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Extended effects of air pollution on cardiopulmonary mortality in Vienna

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Received 7 March 2007; received in revised form 4 July 2007; accepted 10 July 2007

Abstract

Background: Current standards for fine particulates and nitrogen dioxide are under revision. Patients with cardiovascular disease have been identified as the largest group which need to be protected from effects of urban air pollution.

Methods: We sought to estimate associations between indicators of urban air pollution and daily mortality using time series of daily TSP, PM₁₀, PM_{2.5}, NO₂, SO₂, O₃ and nontrauma deaths in Vienna (Austria) 2000–2004. We used polynomial distributed lag analysis adjusted for seasonality, daily temperature, relative humidity, atmospheric pressure and incidence of influenza as registered by sentinels.

Results: All three particulate measures and NO₂ were associated with mortality from all causes and from ischemic heart disease and COPD at all ages and in the elderly. The magnitude of the effect was largest for PM_{2.5} and NO₂. Best predictor of mortality increase lagged 0–7 days was PM_{2.5} (for ischemic heart disease and COPD) and NO₂ (for other heart disease and all causes). Total mortality increase, lagged 0–14 days, per 10 µg m⁻³ was 2.6% for PM_{2.5} and 2.9% for NO₂, mainly due to cardiopulmonary and cerebrovascular causes.

Conclusion: Acute and subacute lethal effects of urban air pollution are predicted by PM_{2.5} and NO₂ increase even at relatively low levels of these pollutants. This is consistent with results on hospital admissions and the lack of a threshold. While harvesting (reduction of mortality after short increase due to premature deaths of most sensitive persons) seems to be of minor importance, deaths accumulate during 14 days after an increase of air pollutants. The limit values for PM_{2.5} and NO₂ proposed for 2010 in the European Union are unable to prevent serious health effects.

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Keywords: Air pollution; Particulate matter; Nitrogen dioxide; Mortality; Time series; Cardiopulmonary mortality

Abbreviations: PM, particulate matter (number denotes aerodynamic diameter in micrometer, 50% cut-off); TSP, total suspended particulates; NO₂, nitrogen dioxide; SO₂, sulfur dioxide, O₃, ozone; COPD, chronic obstructive pulmonary disease

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1. Introduction

During relatively high exposures to TSP and SO₂ in 1972–1983 time-series studies in Vienna found associations of daily air pollutant concentrations with daily mortality of elderly persons independent of temperature and influenza (Neuberger et al., 1987). In the 1980s TSP and SO₂ decreased, Austria being the country with the highest reduction of SO₂

among all signatory states of the Helsinki Protocol. In recent years, relatively low levels of air pollution were monitored in Vienna and 50th (99th) percentile concentrations of daily average SO₂, NO₂, TSP, PM₁₀, PM_{2.5} and PM_{1.0} of 2 (8), 16 (37), 32 (93), 24 (64), 16 (51) and 13 (35) µg m⁻³ were reported (Hauck et al., 2004). Within this concentration range significant associations with daily hospital admissions for respiratory disease were detected among Viennese aged 65 years and older. Admission rates peaked twice in a 14-day period after increases of air pollution and reached 5.5% in males and 5.6% in females per 10 µg m⁻³ increase of PM_{2.5} (Neuberger et al., 2004). Possible explanations for this high increase of respiratory morbidity compared to other studies were: a steeper concentration response function at lower concentrations (backed by observations in a rural control area), a different composition of the aerosol in Vienna (>50% of cars with diesel engines), a high proportion of old persons in the population >65 years of age and the assessment of lagged effects up to 14 days. Meanwhile a multicenter study proved that all nonviolent causes and in particular heart failure increase with PM_{2.5} concentrations lagged 0–2 days (Dominici et al., 2006), but it is still unclear if the risk of dying from cardiovascular disease is higher for a short lag time (Forastiere et al., 2005) or for extended periods (Goodman et al., 2004). There is still a lack of time series studies with extended follow up and on specific outcomes, which might be relevant to understanding mechanisms of air pollution as a trigger for cardiovascular and other disease (Zanobetti and Schwartz, 2006).

This study aims to estimate associations between indicators of urban air pollution and daily cardio-pulmonary mortality in Vienna. To show those associations, statistical models are used, which take into account the exposure of the population to major urban pollutants and the acute, intermediate or prolonged effect involved.

