMA – $Ap \geq 16$, high-speed solar wind (HSSW) in conjunction with days of active-stormy GMA, HSSW occurring after days of active-stormy GMA, and 2 days after the active-stormy GMA level. Days with the mean value of solar wind speed ≥600 km/s were defined as days of HSSW. Data on daily solar wind speed and *Ap* data were downloaded from the National Oceanic and Atmospheric Administration database (ftp://ftp.ngdc.noaa.gov/STP/SOLAR_DATA/).

Statistical analysis

The daily number of EAC for EABP by separate time intervals was presented as mean value (standard error). The association between air pollution variables and the daily number EAC for EABP was evaluated by applying Poisson regression. In the analysis, we used the environmental variables on the day of call and on previous 1–7 days. We examined lag effects of different days including both a single-day lag and the moving average of several days. First, we created the multivariate Poisson regression model for the associations between the risk of EAC and air temperature, WS, RH, BP, and day length; the model included the month of the year and the day of the week as categorical variables. In the model, the WS, RH, and BP were included as piecewise linear (2-piece spline) functions; the cut-offs for all lags were the same and equaled to the median. The graphical analysis of the associations between mean daily air temperature and EAC for EABP in the previous work (Vencloviene et al. 2015a) shows a J-shaped association between air temperature and the mean number of EAC: the daily number of EAC negatively correlated with T above 1 °C, fluctuated around 21.2 in the presence of mean daily T ranging between −1 and 1 °C, and sharply fluctuated at $T < -1$ °C. Therefore, the term of air temperature was a 3-piece linear spline function (Armstrong 2006); the first section $T_{C,t} = \max(T_C - T_t, 0)$, reflected the impact of cold; the middle section was constrained to have zero slope, and the third section $T_{W,t} = \max(T_t - T_W, 0)$ reflected the impact of warmth. The thresholds for cold effect and warm effect were, respectively, $T_C = -1$ °C and $T_W = 1$ °C; the same thresholds were used for all lags.

We evaluated the possible risk of PM_{10}, CO, and O_3 concentrations at lags of 0–7 days; the terms of pollutants on the *t*-th day were expressed as 2-piece linear spline functions. For example, the term of PM_{10} on the *t*-th day was the following:

$$f(PM_{10t}) = \beta_L PM_{10L,t} + \beta_H PM_{10H,t} \quad (1)$$

in which $PM_{10L,t}$ = min(PM_{10t}-median, 0) reflects the impact of PM_{10} concentrations lower than the median; and $PM_{10H,t}$ = max(PM_{10t}-median, 0) reflects the impact of higher than median PM_{10} concentrations. The term of CO was constrained by analogy. The daily ozone concentration positively correlated with air temperature, and a higher air temperature was associated with a lower blood pressure. Additionally, a lower concentration of O_3 is associated with specific weather pattern: low solar radiation levels, high relative humidity, and higher air pollution levels are observed during winter and autumn seasons due to heating, which can be related with adverse effects on human health. Therefore, we analyzed separately the impact of low and high O_3 concentration. The term of O_3 on the t-th day was the following:

$$f(O_{3t}) = \beta_L O_{3L,t} + \beta_H O_{3H,t} \quad (2)$$

in which $O_{3L,t}$ = max(median-O_{3t}, 0) reflects the impact of O_3 concentrations lower than the median; and $O_{3H,t}$ = max(O_{3t}-median, 0) reflects the impact of higher than median O_3 concentrations. To detect the impact of air pollutants, we included the variables $PM_{10L,t-j}$ and $PM_{10H,t-j}$, ($CO_{L,t-j}$, $CO_{H,t-j}$, $O_{3L,t-j}$, and $O_{3H,t-j}$,) into the multivariate model for each *j* = 0, 1,..., 7 one by one, adjusting for significant weather variables detected in the previous multivariate models, for the day of the week, and the month of the year, and additionally adjusting for air temperature. In addition, an unconstrained distributed lag model (DLM) was used. Based on the results of DLM models, significant variables of pollution were identified, such as $PM_{10L,t-j}$, $PM_{10H,t-j}$, $CO_{L,t-j}$, $CO_{L,t-j}$, $O_{3L,t-j}$, and $O_{3H,t-j}$, or analogous variables defined by formula (1–2), replacing the daily concentrations of pollutants with respective moving averages of several days. If the impact of the concentrations below and above the median was similar (coefficients of regression β_L and β_H in (1–2) formulas did not differ), we included the concentration of pollutants as continuous variable into the model. As the concentration of O_3 was a significantly higher in spring–summer, as compared to autumn–winter, we analyzed the impact of ozone during all days and separately on days of spring–summer and autumn–winter. We tested the impact of single pollutants; in addition, the multivariate model included several pollutants. The impact of pollutants was also assessed when additionally including the space weather variable in the created regression model.

The Rate Ratios (RRs) per an increase in interquartile range (IQR) are presented with 95 % confidence intervals (CI) and *p*-value. The analysis was performed separately for the number of daily calls and calls in the morning–before noon, in the afternoon, and at night–early in the morning. We checked the susceptibility based on age and seasonality. Statistical analysis was performed using SPSS 19 software.

Results

There were 17,114 emergency calls for EABP during 911 days: 26 % of the calls were received during the first half of the day, 44.5 % – in the afternoon, and 29.5 % – late in the evening or at night; this distribution was similar for older and younger patients. In total, 78.4 % of the patients were females, and 60.2 % of the patients were older than 65 years of age. The descriptive characteristics of the daily number of EAC for EABP and the environmental variables are presented in Table 1. The IQR of PM_{10} below the median and PM_{10} above the median were, respectively, 7.31 and 12.11 μg/m^3, for CO ≤ median and CO > median, respectively, 0.120 and 0.333 mg/m^3, and for O_3 ≤ median and O_3 > median, respectively 14.5 and 15.4 μg/m^3. A highest pollution with PM_{10} was observed in winter–spring, CO – in winter, and with O_3 – in spring–summer (Table 1). Stronger correlations were detected between air temperature and CO concentration and ozone and relative humidity (Table 2).

Table 1. The decriptive characteristics of the daily number of emergency ambulance calls for elevated arterial blood pressure and environmental variables.

