SHORT-TERM EFFECTS OF AIR POLLUTION ON CARDIOVASCULAR MORTALITY IN ELDERLY IN NIŠ, SERBIA

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SUMMARY

The short-term effects of air pollution on cardiovascular mortality in elderly were investigated in Niš, during the 2001–2005. Daily measurements of black smoke (BS) and sulphur dioxide (SO$_2$), as well as the daily number of cardiovascular death among person ≥ 65 yrs of age, were collected. Generalized linear model extending Poisson regression was applied. The effects of time trend, seasonal variations, day of week, temperature, relative humidity and barometric pressure were analysed. The results did not support findings from previous studies that had shown an increase in the number of cardiovascular death in elderly in association with air pollution.

Key words: elderly, cardiovascular death, mortality, black smoke, sulphur dioxide

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INTRODUCTION

Epidemiological evidence in the last decade confirmed that elevated concentrations of air pollution contributed to the adverse cardiovascular health effects (1–5). These effects refer to cardiovascular morbidity, hospitalization and mortality.

The potential biological mechanisms of influence air pollution on cardiovascular system have two possible interlinks-inflamatory response and abnormal autonomic control (6–8). Inflammatory response leads to the release of prothrombotic and inflammatory cytokines into the circulation resulting in plaque rupture. Abnormal autonomic control leads to an increased risk of arrhythmia in susceptible patients.

Many air pollutants are in the relationship with cardiovascular damage but of special interest are particulate matters with different aerodynamic diameter (9–11). The time series data suggest that an increase in particulate pollution of 10 µg/m$^3$ is associated with an increased cardiovascular mortality of about 1.4% (12, 13). The elderly are the population group which is more sensitive to effects of air pollution (14–17).

This is the second study providing quantitative estimates of the short-term effects of air pollution on mortality in our country. The first one, by Bogdanović et al. (18), has shown that cardiovascular and total non-accidental mortality are related to ambient black smoke (BS) concentrations.

This paper reports the results on the effects on daily BS and sulphur dioxide (SO$_2$) on cardiovascular mortality among person ≥ 65 yrs in Niš.

MATERIAL AND METHODS

The study area is the city of Niš, the second biggest city in Serbia. The urban city area covers 32 km$^2$ with population of around 171,000 inhabitants. A major source of air pollution is fuel combustion including motor vehicle emissions and residential wood, coal and oil burning.

Daily cardiovascular mortality data between 2001 and 2005 were obtained from the Republic Institute for Statistics in charge of coding the medical causes of death according to the International Classification of Diseases – 10$^{th}$ Revision (I00-I99) among person ≥ 65 years old.

Air pollution data were provided by the Public Health Institute of Niš. Daily concentrations of BS and SO$_2$ were monitored using the local monitoring network. BS (µg/m$^3$) was measured by the refractometry method and SO$_2$ (µg/m$^3$) by spectrophotometer. Missing air pollution values for 6% days of the period were treated as being missing completely at random and were dropped from the analyses.

The concentrations of the outdoor air pollutants sulphur dioxide and black smoke, were measured for 24 hours a day during the period from 2001 to 2005. The sampling protocol was carried out by well trained personnel. The laboratory experiments on sulphur dioxide and black smoke were done according to the Regulation of Guideline Values of Immission (Official Register Republic of Serbia 54/92).

The ambient level of black smoke was measured by the reflectance. The sampling was performed by the means of a pump...
operating with a flow rate of 1 l/min through Whatman No. 1 paper filters.

The air concentration of sulphur dioxide was determined simultaneously with that of black smoke. A measured volume of air was bubbled through solution of potassium mercury tetrachloride. The sulphur dioxide which is presented in the air stream reacted with acid-bleached pararosaniline dye and formaldehyde yielding intensely coloured pararosaniline methyl sulphuric acid. The optical density of this species was determined spectrophotometrically at 548 nm and was directly related to the collected amount of sulphur dioxide. The total volume of the air sample was determined from the flow rate and the sampling time. The concentration of sulphur dioxide in the ambient air was computed and expressed in µg/m³ and the lower limit of detection was 1.7 µg/m³.

The daily mean temperature, the mean relative humidity and the mean barometric pressure values for the same period were obtained from Republic Meteorological Department.