To overcome the lack of power for a mortality study in a city with only 1.63 million inhabitants and to enable full adjustment for seasonality we used an observation period of 5 years. We chose generalized additive models (GAMs) (Hastie and Tibshirani, 1990) with distributed lags (Schwartz, 2000a) and for comparability with a multicenter European study (Katsouyanni et al., 2001) the same adjustments for confounders and effect modification. By analysis of associations with different distributed lags we wanted to test the hypothesis

that extended effects of air pollution exceed its acute effects, as discussed for PM (Goodman et al., 2004). While numerous studies (Bell et al., 2004; Nawrot et al., 2006) describe concentration–response relationships between mortality and PM, those of NO₂ are less clear (WHO, 2005). Though studies point to the importance of NO₂ as an indicator of urban air pollution such as a predictor of acute and subacute hospital admissions for respiratory disease (Neuberger et al., 2004) and of acute cardiovascular disease (Barnett et al., 2006), concentration–response functions of European mortality studies are mainly given for PM₁₀ (adjusted for NO₂) and specific mortality has been studied for short lags only (Zeka et al., 2005). From the time course of associations with hospital admissions in Vienna (Neuberger et al., 2004) we decided to study associations of mortality with lags up to 14 days and to use the same statistical analysis for PM and NO₂.

2. Methods

Identical methods as described previously (Hauck et al., 2004) were used for air monitoring and analysis in 2000–2004, with continuous measurement of NO₂, TSP, PM_{2.5} and meteorology at the same central station. PM₁₀ was measured at a second urban background station which showed nearly parallel concentration changes of NO₂ and TSP over time, but reached higher peaks than the other station. Therefore, the 95th percentile of PM₁₀ exceeds that of TSP (Table 1). Because PM_{2.5} was not monitored in Vienna in 2001 and PM₁₀ was unavailable for 2001 and 2002 we modelled these data from daily TSP, NO_x, temperature, relative humidity, atmospheric pressure and day of week,

Table 1
Mean and percentile distribution of daily mean air pollution (rounded to µg m⁻³)

	Mean	5th	25th	50th	75th	95th
NO ₂	31	14	22	30	38	55
SO ₂	5	2	3	4	7	12
O ₃	46	6	25	48	66	87
TSP	31	12	19	27	39	62
PM ₁₀	30	9	17	26	39	67
PM _{2.5}	16	5	9	14	21	36

NO₂: nitrogen dioxide, SO₂: sulfur dioxide, O₃: ozone, TSP: total suspended particulates, PM: particulate matter (number gives aerodynamic diameter in micrometer, 50% cut-off).

using linear regressions with quadratic term for temperature. To justify this procedure the following sensitivity analysis was performed:

1. From subset of all data five 10% samples were selected and removed from the data.
2. Linear model described above was fitted on remaining 90% of data.
3. Results were used to estimate $PM_{2.5}$ on “deleted” data.
4. Estimates of $PM_{2.5}$ were compared with real data.

Histogram of residuals and scattergrams of observed and estimated $PM_{2.5}$ were plotted, showing estimated values close to measured $PM_{2.5}$ and correlation coefficients in the five subsets between 0.91 and 0.96. More information on atmospheric pollution chemistry in Vienna and rural surrounding was given by Puxbaum et al. (2004).

Daily incidence of deaths encoded by age and cause (9th revision of the International Classification of Disease ICD-9) obtained from Statistics Austria for a time-series analysis of all nontrauma deaths is used to study “overall mortality” (80 235 nontrauma deaths) and the specific mortality using the main groups of 42 464 cardiovascular (including 20 827 ‘ischemic heart’—ICD 410–414, 9 064 ‘other heart’—ICD 415–429 and 6372 cerebrovascular—ICD 430–438) deaths and 4114 deaths from respiratory diseases (including 2872 chronic obstructive respiratory diseases ‘COPD’—ICD 490–496) and for control 4213 deaths from diseases of digestive organs (ICD 520–579).

