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Short-term Effects of Air Pollution on Oxygen Saturation in a Cohort of Senior Adults in Steubenville, OH

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Abstract

Objective—We examine whether ambient air pollution is associated with oxygen saturation in 32 elderly subjects in Steubenville.

Methods—We used linear mixed models to examine the effects of fine particles (PM_{2.5}), sulfate (SO₄²⁻), elemental carbon (EC), and gases on median oxygen saturation.

Results—An interquartile range (IQR) increase of 13.4 µg/m³ in PM_{2.5} on the previous day was associated with a decrease of -0.18% (95% CI: -0.31 to -0.06), and a 5.1 µg/m³ IQR increase in SO₄²⁻ on the previous day was associated with a decrease of -0.16% (95% CI: -0.27 to -0.04) in oxygen saturation during the initial 5-min rest period of the protocol.

Conclusions—Increased exposure to air pollution, including the non-traffic pollutant SO₄²⁻ from industrial sources, led to changes in oxygen saturation that may reflect particle-induced pulmonary inflammatory or vascular responses.

Keywords

oxygen saturation; ambient air pollution; particles

INTRODUCTION

Hypoxemia is an important cause of respiratory and cardiovascular morbidity and mortality, and pulse oximetry is a simple non-invasive method of monitoring the percentage of haemoglobin that is saturated with oxygen. Although acute exposure to ambient air pollution

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Conflict of Interest

None of the authors have a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

has been associated with numerous cardiovascular and pulmonary endpoints (1), studies on air pollution and oxygen saturation are fewer and have shown varying results.

Several community-based panel studies showed no consistent associations, (2-5) but two showed small decreases in oxygen saturation in older healthy subjects (6) and subjects with congestive heart failure (7) related to particle exposures. Two chamber studies with exposure to concentrated ambient particles and concentrated ultrafine particles also found significant decrements in oxygen saturation in healthy subjects, subjects with COPD, and asthmatics.(8, 9) Most studies of pollution and oxygen saturation have focused on effects of traffic components of particulate pollution such as black carbon or ultrafine particles.

In a panel study of elders from Steubenville, Ohio, a community that at the time of testing was still dominated by non-traffic pollution from steel mills and power plants, we have documented that elevated levels of fine particle mass ($PM_{2.5}$) and/or its non-traffic sulfur component (SO_4^{2-}) were associated with reduced heart rate variability (10), increased supraventricular arrhythmias (11), and increased pulmonary inflammation, measured as fractional exhaled nitric oxide (FENO) (12). The associations of pollution with pulmonary inflammation were primarily seen in participants with chronic obstructive pulmonary disease (COPD).

In this same population, here we evaluated the associations of oxygen saturation with $PM_{2.5}$ and its components from primarily non-traffic (SO_4^{2-}) and traffic [elemental carbon (EC)] sources. Given our previous findings with FENO, we also examined whether participants with chronic respiratory or cardiac disease were more susceptible to pollutant effects on oxygen saturation than those without these conditions.

SUBJECTS AND METHODS

Study Population and Protocol

Thirty-two non-smoking senior adults from Steubenville, OH participated in a study on air pollution and cardiovascular health during the summer and fall of 2000. Subjects with pacemakers, a recent acute coronary syndrome, atrial flutter or atrial fibrillation and smokers were excluded. The study has been described in detail elsewhere (10,11). The study design was reviewed and approved by the Human Subjects Committees of the Brigham and Women's Hospital and the Harvard School of Public Health.

Study participants were seen weekly, on the same day of the week Monday through Friday, during summer (June 4 – August 18) and fall (September 25 – December 15) of 2000. Each week, a short questionnaire on recent symptoms, hospital or doctor's visits and medication use was administered, followed by electrocardiogram monitoring and parallel oxygen saturation measurement. The protocol included: (1) five minutes of rest in a supine position; (2) three supine blood pressure (BP) measurements (NIBP Vital Signs Monitor, Welch Allyn); (3) five minutes of standing with three standing BP measurements taken after two minutes; (4) five minutes of exercise (walking) outdoors (weather and health permitting); (5) five minutes of rest in a supine position and; (6) two minutes and 20 seconds of paced breathing. Oxygen saturation and pulse rate were continuously monitored during the

protocol through pulse oximetry (Nellcor, Pleasanton, CA) and recorded in 30-second intervals.

All 30-second oxygen saturation data lower than 90% were manually checked by inspection of the trend in the surrounding measurements. If drops in oxygen saturation occurred too suddenly (measurements were not visually in line with trend), the measurements for the time period in question were excluded. We used the median oxygen saturation over the complete 30-min protocol and additionally evaluated the medians over the individual protocol parts as health outcomes.