Variable	Range	Mean (SD)	Percentiles 25	50	75
Daily number of calls					
Daily	5–41	18.8 (5.4)	15	18	22
8:00–13:59	0–14	4.9 (2.4)	3	5	6
14:00–21:59	1–19	8.4 (3.2)	6	8	11
22:00–7:59	0–15	5.5 (2.6)	4	5	7
Age	17–104	67 (15)	58	70	78
Environmental variables					
Air temperature (°C)	−21.8 to 27.2	6.5 (9.7)	−0.1	6.8	14.5
Wind speed (knots)	0.5–17.2	6.3 (2.8)	4.2	6.1	8.0
Barometric pressure (hPA)	977–1032	1005 (9)	1000	1006	1011
Relative humidity (%)	28–100	80 (13)	72	82	90
PM_{10} (μg/m^3)	4.83–176.67	29.3 (19.3)	16.7	25.0	35.0
Carbon monoxide (mg/m^3)	0.08–3.17	0.561 (0.37)	0.333	0.467	0.700
Ozone (μg/m^3)	2.84–101.76	41.7 (18.0)	27.8	41.2	53.9

Environmental variables by seasons (Mean (SD))

	Spring	Summer	Autumn	Winter
Air temperature (°C)	7.22 (6.5)	18.0 (3.7)	7.16 (5.1)	−5.26 (5.6)
Wind speed (knots)	6.18 (2.7)	5.3 (1.9)	6.9 (2.9)	6.9 (3.3)
Barometric pressure (hPA)	1007 (8)	1005 (6)	1005 (9)	1005 (11)
Relative humidity (%)	72 (15)	77 (10)	87 (8)	87 (9)
PM_{10} (μg/m^3)	31.9 (20.0)	22.8 (10.5)	23.0 (12.2)	37.2 (24.9)
Carbon monoxide (mg/m^3)	0.547 (0.3)	0.308 (0.1)	0.536 (0.3)	0.831 (0.5)
Ozone (μg/m^3)	54.9 (15.0)	46.9 (14.9)	26.5 (11.9)	35.0 (14.9)

Notes: SD – standard deviation; PM_{10} – Particulate matter with an aerodynamic diameter less than or equal to 10 μm.

Table 2. Correlation matrix between environmental variables (Spearman's correlation).

	(1)	(2)	(3)	(4)	(5)	(6)
Air temperature (1)	1.00					
Wind speed (2)	−0.181**	1.00				
Barometric pressure (3)	−0.034	−0.351**	1.00			
Relative humidity (4)	−0.357*	0.083*	−0.321**	1.00		
PM_{10} (5)	−0.182**	−0.237**	0.226**	−0.137**	1.00	
Carbon monoxide (6)	−0.602**	−0.135**	0.036	0.312**	0.559**	1.00
Ozone (7)	0.312**	0.237**	−0.021	−0.579	−0.028	−0.298**

Note: PM_{10} – Particulate matter with an aerodynamic diameter less than or equal to 10 μm.
*$p < 0.05$; **$p < 0.01$.

According to unconstrained DLMs (Figure 1), a negative impact of a higher PM_{10} concentration was more pronounced: at lag 1 day and at lag 4 days of PM_{10} levels above the median during the whole day; at lag 4–6 days of PM_{10} above the median and at lag 2–4 days of PM_{10} below the median during 8:00–13:59; at lag 1 day of PM_{10} above the median in the afternoon; and at lag 0–1 days of PM_{10} above the median at night. The risk of EAC for EABP positively correlated with 7-day average PM_{10} (lag 1–7) excluding period 22:00–7:59 (Table 3). For patients aged ≤65 years, the negative impact of a higher 7-day average PM_{10} was stronger before noon, and for the elderly – in the afternoon (Table 3).

A negative impact of CO was observed throughout the day at lag 0–1 and 6–7 days (Figure 1). The risk of EAC for EABP was positively associated with a 7-day average CO concentration. This impact was the same during all the studied periods of the day, but for patients aged ≤65 years, the negative impact was more pronounced before noon and at night, and for the elderly – in the afternoon (Table 3). According to unconstrained DLM, a lower concentration of O_3 on the day of the call was associated with a higher risk of EAC throughout the day, especially during spring–summer period and for the elderly (Table 4). A positive association between the risk of EAC and O_3 levels above the median at