Generalized linear model (GLM) extending Poisson regression was applied allowing over dispersion. This model used mortality counts as the response variable, the natural cubic splines of the calendar time, temperature, relative humidity and barometric pressure, the day of week and season as indicator variables, and air pollution as predictor variable.

To construct the model individual lag 0 (value on a current day) for relative humidity, barometric pressure, BS and SO₂ were used. For temperature individual lag 0 and lag 0–3 (average of values on a current day and three days earlier) were used, both. The model fitting was based on Akaike Information Criteria (AIC). The degrees of freedom for natural spline functions of time and weather variables influence approximation that gave the smallest AIC value were selected. The pollutants were fitted as linear term. The Pearson's correlation coefficients between air pollutants and meteorological variables are presented in Table 2.

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**Persons of All Ages**

\[ \log(\hat{Y}_i) = a + \text{ns}(\text{calendar time, } \text{df} = 30) + \text{indicator} (\text{season}) + \text{indicator} (\text{day of week}) + \text{ns} (\text{mean temperature}_{\text{lag}=0}, \text{df} = 4) + \text{ns} (\text{mean temperature}_{\text{lag}=0,3}, \text{df} = 4) + \text{ns} (\text{mean relative humidity}_{\text{lag}=0}, \text{df} = 2) + \text{ns} (\text{mean air pressure}_{\text{lag}=0}, \text{df} = 2) + \text{air pollution}_{\text{lag}=0} \]

**Persons Older than 65 Years**

\[ \log(\hat{Y}_i) = a + \text{ns} (\text{calendar time, } \text{df} = 30) + \text{indicator} (\text{season}) + \text{indicator} (\text{day of week}) + \text{ns} (\text{mean temperature}_{\text{lag}=0}, \text{df} = 4) + \text{ns} (\text{mean temperature}_{\text{lag}=0,1}, \text{df} = 4) + \text{ns} (\text{mean relative humidity}_{\text{lag}=0}, \text{df} = 2) + \text{ns} (\text{mean air pressure}_{\text{lag}=0}, \text{df} = 2) + \text{air pollution}_{\text{lag}=0} \]

where \( \hat{Y}_i \) are daily mortality counts, \( a \) is the intercept, \( ns \) denotes a natural cubic functions of a covariates, and \( df \) represents the number of degrees of freedom.

**RESULTS**

Table 1 shows the daily number of all age cardiovascular deaths, cardiovascular deaths among person ≥ 65 yrs, pollutants concentrations and weather data. During the 5 years, there were 4,818 all age cardiovascular deaths in the city of Niš, and 4,006 cardiovascular deaths among person ≥ 65 yrs. The daily mean number of all age cardiovascular deaths was 2.64±1.69 (0 to 10) and 2.19±1.51 (0 to 3) among person ≥ 65 yrs. The daily mean level for BS was 22.83±21.82 µg/m³, minimum 1.00 µg/m³ and maximum 225.00 µg/m³. The daily mean level for SO₂ was 14.69±12.57 µg/m³, minimum 1.00 µg/m³ and maximum 107.00 µg/m³. The daily mean temperature, the mean relative humidity and the mean barometric pressure values for the same period were 22.83±21.82 °C, 96.60±21.82 %, and 107.00±21.82 mBar.

The Pearson’s correlation coefficients between air pollutants and meteorological variables are presented in Table 2.

Table 2 and Fig. 1 summarize the results of SO₂ influence on all age cardiovascular deaths and among person ≥ 65 yrs. According to the results of unipollutant regression model, the risk of cardiovascular deaths because of an increase of 10 µg/m³ in SO₂ in all age increases by 2.50% (OR=1,02503; 95% CI: 0.99020 to 1.06109), and among person ≥ 65 yrs by 2.83% (OR=1.02834; 95% CI: 0.99929 to 1.06785), but was not significant. Estimated OR of bio pollutant regression model for among person ≥ 65 yrs was 1.01012 (95% CI: 0.99195 to 1.02863), that is, an increase of 10 µg/m³ in SO₂ augmented 1.81% the probability of death on a given day, this again being not significant.

Table 3 and Fig. 2 summarize the results of BS influence on cardiovascular deaths among person ≥ 65 yrs. Estimated OR of unipollutant regression model for among person ≥ 65 yrs was 1.01312 (95% CI: 0.99581 to 1.03072), and estimated OR of bipollutant model was 1.01012 (95% CI: 0.99195 to 1.02863).