We collected 24-hour integrated PM_{2.5}, SO₄²⁻, EC and gaseous pollutant (O₃, NO₂, SO₂) samples beginning at 9 a.m. each day (except Saturday) at a central ambient site at the Franciscan University of Steubenville, located within one mile of participants' residences, using a Harvard multi-pollutant monitor (13). As the study was designed to evaluate short-term effects of air pollution on health outcomes, our monitoring station only operated during the period when health outcomes were measured (i.e., no Saturday measurements). PM_{2.5} was measured gravimetrically at the Harvard School of Public Health, and the SO₄²⁻, O₃, NO₂ and SO₂ filters were analyzed through ion chromatography and EC filters through thermal optical transmission by CONSOL Energy Inc. Research & Development. Exposure collection methods have been previously described in detail (14).

The concentration of the non-sulfate fraction of PM_{2.5} was calculated as the difference between the measured PM_{2.5} and sulfate concentration, with sulfate assumed to be in the form of ammonium sulfate ([NH₄]₂SO₄): non-sulfate fraction of PM_{2.5} = PM_{2.5} - (SO₄²⁻ · 132/96).

Temperature, relative humidity, and dew point were collected continuously by CONSOL Energy Inc. Research & Development at the same site using a Met-1 10 meter station.

Statistical Methods

We examined the associations between ambient air pollution exposure and median oxygen saturation over the entire 30-minute protocol with linear mixed models including random subject effects, age, gender, race, body mass index (kg/m²), time of the day (7-9, 9-11, 11-13, 13-15, 15-18), temperature during the hour of the test as a linear term, and a first-order auto-regressive process for the within-subject residuals (15). We chose several air pollution exposure metrics for assessment in our models: the previous day (lag 1), two-day moving average (of lags 1-2), and 3-day moving average (of lags 1-3) to reflect short-term exposure, and the 14-day moving average to reflect a slightly longer exposure window; we required 75% data completeness for calculating the moving averages. The basic demographic covariates (age, gender, race, BMI) were selected a priori. Of the weather and seasonal variables only temperature improved the model fit by AIC and was included in the final model. To evaluate effects of co-morbidities and medication intake, diagnoses and medications were added (each separately) to the base model. Using interaction terms, we evaluated patient characteristics as potential modifiers of the association between air pollution and oxygen saturation.

Results are reported as estimated difference in percent oxygen saturation and the 95% confidence interval (CI) associated with an interquartile range (IQR) increase in air pollution exposure. All analyses were performed with SAS software version 9.3 (SAS Institute, Inc; Cary, NC).

RESULTS

Study Population

Participants' characteristics and the oxygen saturation distribution are shown in Table 1. Thirty-two subjects completed a total of 645 health visits, with an average of 20 visits (range 4-24) per subject. The mean age at screening was 71 years; 91% of the participants were female, and 69% were white. Most participants (84%) had one or more cardiovascular condition, 22% were diabetics, and 66% were on one or more medications. Valid oxygen saturation measurements were obtained from 644 visits. The median oxygen saturation value per visit ranged from 89% to 100% with a mean of 96.4%.

Ambient Air Pollutant Concentrations

A detailed assessment of air pollution in Steubenville during the study period is reported elsewhere (10, 14). Ambient concentrations of the measured criteria gases were moderate in Steubenville (average concentration: 6.0 ppb NO₂, 0.4 ppb SO₂, and 12.1 ppb O₃) while ambient fine particle and sulfate concentrations were relatively high with averages of 19.7 µg/m³ and 6.9 µg/m³ and interquartile ranges (IQR) of 13.4 µg/m³ and 5.1 µg/m³ respectively.

Associations between Air Pollution and Oxygen Saturation

Adjusted for demographic and meteorological covariates, oxygen saturation during the initial protocol segments (the rest and blood pressure measurement periods) before the exercise period was negatively associated with levels of PM_{2.5} and sulfate during the two previous days (Figure 1). For the initial rest period, an IQR increase of PM_{2.5} on the previous day was associated with a decrease of -0.18% (-0.31 to -0.06) in oxygen saturation and an IQR increase of SO₄²⁻ was associated with a decrease of -0.16% (-0.27 to -0.04) in oxygen saturation (Table 2), for the blood pressure measurement segment the estimated decreases were -0.20% (-0.34 to -0.06) for PM_{2.5} and -0.17% (-0.29 to -0.04) for SO₄²⁻ respectively. For the non-sulfate fraction of PM_{2.5} as an indicator for the traffic-related particles, the estimated decrease was -0.08% (-0.17 to 0.01) and considerably smaller than for total PM_{2.5} and SO₄²⁻. The associations are strongest during the initial rest period and during supine blood pressure measurements and less pronounced during standing blood pressure measurements. We did not observe any associations during exercise, and only weak (non-significant) associations during the rest and paced breathing periods after exercise (Figure1).