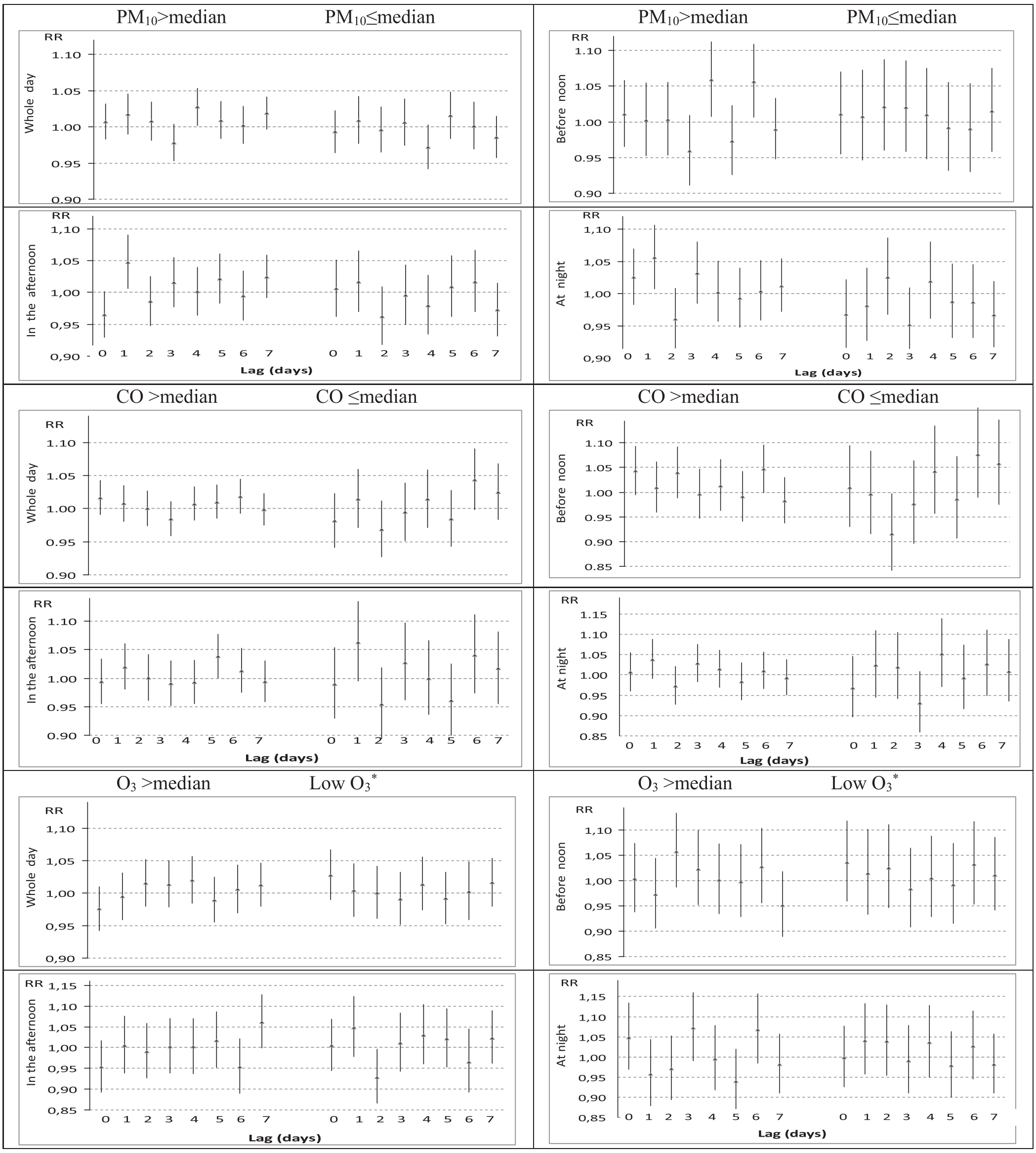

Figure 1. The results of the unconstrained distributed time-lag threshold model for particulate matter with an aerodynamic diameter ≤10 µm (PM_{10}), for the highest 8-h moving average of carbon monoxide (CO) concentration and for ozone, adjusted for the month, the day of the week, weather variables presented in Table 3, and for air temperature and relative humidity.

Notes: RR per interquartile range (7.9 and 18.8 µg/m^3 for PM_{10} ≤ median and PM_{10} > median, respectively; 146 and 345 µg/m^3 for CO ≤ median and CO > median, respectively; 15.4 µg/m^3 for O_3 > median) increase and per IQR (14.5 µg/m^3) decrease for low O_3; *max(median-O_{3t}, 0).

lag 2 day was observed in the afternoon during spring–summer, and a negative association – at night at lag 0–2 days (Figure 1, Table 4). Additional adjustment for the space weather variable showed that the significance of the variables of PM_{10} and CO decreased (Table 5).

In the multivariate model of pollutants, a higher daily number of EAC for EABP was associated with a higher PM_{10} concentration above the median at lag 4 days, a higher CO concentration at lag 6–7 days, and a lower O_3 concentration on the day of the call; a stronger impact of O_3 was observed during summer (Table 6). The patients aged ≤65 years were more sensitive to CO above the median at lag 0–1 days, especially during the equinox, and to PM_{10} > median at lag 4–6 days during winter.

Table 3. The association between PM_{10} and CO and EAC for EABP, adjusting for month, years, the day of the week, the day length, and weather variables*. Rate ratios with 95 % CI per increase in IQR** of PM_{10}, and CO.

		All patients		Age ≤ 65 years		Age > 65 years	
Variable	Lag	RR (95 % CI)	*p*	RR (95 % CI)	*p*	RR (95 % CI)	*p*
Whole day							
PM_{10}	1	1.02 (1.00–1.04)	0.019	1.03 (1.01–1.06)	0.016	1.02 (0.99–1.04)	0.197
PM_{10} > median	4–6	1.04 (1.01–1.06)	0.002	1.04 (1.00–1.08)	0.033	1.03 (1.00–1.06)	0.064
PM_{10}	4–6	1.03 (1.01–1.05)	0.006	1.03 (1.00–1.06)	0.063	1.02 (1.00–1.04)	0.125
PM_{10}	1–7	1.04 (1.01–1.07)	0.006	1.04 (0.99–1.08)	0.103	1.03 (1.00–1.07)	0.065
CO	1	1.03 (1.01–1.05)	0.011	1.03 (1.00–1.06)	0.077	1.02 (1.00–1.05)	0.066
CO	0–1	1.03 (1.01–1.06)	0.008	1.04 (1.00–1.07)	0.051	1.03 (1.00–1.06)	0.049
CO > median	0–1	1.03 (1.00–1.06)	0.005	1.04 (1.01–1.08)	0.021	1.03 (1.00–1.06)	0.064
CO	6–7	1.03 (1.01–1.05)	0.014	1.01 (0.98–1.05)	0.529	1.04 (1.01–1.07)	0.007
CO < median	6–7	1.04 (1.00–1.09)	0.035	1.05 (0.98–1.11)	0.151	1.03 (0.98–1.08)	0.317
CO > median	6–7	1.02 (1.00–1.04)	0.037	1.00 (0.97–1.04)	0.866	1.03 (1.01–1.06)	0.018
CO	1–7	1.05 (1.02–1.09)	0.004	1.05 (1.00–1.11)	0.063	1.05 (1.00–1.10)	0.031
*Adjusted for weather variable (lag)		T_W (0–1); WS (6); BP_L (0–2); BP_H (4), WS_L (0–6)		T_W (0–1); WS (6),BP_L (2); ΔBP_L (0 and 5); RH_L (0)		T_W (0–1 and 5–7); WS_L (0–4); BP_L (0–2); BP_H (4)	
Morning-early afternoon							
PM_{10} < median	2–4	1.07 (1.00–1.14)	0.045	1.00 (0.91–1.09)	0.945	1.13 (1.04–1.23)	0.004
PM_{10} > median	4–6	1.06 (1.01–1.12)	0.026	1.11 (1.03–1.19)	0.004	1.02 (0.96–1.09)	0.518
PM_{10}	4–6	1.05 (1.01–1.09)	0.025	1.09 (1.03–1.15)	0.005	1.02 (0.97–1.08)	0.409
PM_{10}	1–7	1.06 (1.00–1.12)	0.055	1.10 (1.02–1.19)	0.014	1.03 (0.97–1.10)	0.371
CO	0–1	1.02 (0.99–1.06)	0.217	1.05 (0.98–1.12)	0.148	1.03 (0.98–1.09)	0.222
CO	6–7	1.05 (1.00–1.09)	0.034	1.03 (0.96–1.10)	0.444	1.05 (1.00–1.11)	0.067
CO > median	6–7	1.03 (0.98–1.07)	0.218	1.01 (0.94–1.08)	0.800	1.03 (0.98–1.09)	0.275
CO < median	6–7	1.11 (1.03–1.19)	0.009	1.09 (0.97–1.22)	0.146	1.12 (1.01–1.24)	0.027
CO	1–7	1.06 (0.99–1.14)	0.091	1.09 (0.99–1.21)	0.085	1.02 (0.93–1.11)	0.656
*Adjusted for weather variable (lag)		T_W (0–1, 5–7); WS_L (4–6); BP_L (0–2, 5); BP_H (4–6); ΔRH_H (0); ΔRH_L (3–4, 6)		ΔT (1); ΔWS_L (6); ΔBP_L (0, 3–4); BP_L (6); ΔRH (0); ΔRH_H (4)		ΔT of T_W (3–4); WS_L (4–6); BP_L (0–2); ΔRH_H (0); ΔRH_L (3–4, 6)	
In the afternoon							
PM_{10}	1	1.03 (1.00–1.05)	0.033	1.02 (0.98–1.06)	0.259	1.02 (0.98–1.05)	0.346
PM_{10} > median	1	1.04 (1.01–1.07)	0.023	1.03 (0.98–1.08)	0.236	1.02 (0.98–1.07)	0.306
PM_{10} > median	1–7	1.06 (1.01–1.11)	0.024	1.00 (0.93–1.08)	0.952	1.08 (1.01–1.15)	0.016
PM_{10}	1–7	1.04 (1–00–1.08)	0.046	1.00 (0.94–1.07)	0.930	1.05 (1.00–1.10)	0.045
CO	1	1.03 (0.00–1.06)	0.043	1.02 (0.98–1.07)	0.339	1.03 (0.99–1.06)	0.187
CO > median	1–7	1.05 (1.00–1.11)	0.050	0.99 (0.91–1.08)	0.845	1.09 (1.02–1.16)	0.010
CO	1–7	1.05 (1.00–1.10)	0.076	0.99 (0.91–1.08)	0.851	1.08 (1.01–1.15)	0.019
*Adjusted for weather variable (lag)		T_W (0–1); WS (6); WS_L (0–4); BP_L (6);		T_W 1 (0–1); WS (6); BP_L (0); RH_L (0); RH_H (1); ΔRH_H (4)		T_W (0–1); T_C (1); WS_L (0–4); BP_L (6);	
At night							
PM_{10} > median	0–1	1.06 (1.01–1.10)	0.013	1.04 (0.97–1.11)	0.292	1.07 (1.01–1.13)	0.025
PM_{10}	0–1	1.04 (1.00–1.07)	0.047	1.02 (0.97–1.08)	0.392	1.05 (1.00–1.10)	0.045
CO	1–7	1.05 (0.99–1.12)	0.085	1.18 (1.06–1.30)	0.002	1.02 (0.94–1.10)	0.644
*Adjusted for weather variable (lag)		T_W (0); BP_H (3); RH_L (1); RH_H (4);		T_W (7); T (7); ΔWS_L (6); BP (2) RH (0, 6); RH_H (4);		T_W (0); WS_L (0); ΔBP_H (1); ΔRH_L (4); RH_H (4)	