We investigate associations between the ambient particulate and gaseous pollutants with daily non-accidental mortality for all ages and for the elderly (65+ years), by three different models of the temporal association of exposure and effect: for acute effects we estimate the relative rate (RR) of mortality associated with mean exposure on the current and previous day, for intermediate effects we apply a 7-day polynomially distributed lag (pdl) model and for prolonged effects a 14-day pdl model, using overdispersed Poisson GAMs (Hastie and Tibshirani, 1990), pdl analysis (Schwartz, 2000a), stringent convergence criteria (Dominici et al., 2002, 2004) and considering seasonal, daily meteorological influences (temperature, relative humidity, pressure and change of temperature and pressure between consecutive days), day of the week and incidences of influenza (as registered by sentinels) as

confounders. Seasonal and meteorological factors are modelled using spline functions (Katsouyanni et al., 2001), minimizing sum of partial autocorrelation function. For time trends, we checked from three to eight degrees of freedom per year and based our selection on the minimum sum of 30 lags of partial autocorrelation function.

For weather indicators smoothing parameters along with lagged effect (days 0, 1 and 2) are chosen. Meteorological variables were entered to the model sequentially: mean temperature, humidity, pressure and next change between consecutive days of temperature and pressure. For each factor the best combination of lag and smoothing parameter was selected on the basis of the Akaike (1973) information criterion.

Influenza has been encoded as a binary variable according to earlier results (Neuberger et al., 1987), showing epidemic influenza if incidence per week exceeded 10 000 cases.

We assume a linear dose–response function after having checked the validity of this assumption by visual inspection of plots (spline functions). Significance is assessed by the posterior probability that the RR is larger than zero. Values >0.95 are considered significant. Calculations were performed in S-Plus 2000 using the GAM exact procedure suggested by Dominici et al. (2004) assuming that the daily number of counts follow an overdispersed Poisson distribution.

3. Results

Daily concentrations of air pollutants monitored continuously are given in Table 1. Most values complied with EU standards. In the 5 years of observation no annual standard but the daily PM_{10} standard of $50 \mu\text{g m}^{-3}$ was exceeded on 22–59 days (allowed: 35 days per year). The highest NO_2 concentration per hour was $156 \mu\text{g m}^{-3}$ and never exceeded the EU standard of $200 \mu\text{g m}^{-3}$.

Table 2 shows that all (nontrauma) cause mortality increase is associated with daily NO_2 , with higher associations for longer lags. Associations of overall mortality with TSP are significant for prolonged effects (14-day pdl model) only. Table 2 shows that NO_2 is the better predictor of mortality, with significant associations also for intermediate deaths (within 7 days after its increase), caused by significant increases of all groups of deaths except cerebrovascular ones. Effects of TSP are seen mainly on ischemic heart disease and

Table 2

Percent increase of mortality (with 95% confidence intervals) related to a $10 \mu\text{g m}^{-3}$ increase in pollution by NO_2 or TSP

	NO_2			TSP		
	Lag 0–1 day	Lag 0–7 days	Lag 0–14 days	Lag 0–1 day	Lag 0–7 days	Lag 0–14 days
All deaths	0.8* (0.0; 1.6)	2.1* (0.8; 3.5)	2.9* (1.6; 4.1)	0.3 (–0.3; 0.9)	0.9 (–0.0; 1.9)	0.8* (0.0; 1.6)
Cardiovascular	0.7 (–0.4; 1.8)	3.1* (1.2; 5.0)	4.6* (2.9; 6.3)	0.3 (–0.5; 1.2)	1.6* (0.3; 3.0)	1.7* (0.7; 2.8)
Ischemic heart	0.4 (–1.2; 1.9)	2.8* (0.3; 5.3)	4.5* (2.4; 6.6)	0.8 (–0.4; 2.1)	2.6* (0.8; 4.5)	3.4* (1.9; 4.9)
Other heart	1.6 (–1.1; 4.5)	4.6* (0.4; 9.1)	3.9* (0.4; 7.6)	0.3 (–1.8; 2.4)	0.9 (–2.2; 4.1)	–1.3 (–3.7; 1.2)
Cerebrovascular	1.0 (–1.7; 3.9)	2.4 (–1.8; 6.7)	4.4* (0.8; 8.2)	0.1 (–2.0; 2.3)	0.9 (–2.3; 4.1)	1.7 (–0.9; 4.3)
Respiratory	2.3 (–0.6; 5.2)	5.7* (1.1; 10.6)	6.7* (2.7; 10.8)	2.3* (0.0; 4.7)	3.7* (0.1; 7.4)	2.7 (–0.1; 5.6)
COPD	1.9 (–2.4; 6.4)	9.9* (3.0; 17.3)	8.9* (3.0; 15.2)	3.6* (0.2; 7.1)	8.5* (3.1; 14.2)	5.0* (0.7; 9.4)

* $p < 0.05$.