Table 1. Summary statistics of daily data in Niš

<table>
<thead>
<tr>
<th>Description</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>25%</th>
<th>Median</th>
<th>75%</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>All age cardiovascular deaths (n)</td>
<td>2.64</td>
<td>1.69</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Cardiovascular deaths among person ≥ 65 yrs (n)</td>
<td>2.19</td>
<td>1.51</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>BS (µg/m³)</td>
<td>22.83</td>
<td>21.82</td>
<td>0.00</td>
<td>9.50</td>
<td>17.00</td>
<td>26.50</td>
<td>225.00</td>
</tr>
<tr>
<td>SO₂ (µg/m³)</td>
<td>14.69</td>
<td>12.57</td>
<td>1.00</td>
<td>6.00</td>
<td>19.00</td>
<td>107.00</td>
<td></td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>12.10</td>
<td>8.80</td>
<td>-11.60</td>
<td>4.90</td>
<td>12.80</td>
<td>19.40</td>
<td>30.50</td>
</tr>
<tr>
<td>Humidity (%)</td>
<td>70.33</td>
<td>13.08</td>
<td>26.00</td>
<td>6.10</td>
<td>71.00</td>
<td>80.00</td>
<td>108.00</td>
</tr>
<tr>
<td>Air pressure (mBar)</td>
<td>993.80</td>
<td>67.00</td>
<td>966.20</td>
<td>989.60</td>
<td>993.30</td>
<td>997.90</td>
<td>1014.80</td>
</tr>
</tbody>
</table>
DISCUSSION

This mortality time series study have shown, that all age cardiovascular mortality and among person ≥ 65 yrs are not related to ambient air pollutants concentrations. There is a risk of cardiovascular death with increase of 10 $\mu g/m^3$ in SO$_2$ and BS, but it is statistically insignificant.

Low quality of the fuel and vehicles results in incomplete fossil burning during the heating and traffic in our country. Growing epidemiological evidence suggests that exposure to the particulate matter such as PM$_{10}$ and PM$_{2.5}$ causes negative health effects. Due to shortage of the equipment for measuring this particulate matter we use BS measurement data for calculation. However, WHO documents (19) indicate that BS could serve as a useful marker in epidemiological studies. Levels of BS and SO$_2$ measured in our study were not very high, and were generally below the national standard (50 $\mu g/m^3$).

The majority of the published studies have found significant associations between a 10 $\mu g/m^3$ increase in air pollutants and increase in daily number of death (20–22). Zmirou et al. (23) found that daily deaths of cardiovascular conditions increased 2% with BS and 4% with SO$_2$. In a study in the city of Dublin, Ireland (24), a reduction in BS concentration by 35.6 $\mu g/m^3$ was associated with a 10.3% decrease in annual cardiovascular mortality.

There is lot of evidence that air pollution has harmful effect on the elderly population. The results of the APHEA2 project (25) indicated that the per cent increase of daily number of death associated with a 10 $\mu g/m^3$ increase in PM$_{10}$ was in elderly 0.8% and the corresponding number for BS was 0.6%. In the elderly, a 3–4% increase in daily deaths for all causes and for cardiovascular

Table 2. Correlation between air pollutants and weather variables

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Humidity</th>
<th>Air pressure</th>
<th>Temperature</th>
<th>SO$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>BS</td>
<td>0.181**</td>
<td>0.197**</td>
<td>-0.305**</td>
<td>0.389**</td>
</tr>
<tr>
<td>SO$_2$</td>
<td>-0.007</td>
<td>0.344**</td>
<td>-0.556**</td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>-0.512**</td>
<td>-0.313**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air pressure</td>
<td>0.020</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

** Significant at the 0.01 level

Table 3. ORs (95% CIs)/10 $\mu g/m^3$ increase in concentration of SO$_2$ for daily numbers of all age cardiovascular deaths and among person ≥ 65 yrs