**IQR: 18.3, 7.9, and 18.8 μg/m³ for PM_{10}, PM_{10} below the median, and PM_{10} above the median, respectively; 0.367. 0.146, and 0.345 mg/m³ for CO, CO below the median, and CO above the median, respectively; T – air temperature; BP – barometric pressure; WS – wind speed; RH – relative humidity; $T_W = \max(T - 1,0)$; $T_C = \max(-1 - T,0)$; BP_L = max(1006-BP,0); BP_H = max(BP-1006,0); RH_L = min(RH-82,0); RH_H = max(RH-82,0); WS_L = min(WS-6.1,0); WS_H = max(WS-6.1,0); Δ daily change.

The elderly were more sensitive to a decreased O_3 concentration below the median (Table 6). During the period of 8:00–13:59, positive associations were detected between the risk of EAC and PM_{10} at lag 2–4 days below the median and CO at lag 6–7 days below the median; a stronger impact of these pollutants was observed in the elderly. In the afternoon, an increased risk of EAC was associated with a higher PM_{10} above the median on previous day, and for the elderly – with the 7-day average CO above the median. At night–early in the morning, a negative impact on the risk of EAC was associated with a lower O_3 at lag 0–2 days below the median, a higher mean PM_{10} at lag 0–1 days above the median for the elderly, and a higher CO at lag 1–7 days for younger patients (Table 6).

Table 4. The association between O_3 and EAC for EABP, adjusting for month, years, the day of the week, day length, relative humidity, and weather variables in Table 3. Rate ratios with 95 % CI per an increase of IQR[a] of O_3, O_3 > median, and a decrease in IQR of low O_3 (O_3 < median).