Table 3

Percent increase of mortality (with 95% confidence intervals) related to a $10 \mu\text{g m}^{-3}$ increase in pollution by $\text{PM}_{2.5}$ or PM_{10}

	$\text{PM}_{2.5}$			PM_{10}		
	Lag 0–1 day	Lag 0–7 days	Lag 0–14 days	Lag 0–1 day	Lag 0–7 days	Lag 0–14 days
All deaths	0.5 (–0.6; 1.5)	1.8 (–0.0; 3.7)	2.6* (1.1; 4.1)	0.2 (–0.4; 0.7)	0.9 (–0.1; 1.9)	1.2* (0.4; 2.1)
Cardiovascular	0.4 (–1.0; 1.8)	2.7* (0.3; 5.2)	3.8* (1.9; 5.8)	–0.2 (–0.6; 1.0)	1.4* (0.1; 2.8)	2.0* (0.9; 3.1)
Ischemic heart	1.0 (–1.0; 3.1)	3.8* (0.6; 7.1)	5.5* (3.0; 8.1)	0.4 (–0.7; 1.6)	2.1* (0.4; 3.9)	3.2* (1.8; 4.6)
Other heart	0.9 (–2.6; 4.6)	3.0 (–2.2; 8.5)	1.5 (–2.5; 5.7)	0.4 (–1.5; 2.4)	1.3 (–1.6; 4.3)	–0.1 (–2.4; 2.2)
Cerebrovascular	0.4 (–3.2; 4.1)	2.7 (–2.7; 8.4)	4.9* (0.7; 9.3)	0.3 (–1.6; 2.4)	1.4 (–1.6; 4.4)	2.6* (0.3; 5.0)
Respiratory	3.9* (0.1; 7.8)	7.0* (0.9; 13.4)	6.4* (1.9; 11.2)	2.1* (0.0; 4.2)	3.5* (0.1; 6.9)	3.0* (0.5; 5.5)
COPD	6.4* (0.6; 12.5)	14.0* (4.9; 24.0)	9.0* (1.9; 16.6)	3.5* (0.4; 6.7)	7.9* (3.0; 12.9)	5.1* (1.3; 9.1)

* $p < 0.05$.

COPD, but NO_2 is associated with other heart disease and respiratory disease as well.

The highest estimate for TSP is seen for intermediate effects on respiratory mortality. If prolonged effects up to 14 days are included, only the estimate for ischemic heart disease from TSP enlarges, while for NO_2 effects most estimates increase and the estimate for cerebrovascular disease becomes significant. In summary, Table 2 shows more pronounced effects per $10 \mu\text{g m}^{-3}$ increase of NO_2 than per $10 \mu\text{g m}^{-3}$ increase of TSP, with highest effects on respiratory (mainly COPD) and cardiovascular (ischemic heart and cerebrovascular) deaths.

Table 3 gives the estimates for subfractions of TSP (partly modeled). The hypothesis that extended effects of air pollution (intermediate and prolonged) exceed that of acute effects is supported also for $\text{PM}_{2.5}$ and PM_{10} , in particular for overall mortality and for mortality from ischemic heart disease and cerebrovascular disease (Table 3). An increase of $\text{PM}_{2.5}$ predicts lethal ischemic heart disease even better than an increase of NO_2 of comparable

weight concentration. The same is true for respiratory disease, in particular COPD, if associated with premature death within 7 days after the increase of the pollutant. NO_2 and $\text{PM}_{2.5}$ predict prolonged respiratory mortality increases equally well. The estimates for TSP and PM_{10} are of comparable magnitude and lower than the ones for $\text{PM}_{2.5}$. There are no significant associations between total, cardiac and cerebrovascular mortality on one hand and the differences between TSP and $\text{PM}_{2.5}$ on the other hand (data not shown).