<table>
<thead>
<tr>
<th>Model</th>
<th>Age</th>
<th>$\beta$</th>
<th>SE</th>
<th>OR</th>
<th>Lower 95%</th>
<th>Upper 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unipolutant</td>
<td>Total</td>
<td>0.02473</td>
<td>0.01764</td>
<td>1.02503</td>
<td>0.99020</td>
<td>1.06109</td>
</tr>
<tr>
<td></td>
<td>≥ 65</td>
<td>0.02795</td>
<td>0.01923</td>
<td>1.02834</td>
<td>0.99029</td>
<td>1.06785</td>
</tr>
<tr>
<td>Bipolutant</td>
<td>Total</td>
<td>0.02128</td>
<td>0.02020</td>
<td>1.02150</td>
<td>0.98185</td>
<td>1.06276</td>
</tr>
<tr>
<td></td>
<td>≥ 65</td>
<td>0.01796</td>
<td>0.01853</td>
<td>1.01812</td>
<td>0.98180</td>
<td>1.05578</td>
</tr>
</tbody>
</table>

Table 4. ORs (95% CIs)/10 $\mu g/m^3$ increase in concentration of BS for daily numbers of all age cardiovascular deaths and among person ≥ 65 yrs

<table>
<thead>
<tr>
<th>Model</th>
<th>Age</th>
<th>$\beta$</th>
<th>SE</th>
<th>OR</th>
<th>Lower 95%</th>
<th>Upper 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unipolutant</td>
<td>total</td>
<td>0.01268</td>
<td>0.00806</td>
<td>1.01276</td>
<td>0.99689</td>
<td>1.02889</td>
</tr>
<tr>
<td></td>
<td>≥ 65</td>
<td>0.01303</td>
<td>0.00879</td>
<td>1.01312</td>
<td>0.99581</td>
<td>1.03072</td>
</tr>
<tr>
<td>Bipolutant</td>
<td>total</td>
<td>0.01017</td>
<td>0.00849</td>
<td>1.01022</td>
<td>0.99354</td>
<td>1.02718</td>
</tr>
<tr>
<td></td>
<td>≥ 65</td>
<td>0.01007</td>
<td>0.00926</td>
<td>1.01012</td>
<td>0.99195</td>
<td>1.02863</td>
</tr>
</tbody>
</table>

Fig. 1. Association between SO$_2$ concentration and the number of all age cardiovascular deaths and among person ≥ 65 yrs.

Fig. 2. Association between BS concentration and the number of cardiovascular deaths in all age and in person ≥ 65 yrs.
diseases was associated with an increase in fine particulate matter and in sulphur dioxide from the 10th to the 90th percentile (26). In 20 U.S. cities (27) the level of PM\(_{2.5}\) is associated with the rate of death from all causes and from cardiovascular and respiratory illnesses. The estimated increase in the relative rate of death from cardiovascular and respiratory causes was 0.68% (95% posterior interval, 0.20 to 1.16 %) for each increase in the PM\(_{2.5}\) level of 10 µg/m\(^3\). Levels of SO\(_2\) were not significantly related to the mortality rate.

In two French cities no coherent results were found between SO\(_2\) pollution and cardiovascular deaths (28). Ballester et al. (29) found that the estimated relative risk (RR) of dying corresponding to a 10 µg/m\(^3\) increase in mean daily BS over the whole study period was 1.009 (95% CI: 1.003, 1.015). For mortality in the group aged more than 70 years and for cardiovascular mortality, the RR\(_s\) were 1.008 (95% CI: 1.001, 1.016) and 1.012 (95% CI: 1.003, 1.022) respectively. The association with SO\(_2\) was less clear: it was evident during the warm season only. The estimated RR\(_s\) in this case were 1.007 (95% CI: 0.999, 1.015) for total mortality, 1.009 (95% CI: 1.00, 1.21) for total mortality in those older than 70, and 1.012 (95% CI: 0.995, 1.026) for cardiovascular deaths.

The associations which could be explained partially by the small number of pollution measurements available for the period analyzed were statistically insignificant. The results were also partly dependent on season and type of climate. In our country the climate is moderate continental and higher air pollutants effects are generally found in warmer and drier climates. The results from 29 European cities within due to APHEA2 project (30) suggest that in population with higher underlying mortality rate due to effects of PM on the elderly are smaller.

However, in response to air pollution exposure, different age groups may respond differently. Who is at risk and who is more susceptible to the adverse health effects of air pollution are important questions which have not been fully clarified (31, 32).

REFERENCES