		All patients		Age ≤ 65 years		Age > 65 years	
Variable	Lag	RR (95 % CI)	*p*	RR (95 % CI)	*p*	RR (95 % CI)	*p*
Whole day							
O_3	0	0.96 (0.92–0.99)	0.014	0.97 (0.91–1.02)	0.247	0.94 (0.89–0.98)	0.008
Autumn–winter		0.96 (0.91–1.02)	0.185	0.93 (0.85–1.02)	0.116	0.99 (0.92–1.06)	0.714
Spring–summer		0.95 (0.90–1.00)	0.037	0.99 (0.91–1.07)	0.756	0.91 (0.85–0.97)	0.004
Low O_3[b]	0	1.03 (1.00–1.08)	0.032	1.01 (0.96–1.06)	0.700	1.06 (1.02–1.11)	0.005
Autumn–winter		1.03 (0.99–1.08)	0.137	0.96 (0.97–1.10)	0.264	1.03 (0.98–1.09)	0.255
Spring–summer		1.06 (1.00–1.14)	0.053	0.99 (0.89–1.10)	0.835	1.12 (1.04–1.22)	0.005
High O_3[c]	0	0.97 (0.94–1.01)	0.105	1.00 (0.92–1.12)	0.922	0.97 (0.93–1.01)	0.195
Autumn–winter		0.99 (0.92–1.06)	0.775	0.97 (0.93–1.05)	0.447	1.05 (0.96–1.14)	0.319
Spring–summer		0.97 (0.93–1.01)	0.102	0.99 (0.92–1.06)	0.800	0.95 (0.90–0.99)	0.027
O_3	2–4	1.04 (0.99–1.09)	0.162	1.00 (0.93–1.08)	0.982	1.03 (0.96–1.10)	0.415
Autumn–winter		0.97 (0.89–1.05)	0.396	0.99 (0.88–1.12)	0.900	0.97 (0.87–1.08)	0.552
Spring–summer		1.07 (1.00–1.15)	0.043	1.02 (0.92–1.13)	0.706	1.06 (0.96–1.16)	0.258
High O_3[c]	2–4	1.03 (0.99–1.08)	0.111	1.00 (0.94–1.07)	0.930	1.03 (0.97–1.09)	0.299
Autumn–winter		0.97 (0.87–1.09)	0.630	1.05 (0.89–1.25)	0.570	0.95 (0.82–1.09)	0.462
Spring–summer		1.06 (1.01–1.12)	0.017	1.01 (0.95–1.09)	0.700	1.05 (0.98–1.12)	0.169
Additionally adjusting for space weather variable							
O_3	0	0.96 (0.92–0.99)	0.014			0.94 (0.89–0.98)	0.006
Spring–summer		0.95 (0.90–1.00)	0.045			0.91 (0.85–0.97)	0.003
Low O_3[b]	0	1.04 (1.01–1.08)	0.021			1.06 (1.02–1.11)	0.003
Spring–summer		1.08 (1.00–1.14)	0.039			1.14 (1.04–1.14)	0.003
Low O_3[b] SS	0	1.03 (0.99–1.06)	0.112			1.05 (1.00–1.11)	0.031
O_3 SS	2–4	1.07 (1.00–1.15)	0.052				
High O_3[c] SS	2–4	1.06 (1.01–1.12)	0.019				
In the afternoon							
Low O_3[b]	2	0.95 (0.90–1.00)	0.049	0.93 (0.85–1.00)	0.058	0.98 (0.95–1.02)	0.346
Autumn–winter		0.94 (0.88–1.01)	0.101	0.95 (0.86–1.04)	0.303	0.95 (0.88–1.03)	0.257
Spring–summer		0.97 (0.87–1.08)	0.544	0.86 (0.73–1.02)	0.090	1.01 (0.88–1.15)	0.924
Additionally adjusting for space weather variable							
Low O_3[b]	2	0.95 (0.90–1.00)	0.051	0.93 (0.85–1.00)	0.055		
At night							
O_3	1–2	0.92 (0.84–0.99)	0.030	0.92 (0.81–1.04)	0.177	0.95 (0.86–1.06)	0.350
Autumn–winter		0.88 (0.78–1.00)	0.052	0.93 (0.76–1.13)	0.464	0.80 (0.68–0.94)	0.005
Spring–summer		0.95 (0.85–1.06)	0.362	0.91 (0.76–1.08)	0.277	1.08 (0.93–1.24)	0.323
Low O_3[b]	1–2	1.11 (1.03–1.19)	0.004	1.05 (0.94–1.18)	0.338	1.11 (1.02–1.23)	0.015
Autumn–winter		1.11 (1.02–1.22)	0.019	1.09 (0.94–1.25)	0.269	1.16 (1.04–1.30)	0.008
Spring–summer		1.08 (0.93–1.25)	0.317	0.99 (0.78–1.25)	0.925	1.06 (0.88–1.30)	0.530
Low O_3[b]	0–2	1.12 (1.04–1.12)	0.003	1.05 (0.93–1.19)	0.429	1.16 (1.05–1.28)	0.004
Autumn–winter		1.09 (0.99–1.19)	0.087	1.04 (0.89–1.202)	0.627	1.19 (1.05–1.36)	0.006
Spring–summer		1.19 (1.01–1.30)	0.042	1.10 (0.85–1.43)	0.453	1.16 (0.93–1.45)	0.187
Additionally adjusting for space weather variable							
O_3	1–2	0.92 (0.85–1.00)	0.045				
O_3 AW	1–2	0.87 (0.77–0.99)	0.039			0.79 (0.67–0.93)	0.005
Low O_3[b]	1–2	1.11 (1.03–1.19)	0.003			1.12 (1.02–1.22)	0.014
Low O_3[b] AW	1–2	1.12 (1.02–1.22)	0.014			1.18 (1.04–1.32)	0.007
Low O_3[b]	0–2	1.12 (1.04–1.22)	0.004			1.16 (1.05–1.28)	0.004
Low O_3[b] AW	0–2	1.09 (0.99–1.20)	0.084			1.20 (1.05–1.37)	0.006
Low O_3[b] SS	0–2	1.19 (1.01–1.41)	0.043				

[a]IQR: 26.1, 14.5, and 15.4 μg/m^3 for O_3, O_3 below the median, and O_3 above the median, respectively.
[b]LowO_3 = max(median-O_3, 0).
[c]HighO_3 = max(O_3-median, 0); AW – autumn–winter; SS – spring–summer.

Discussion

According to our results, significant increases in the daily number of EAC for EABP occurred in association with a higher level of CO and PM_{10} and a lower level of O_3 in the multivariate pollutants

Table 5. The association between air pollutants and emergency calls for EABP, adjusting for month, years, the day of the week, the day length, weather variables in Table 3, and the space weather variable. Rate ratios with 95 % CI per an increase in IQR[a] of PM_{10} and CO.

		All patients		Age ≤ 65 years		Age > 65 years	
Variable	Lag	RR (95 % CI)	*p*	RR (95 % CI)	*p*	RR (95 % CI)	*p*
Whole day							
PM_{10}	1	1.02 (1.00–1.04)	0.044	1.03 (1.01–1.06)	0.019		
PM_{10} > median	4–6	1.04 (1.01–1.06)	0.006	1.05 (1.01–1.09)	0.024	1.02 (0.99–1.05)	0.287
PM_{10}	4–6	1.03 (1.01–1.05)	0.012	1.03 (1.00–1.07)	0.043		
PM_{10}	1–7	1.04 (1.01–1.07)	0.017			1.02 (0.99–1.06)	0.190
CO	1	1.02 (1.00–1.04)	0.019	1.03 (1.00–1.06)	0.068	1.02 (1.00–1.04)	0.120
CO	0–1	1.03 (1.01–1.05)	0.015	1.04 (1.00–1.07)	0.051	1.03 (1.00–1.06)	0.089
CO > median	0–1	1.03 (1.01–1.06)	0.009	1.04 (1.01–1.08)	0.019	1.03 (0.99–1.06)	0.114
CO	6–7	1.03 (1.00–1.05)	0.034			1.03 (1.00–1.06)	0.053
CO < median	6–7	1.04 (1.00–1.09)	0.037			1.02 (0.97–1.08)	0.363
CO > median	6–7	1.02 (1.00–1.04)	0.085			1.02 (1.00–1.05)	0.103
CO	1–7	1.04 (1.01–1.09)	0.010	1.06 (1.00–1.11)	0.050	1.04 (0.99–1.09)	0.088
Before noon							
PM_{10} < median	2–4	1.07 (1.00–1.14)	0.045			1.13 (1.04–1.23)	0.004
PM_{10} > median	4–6	1.05 (1.00–1.11)	0.059	1.11 (1.03–1.19)	0.005		
PM_{10}	4–6	1.04 (1.00–1.09)	0.055	1.09 (1.03–1.15)	0.005		
PM_{10}	1–7	1.05 (1.00–1.12)	0.068	1.11 (1.02–1.20)	0.012		
CO	6–7	1.04 (0.99–1.08)	0.099			1.04 (0.98–1.09)	0.168
CO < median	6–7	1.10 (1.02–1.19)	0.013			1.12 (1.01–1.24)	0.027
CO	1–7	1.05 (0.98–1.13)	0.160	1.09 (0.98–1.21)	0.098		
In the afternoon							
PM_{10}	1	1.02 (1.00–1.05)	0.080				
PM_{10} > median	1	1.04 (1.00–1.07)	0.031				
PM_{10} > median	1–7	1.05 (1.00–1.10)	0.061			1.06 (1.00–1.13)	0.065
PM_{10}	1–7	1.04 (1.00–1.08)	0.084			1.04 (0.99–1.09)	0.127
CO	1	1.03 (1.00–1.06)	0.056				
CO > median	1–7	1.05 (1.00–1.11)	0.063			1.08 (1.01–1.15)	0.026
CO	1–7	1.05 (0.99–1.10)	0.091			1.07 (1.00–1.14)	0.043
At night							
PM_{10} > median	0–1	1.05 (1.01–1.10)	0.015			1.06 (1.01–1.13)	0.032
PM_{10}	0–1	1.04 (1.00–1.07)	0.057			1.05 (1.00–1.09)	0.059
CO	1–7	1.05 (0.99–1.12)	0.091	1.18 (1.07–1.31)	0.002		