For NO_2 and $\text{PM}_{2.5}$ predicting the highest increase of mortality with a similar time course no indication of important harvesting was seen over 2 weeks (Fig. 1). For NO_2 , Fig. 1 shows a decrease of the association during the first week with overall and respiratory deaths, but an increase with cardiovascular deaths. During the first week an increase of the association with cardiovascular and cerebrovascular deaths was also seen for $\text{PM}_{2.5}$.

Very similar but slightly higher estimates are found for deaths at age 65+ years: e.g. the total mortality increase per $10 \mu\text{g m}^{-3}$ lagged 0–14 days

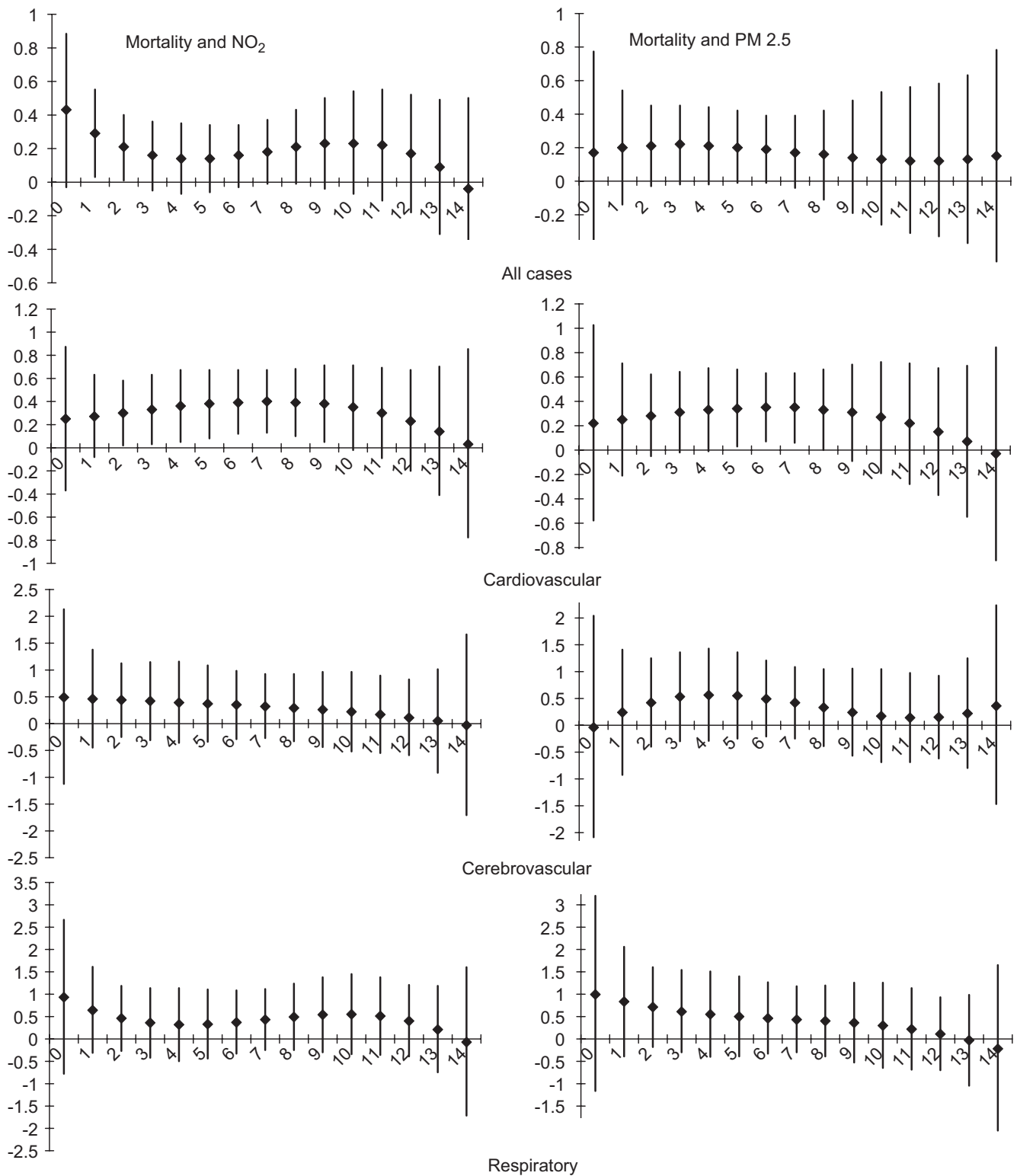


Fig. 1. Time course of the association between an air pollutant (NO₂, PM_{2.5}) and the total and specific mortality in Vienna over 14 days. x-axis: days, y-axis: percent change per 10 µg m⁻³.

was 3.2% (95% CI: 1.7–4.6%) for NO₂ and 2.8% (95% CI: 1.1–4.6%) for PM_{2.5}. No significant associations were detected with deaths at age

15–64 years. Deaths from diseases of the digestive system (used for control) were not associated with any pollutant in any age group, and in the groups

reported no significant associations of mortality with SO₂ or O₃ concentrations were found (data not shown).

4. Discussion

While the mechanisms linking cardiovascular events and mortality with air pollution are still under debate, numerous studies describe day-to-day variations in atmospheric pollutants with daily variations in deaths or disease (Maître et al., 2006; Nawrot et al., 2006). Most of them, however, investigated only immediate responses to an increase in pollution (on the same day and the day afterwards) and found an average increase in total mortality of about 0.5% per 10 µm³ of PM₁₀. In this study, the estimates per microgram increase of NO₂ or PM_{2.5} are found higher compared to studies focusing on short lags (Katsouyanni et al., 2001; Bell et al., 2004), but they are in line with earlier results on hospital admissions in Vienna (Neuberger et al., 2004), which had found stronger associations than reported for other cities with comparable pollution. One of the possible explanations is a different composition of the urban aerosol in Vienna (Puxbaum et al., 2004) where nearly all trucks and half of passenger cars use diesel engines. This is supported by the observation that the associations of mortality with NO₂ is higher than the association of mortality with TSP and PM₁₀, indicating an important influence of local motor traffic exhaust, contributing both NO₂ and fine combustion particulates of high toxicity. Another reason for a steeper dose–response function could be a higher proportion of sensitive persons in the population compared to other studies. Unfortunately most time series studies do not report the age distribution above 65 years. At the census of 2001, 16% of the total Viennese population was at age 65 or older. Of these 23.3%, 25.0%, 24.7%, 13.2%, 9.1%, 3.9% and 0.8% were at age 65–69, 70–74, 75–79, 80–84, 85–89, 90–94 and 95 years or older. This population at age 65+, however, showed only slightly higher estimates per 10 µg m⁻³ for all deaths lagged 0–14 days than shown in Tables 2 and 3 for the total population: 3.2% for NO₂, 1.1% for TSP and 2.8% for PM_{2.5}, making age distribution an unlikely cause for higher effects in this population.

The damage of short-term exposures could be immediate, latent and cumulative. Effects of particulate air pollution on mortality were reported to be strongest on the day of and the few days after

exposure, but to extend out through about 40 days after exposure (Goodman et al., 2004). On the other hand, “harvesting” has been reported in time-series studies (increased mortality of very sick and sensitive persons during the first days of an air pollution episode and decreased mortality thereafter) (Schwartz, 2000b), leading to reduced mortality increase in longer periods of observation. From comparing results of this study for pdl 0–7 days with pdl 0–14 days some harvesting effect is indicated for COPD, in particular for the association with PM_{2.5} (Table 3), but not for overall mortality. For cardiovascular deaths associations with PM_{2.5} and NO₂ increase during the first week (Fig. 1). A significant risk for cerebrovascular death would not have been detected if only lagged effects of 0–7 days were analyzed. An effect on mortality from stroke at shorter lags (Hong et al., 2002; Chan et al., 2006) might be detectable in studies on larger populations only.

Also for NO₂ we observed no harvesting but an increase in total mortality from lag 0–1 day (0.8% per 10 µg m⁻³) to pdl 0–7 days (2.1% per 10 µg m⁻³) and pdl 0–14 days (2.9% per 10 µg m⁻³). Therefore, we do not think to have captured a short-term toxic effect of the irritant gas NO₂ but rather a sum of acute and subacute effects of the gaseous indicator of motor traffic. Similar interpretations have been given recently for associations of NO₂ with hospital admissions for cardiovascular disease (Barnett et al., 2006) and coronary heart disease deaths in an ecological study (Maheswaran et al., 2005).