[a]IQR: 18.3, 7.9, and 18.8 μg/m^3 for PM_{10}, PM_{10} below the median, and PM_{10} above the median, respectively; 0.367. 0.146, and 0.345 mg/m^3 for CO, CO below the median, and CO above the median, respectively.

model. Unlike previous authors, we adjusted the RRs for the space weather variable because elevated GMA associated with an EABP (Dimitrova et al. 2004).

In our study, we found a significant positive association between the risk of EAC for EABP and PM_{10} at lag 1 and lag 4–6 days above the median. Other authors obtained similar results. The increase in the risk of emergency hospital visits for AH was associated with an increase in PM_{10} at lag 2 day in Beijing, China (Guo et al. 2010a) and at lag 3–4 and 6 days in Canada (Szyszkowicz et al. 2012). In the latter study, the concentrations of pollutants were similar to those found in our study. Most of the studies on the link between air pollution and human health found a positive association between PM_{10} exposure and blood pressure (Cai et al. 2016; Giorgini et al. 2016). We found a significant association with mean CO above the median at lag 0–1 days and CO at lag 6–7 days. Other researchers (Qorbani et al. 2012; Szyszkowicz et al. 2012) did not find any significant associations between CO levels and visits to emergency departments for AH. However, Qorbani et al. (2012) found that the association between exposure to CO and the risk of acute coronary syndrome was stronger in females than in males. In our study, 78.4 % of the patients were females, to which a significant effect of CO exposure might be attributed. There are few studies on the association between short-term exposure to outdoor CO and blood pressure (Giorgini et al. 2016). Only Huang et al. (2012) found a statistically significant positive association between 12-h exposure to outdoor CO and systolic and diastolic blood pressure in patients with cardiovascular disease. A significant positive association was found between mean

Table 6. The multivariate pollutants models. Rate ratios per the increase in IQR[a] of PM_{10}, CO, and O_3, adjusted for the month, years, the day of the week, the day length, weather variables, and the space weather variable.

		All period		Winter	Equinox	Summer
Variable	Lag	RR (95 % CI)	*p*	RR (95 % CI)	RR (95 % CI)	RR (95 % CI)
All patients whole day						
PM_{10} > median	4	1.02 (1.00–1.04)	0.039	1.02 (0.99–1.06)	1.02 (0.99–1.06)	0.98 (0.88–1.09)
CO	6–7	1.04 (1.02–1.07)	0.001	1.05 (1.02–1.09)	1.05 (1.02–1.09)	1.02 (0.88–1.18)
O_3	0	0.95 (0.92–0.99)	0.005	0.98 (0.93–1.03)	0.98 (0.93–1.03)	0.91 (0.84–0.99)
All patients before noon						
PM_{10} < median	2–4	1.08 (1.01–1.15)	0.031	1.11 (0.94–1.31)	1.16 (1.05–1.27)	0.91 (0.72–1.16)
CO < median	6–7	1.05 (1.01–1.10)	0.028	1.02 (0.94–1.11)	1.09 (1.02–1.16)	1.02 (0.74–1.40)
All patients in the afternoon						
PM_{10} > median	1	1.04 (1.00–1.07)	0.031	1.03 (0.98–1.08)	1.03 (0.98–1.08)	0.88 (0.73–1.07)
All patients at night						
O_3 < median[b]	0–2	1.10 (1.02–1.18)	0.018	1.15 (1.01–1.32)	1.03 (0.92–1.14)	1.23 (0.97–1.59)
PM_{10} > median	1	1.04 (1.00–1.08)	0.059	1.03 (0.97–1.09)	1.04 (0.97–1.11)	1.12 (0.91–1.37)
Age ≤ 65 years whole day						
CO > median	0–1	1.04 (1.00–1.08)	0.028	1.04 (0.99–1.09)	1.06 (1.00–1.13)	2.05 (0.95–4.41)
PM_{10} > median	4–6	1.03 (0.99–1.07)	0.185	1.09 (1.01–1.17)	1.01 (0.95–1.06)	1.13 (0.91–1.39)
Age ≤ 65 years before noon						
PM_{10} > median	4–6	1.11 (1.03–1.19)	0.005	1.16 (1.01–1.34)	1.09 (0.99–1.21)	1.07 (0.74–1.58)
Age ≤ 65 years at night						
CO	1–7	1.18 (1.07–1.31)	0.002	1.12 (0.93–1.35)	1.34 (1.12–1.59)	0.99 (0.52–1.86)
Age > 65 years whole day						
O_3 < median[b]	0	1.05 (1.01–1.10)	0.012	1.09 (1.01–1.16)	1.02 (0.96–1.09)	1.12 (0.99–1.28)
Age > 65 years before noon						
PM_{10} < median	2–4	1.13 (1.04–1.23)	0.005	1.23 (0.99–1.52)	1.12 (1.00–1.26)	1.13 (0.88–1.45)
CO < median	6–7	1.12 (1.02–1.24)	0.024	1.11 (0.74–1.66)	1.22 (1.06–1.42)	1.14 (0.84–1.37)
Age > 65 years in the afternoon						
CO > median	1–7	1.08 (1.01–1.15)	0.026	1.07 (0.95–1.19)	1.04 (0.95–1.14)	0.99 (0.29–3.35)
Age > 65 years at night						
O_3 < median[b]	0–2	1.12 (1.02–1.25)	0.021	1.23 (1.02–1.47)	1.03 (0.89–1.18)	1.33 (0.97–1.85)
PM_{10} > median	0–1	1.07 (1.01–1.13)	0.030	1.05 (0.95–1.15)	1.01 (0.91–1.12)	1.11 (0.80–1.54)

[a]IQR: 18.3, 7.9, and 18.8 μg/m^3 for PM_{10}, PM_{10} below the median, and PM_{10} above the median, respectively; 0.367. 0.146, and 0.345 mg/m^3 for CO, CO below the median, and CO above the median, respectively; 26.1, 14.5, and 15.4 μg/m^3 for O_3, O_3 below the median, and O_3 above the median, respectively.
[b]RR per decrease in IQR.

72-h-averaged personal CO exposure and diastolic blood pressure in pregnant women in Ghana (Quinn et al. 2016).

According to research of other authors (Brook et al. 2010), a negative impact of PM exposure manifests itself by direct interaction of pollutants with blood, systemic inflammation with an increase in pro-inflammatory biomarkers, and the modification of the autonomic nervous system. The overlapping of these three mechanisms eventually may cause an increase in EAC for EABP on 4–6 day after elevated exposure to PM_{10}, especially above the median. The effect of PM_{10} on the previous day might be explained by the rapid impact of some components of PM_{10} – such as endotoxin and β-1,3-d-glucan (Cascio et al. 2015). In our study, a stronger impact of exposure to PM_{10} was found for younger patients. In a systemic review and meta-analysis (Cai et al. 2016), a negative association between age and the severity of the effect of air pollution was stated. The protective effect of age might be related to the different medication use: older people usually use more medication than young people do, and not taking medication was a strong predictor of an increase in blood pressure (Szyszkowicz et al. 2012). Low levels of CO act as a gasotransmitter activating signaling pathways (Reboul et al. 2017). This may explain the negative effect of CO at lag 0–1 days. It has been proposed that exposure to CO is associated with oxidative stress (Brook et al. 2010). It is possible oxidative stress is responsible for the negative impact after 6–7 days.

Our study revealed a negative association between O_3 exposure on the day of the call and daily EAC and a positive association between exposures to O_3 above the median at lag 2–4 days during spring–summer. Many researchers stated a negative effect of short-term exposure to O_3 on human health. Systematically reviewed epidemiologic evidence regarding sensitivity to mortality or hospital admission due to asthma from short-term ozone exposure indicates higher associations for mortality among women than among men (Bell et al. 2014). In the studies on the exposure to air pollutants and emergency visits or hospitalizations due to AH, only one study found a significant association with O_3. According to studies conducted in Canada (Brook and Kousha 2015), a statistically significant increase in the risk of emergency department (ED) visits for hypertension was associated with an increase in O_3 concentration at lag 3 and 4 days for females during the warm season. During the cold season (October–March), a statistically significant increase in the risk of ED visits for hypertension was associated with a decrease in O_3 concentration at lag 7 days for females. However, some studies indicated a protective impact of a higher concentration of troposphere ozone. A study (Middleton et al. 2008) that associated exposure to O_3 with hospital admissions for respiratory or cardiovascular diseases found that the impact of exposure to O_3 was similar to that found in our study. In addition, a negative association between the risk of hospital admission and O_3 levels on the day of the call and positive associations with levels of ozone at lag 2 day were observed (Middleton et al. 2008). The results obtained by other researchers showed that the effect of exposure to troposphere ozone on the risk of myocardial infarction was both positive and negative (Mustafic et al. 2012). In subjects with diabetes mellitus, an interquartile increase in a 5-day mean concentration of ozone (13.3 ppb) was associated with a 5.2 mm Hg (95 % CI: −8.6, −1.8 mm Hg) decrease in systolic blood pressure (Hoffmann et al. 2012). The negative association between O_3 concentration and the risk of EAC during spring–summer might be explained by the impact of weather conditions associated with higher O_3 levels. Lower O_3 levels are associated with overcast and rainy conditions and higher air pollution levels (Milanchus et al. 1998). These environmental conditions may negatively affect human health causing an increase in EAC. A higher O_3 concentration is associated with light wind, sunny days, a higher air temperature, low cloudiness, and a lower relative humidity. These conditions (especially sunny days) may be associated with reduced stress and better mood and well-being, which reduces the incidence of AH flare-ups. In addition, a higher air temperature is associated with a lower blood pressure (Barnett et al. 2007).

Another main finding in our study was that the impact of pollutants was not identical for different time of the day. In the morning–early afternoon, a negative impact of pollutants (PM_{10} and CO) only on lag 2–6 days was observed. The weakest impact of pollutants was observed in the afternoon – for PM_{10} above the median on the previous day for all patients and for CO at lag 1–7 days above the median. For all patients and for the elderly, a negative impact of pollutants at lags 0–2 days was observed. In addition, a negative impact of low ozone levels was found.

In our study, an instantaneous effect of PM_{10} above the median (lag 0–1 days) was observed at night–early in the morning. This effect might be explained by the impact of PM_{10} on the quality of the sleep. A study that also focused on the impact of PM_{10} on the circadian rhythm of blood pressure also showed a stronger impact of exposure to PM_{10} at lag 0–2 days during nighttime: an increase in PM_{10} concentration was associated with an increase in nighttime systolic blood pressure on the same day and 1 day before (Tsai et al. 2012). In addition, PM exposure can also reduce daytime sodium excretion and blunt the normal nocturnal reduction in blood pressure. If this happens repeatedly, the impaired renal handling of excess sodium may partly contribute to elevated blood pressure (Tsai et al. 2012). The effect at night may be due to the adverse effects of PM_{10} on the quality of sleep. A decrease in sleep efficiency has been associated with an increase in short-term variation of PM_{10} (Zanobetti et al. 2010). It has been hypothesized that sleep is a mediator in the pathway linking environmental factors to hypertension (Akinseye et al. 2015) and in the afternoon.

During 8:00–13:59, a higher risk of EAC was associated with an increase in PM_{10} at lag 2–4 days below the median; a stronger impact was observed in the elderly. The absence of a positive association between PM_{10} above the median may also be explained by exhaust particles being larger when the levels of PM_{10} are lower. Inhalation of this particulate matter may be associated with its direct translocation into blood (Mannucci 2013). In addition, adverse vascular effects of diesel exhaust inhalation in healthy volunteers were detected (Mills et al. 2011); the elderly might have been more sensitive to pollutants.

Higher PM_{10} in winter might mean more crusted material (road dust) and more abundant soot and organic particles from wood smoke with different deposition and toxicity. The impact of PM_{10} at lag 2–4 days below the median may be explained by oxidative stress and an increase in inflammatory markers related to endothelial dysfunction, vasoconstriction, and blood metabolism (Brook et al. 2010). These factors may be important in obtaining appropriate EAC readings in the morning, when the sympathetic nervous system is more active.