Chronic effects of urban pollution indicated by long-term averages of NO₂ (Nafstad et al., 2004) or PM (Pope et al., 2002) exceed the acute and subacute effects of current exposure termed “intermediate” and “prolonged” in this study, but these results are more vulnerable to spatial differences of air pollutants monitored (Hoek et al., 2002). The question whether NO₂ is an indicator only for living close to motor traffic is more relevant for studying spatial distributions (Gauderman et al., 2005) than for time series (Moshhammer et al., 2006a). Morbidity studies underline the importance of NO₂ as a predictor of short-term health effects, both outdoor (Neuberger et al., 2002) and indoor (Moshhammer et al., 2006b); however, increased mortality has rather been associated with chronic exposure to NO₂ from traffic and industrial sources (Nafstad et al., 2004; Gehring et al., 2006). Also associations of maximal NO₂ concentrations lagged 0–1 day with total daily mortality were reported, with a stronger effect on

respiratory mortality (Samoli et al., 2006); however, this association became nonsignificant when controlling for SO₂. In the present study, there was no evidence of confounding by SO₂. By contrast to the present situation in other European cities (Sunyer et al., 2003) and by contrast to earlier studies in Vienna when SO₂ had been an indicator for industrial and heating emissions and a predictor of health effects including acute cardiopulmonary mortality (Neuberger et al., 1987), we did not find significant associations with the rather low SO₂ concentrations of today. Nevertheless, the monitoring of SO₂ should be continued as long as sulfur containing fuels are used in Europe.

In contrast to larger and southern cities ozone in Vienna is usually low when NO₂ and PM_{2.5} are high and we did not find a positive association of O₃ with acute and subacute mortality in this study nor with hospital admissions for respiratory disease (Neuberger et al., 2004). Effects of O₃ on morbidity in Vienna, however, cannot be excluded and O₃ monitoring must be continued. But at present monitoring of PM_{2.5} which in many European cities is still lacking, seems to be the most important.

In Vienna PM_{2.5} proved to be a reliable predictor for acute and subacute hospital admissions (Neuberger et al., 2004). The present study confirms the necessity of monitoring PM_{2.5} as a predictor of overall mortality lagged 0–14 days after its increase (Table 3), but also points to other properties of the urban aerosol which are captured better by surveillance of NO₂, predicting an earlier increase of overall mortality (Table 2), mainly caused by heart disease. Monitoring of NO₂ is available in most cities and serves as an indicator of motor traffic. From the results of this study, we conclude that NO₂ predicts cardiovascular and non-ischemic heart death even better than PM_{2.5}. At distributed lag of 0–14 days an increase of NO₂ (per microgram) predicted a higher increase of cardiovascular deaths and about the same increase of respiratory deaths. On the other hand, PM_{2.5} was the better predictor of early increases in respiratory deaths, mainly from COPD (Tables 2 and 3).

Also monitoring of TSP or PM₁₀ predicted acute and subacute mortality, but if PM_{2.5} was deducted from TSP, no significant association with cardiopulmonary mortality was found in this study. Therefore, we conclude that coarse (resuspended, mineral) dust is of minor importance for the health outcome in this study and in similar environmental settings. The situation was reported to be different

in desert areas or cities with unpaved roads where coarse dust is an important fraction of TSP (Lippset et al., 2006).

Concentration–response plots (not shown) were consistent with the lack of a threshold of effects of NO₂ or particulate matter on mortality.

The causality of the associations is supported by cohort studies showing a decrease in mortality with a reduction of PM_{2.5} (Laden et al., 2006) and an increase in respiratory function with a reduction of NO₂ (Moshhammer et al., 2006b). This study adds to the growing evidence that both ambient PM_{2.5} and NO₂ need to be reduced further. The foreseen targets in the European Union for limitation of annual concentrations (25 µg m⁻³ of PM_{2.5} and 40 µg m⁻³ of NO₂) in 2010 had never been violated during the 5 years of our study. These standards are certainly insufficient for prevention of serious health effects.

Acknowledgments

This work was supported financially by the Municipality of Vienna (department for the environment—MA22). A travel grant was given by the Clean Air Commission of the Austrian Academy of Science.

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