A significant impact of PM_{10} exposure at lag 4–6 days was observed only during time period of 8:00–13:59 and only in patients aged ≤65 years. This may be explained by the fact that after some time, the effect of PM_{10} occurs in the presence of a more active sympathetic nervous system. The central nervous system suffers adverse health effects of air pollution with PM_{10}, which may contribute to neurodevelopmental and neurodegenerative disorders, and may lead to neurotoxicity (Costa et al. 2015). The cerebellum and hippocampus seem to be more susceptible to direct PM exposure than other brain structures are, and the oxidative stress pathway catalyzes the neurotoxic effect of PM exposure (Fagundes et al. 2015). The difference in the impact of the exposure to PM_{10} in the morning–early afternoon between younger and elderly patients might be related to the different medication use between young age and elderly individuals.

In our study, an increase in CO at lag 6–7 days below the median was associated with an elevated risk of EAC before noon, especially for the elderly and during the equinox. A clear mechanism of action underlying the potentially toxic effects of low-level CO exposure is the decreased oxygen-carrying capacity of blood and subsequent reduction in oxygen release at the tissue level (Raub 1999). In animal studies, exposure to CO was associated with oxidative stress (Meyer et al. 2010; Reboul et al. 2017), and this may explain the reduction of the effects of CO after 6–7 days. We think that this effect was stronger before noon, when the sympathetic nervous system was more active. In addition, the decrease in heart rate variability was stronger in cardiovascular patients with elevated inflammatory markers and with overweight (Huang et al. 2012). This explains the stronger impact of exposure to CO at lag 6–7 days below the median during the equinox because during this period, there were cases associated with inflammatory processes and with the elderly because the risk of overweight was related to age (Snijder et al. 2006).

In our study, an increase in CO at lag 1–7 days above the median was associated with an elevated risk of EAC in the afternoon for the elderly. CO binding in the lungs with hemoglobin in the blood forms carboxyhemoglobin (COHb) and induces hypoxia, neurological deficits, and neurobehavioral changes, and also increases daily mortality and hospital admissions for cardiovascular diseases (Schwela 2000). Experimental studies have shown that low levels of CO adversely affect patients with heart disease on exertion: the exercise tolerance test (time to the onset of angina) was shorter in patients exposed to CO (Allred et al. 1989; Raub 1999). During daytime, people may be more physically active, which may strengthen the impact of pollution with CO – and thus higher CO concentrations may affect EAC in the afternoon and in the elderly. For younger patients, an increased weekly exposure to CO was associated with a higher EAC at night–nearly in the morning. This could possibly happen due to prolonged impact of CO during the active period of the day. In addition, CO concentration correlated with PM_{10} concentration. In total, the aforementioned negative impact of CO might have been due to impact of exposure to PM_{10}.

A significant negative impact of low ozone concentration was detected only during time period of 22:00–7:59, especially for the elderly and in autumn–winter. The negative associations between ozone at lag 0–2 days below the median and EAC for EABP might be explained by the fact that ozone is associated with an enhancing release of NO and at low concentrations may affect as a vasodilator (Valacchi and Bocci 2000). This impact of ozone below the median on emergency calls at night–early in the morning may be explained by the fact that ozone is an oxidant with immediate effect on pulmonary reflexes (Lee and Pisarri 2001), and the exposure to ozone is stronger when parasympathetic nervous system is more active because parasympathetic nervous receptor are more numerous in the lungs (Beckett et al. 1985; McCorry 2007). Therefore, these possible effects attributed to vasodilatation in the afternoon reduced EAC at night. In addition, low O_3 concentrations are associated with overcast and rainy conditions, which may have a negative effect at night – especially in the elderly.

The inclusion of the space weather variable in the Poisson regression model decreased the RRs and increased its *p*-value up to 0.05 for PM_{10} – especially in the afternoon and for the elderly. Elderly patients were likely to be more sensitive to these space weather events (Mendoza and Diaz-Sandoval 2004; Vencloviene et al. 2014) as well as to air pollution (Carey et al. 2016; Costa et al. 2017), and therefore the impact of the space weather variable may affect the data for older patients.

In some cases, the association between the pollutant and the risk of emergency event is non-linear (de Souza et al. 2014; Taj et al. 2016; Xia et al. 2017). In our study, a non-linear association between pollutants and EAC for EABP was observed. In the analysis, we used the linear spline models to evaluate the relationship between EAC and air pollution data. Popular models for this purpose are natural cubic spline curves, but simpler models allow for a better interpretation of risk estimates as well as for their comparison between different times of the call or population subgroups (Armstrong 2006). The interpretation of the results obtained by using spline functions is difficult, but in our study and in the previous study (Vencloviene et al. 2017), a significant impact of pollutants only below or above the median was observed.

We found no clear effect modification of the pollutants' effect by season, but the estimate before noon was somewhat higher during the equinox. The impact of ozone was more pronounced in summer. A possible explanation includes a different chemical composition of the PM mixture during the warm season when, in the absence of household heating, traffic emissions cause a greater fraction of the overall particle mass or varying ventilation patterns in warm and cold seasons, resulting in different personal exposure (Fuks et al. 2011).

Limitations

Our study is limited in that we had no data on personal risk factors – e.g. alcohol use or smoking, stress, or co-morbidities. In addition to that, we did not have any data on other environmental factors that might have increased the risk of EAC for EABP – i.e. the climatic conditions within peoples' homes (indoor air temperature and air quality), the exposure to environmental noise, and the time spent indoors. In this study, we did not evaluate the effectiveness of pharmacological treatment. All these factors may be seen as confounding factors.

Conclusions

Our results showed that significant increases in the daily number of EAC for EABP occurred in association with a higher level of CO and PM_{10} and a lower level of O_3 in the multivariate pollutants model. The space weather variable included as the impact of elevated GMA and HSSW may be used as a confounding factor in studies on the association between short-term air pollution and the exacerbation of AH. In addition, the impact of pollutants was not identical for different time of the day. During the period of 8:00–13:59, positive associations were detected between the risk of EAC and PM_{10} at lag 2–4 days below the median and CO at lag 6–7 days below the median; a stronger impact of exposure to these pollutants being observed in the elderly. In the afternoon, an increased risk of EAC was associated with a higher PM_{10} concentration above the median on the previous day, and for the elderly – with a 7-day average CO above the median. At night–early in the morning, the risk of EAC was negatively affected by a lower O_3 at lag 0–2 days below the median and a higher mean PM_{10} at lag 0–1 days above the median for the elderly, and a higher CO concentration at lag 1–7 days for younger patients.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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