We also found associations between SO₂ and decreased oxygen saturation, but no associations with EC or NO₂. We did not find any associations between oxygen saturation and particle or SO₂ exposure metrics beyond the two previous days. The ozone 14-day moving average was positively associated with oxygen saturation.

There was no association of pollution with oxygen saturation during exercise, and the median oxygen saturation over the whole 30-minute protocol was associated with a decrease of around -0.1% ($p < 0.10$) (Figure 1).

Covariate Effects and Interactions

In general, subjects with diagnosed co-morbidities and subjects on medications had lower oxygen saturation. This was most pronounced for those with hypertension and those on statins (Figure 2). There was considerable overlap of subjects between the medication groups (7 of the 12 subjects on beta blockers and 5 of the 11 subjects on calcium channel blockers were also on statins; 5 subjects were on beta blockers, calcium channel blockers, and statins), and our subject number was too low to fully elucidate which diagnoses or medications were drivers of low oxygen saturation. Including terms for each diagnosis or medication (only one at a time) in our models did not impact the observed particle effects. In interaction models the $PM_{2.5}$ associations are slightly stronger in subjects without diagnosed comorbidities, but no interaction term was significant (Figure 3). We did not find any effect modification by low ($<96\%$) baseline oxygen saturation level (based on average levels across all visits).

Subgroup analyses by season resulted in similar point estimates but wider confidence intervals, and interaction models showed no effect modification by season.

DISCUSSION

In a repeated measures study of elderly subjects living in Steubenville, Ohio, we found that increases in ambient pollutant concentrations, especially those related to fossil fuel combustion from power plants and other industrial facilities, were associated with reduced oxygen saturation in the following 1-2 days. These pollutants included overall $PM_{2.5}$, the sulfate component of $PM_{2.5}$, and SO_2 . Pollutants whose primary sources are traffic – EC, NO_2 , and the secondary pollutant O_3 – did not predict lower oxygen saturation in this community. While oxygen saturation was lower in participants with some cardiopulmonary diagnoses or on cardiac medications, associations of pollution with oxygen saturation were not modified in these participants.

All pollutants for our study were measured within one mile of the subjects' residences, and we anticipate little measurement error due to ambient spatial variability. A subset of 15 participants of this cohort took part in a more extensive exposure assessment study with two 24-hour periods of personal exposure measurements during each week of the study (14). Because of their age and their general health status the study participants spent most of their time in close proximity to their residences and indoors (summer = 90.5%, fall = 95.2%) (14). We found strong associations between ambient particle concentrations and corresponding personal exposures, and low to moderate associations between ambient gases and their corresponding personal exposures for both the summer and the fall season.

We hypothesize that the lack of associations between air pollution exposure and oxygen saturation during the more active parts of the protocol can possibly be explained by the loosening of the probe which might result in noisier data. With 72% of the subjects suffering

from hypertension and 34% from coronary artery disease (table 1), it is also possible that the stress of standing or walking overshadowed the air pollution associations through temporary periods of shortness of breath.

The fact that associations between air pollution exposures and oxygen saturation were only observed for the previous two days and not for longer exposure windows, confirmed our initial assumption of a short-term effect. While some previous population-based panel studies (6, 7) and controlled exposure chamber studies (8, 9) found short-term increases in pollution exposures associated with reduced oxygen saturation, others have not (2-5). Most previous studies have focused on total particle mass (PM₁₀ or PM_{2.5}) effects and have not separated the effects of pollutants from different emission sources (e.g., traffic vs. non-traffic). Few studies have investigated sources of susceptibility to the effects of ambient pollution (6, 8, 9).

In a 12-week repeated-measures study in 1999 (similar in design to the current study in Steubenville) of 28 older Boston residents, PM_{2.5} concentrations were associated with reduced oxygen saturation during the baseline rest period, post-exercise, but not during exercise (6), as in the current study. Daily oxygen saturation measured over a 2-month period on 31 subjects with congestive heart failure in Montreal from 2002-2003 was negatively associated with concentrations of fine particulates, ozone, and SO₂ during the previous day, but only SO₂ was significant after adjustment for weather effects (7). The association between PM_{2.5} and oxygen saturation in this study (-0.18% for an IQR increase of 13.4 µg/m³) is similar in magnitude to the effect size observed in the earlier Boston panel study (-0.17% for an IQR increase of 10.6 µg/m³) (6), but stronger than in the Montreal panel study (-0.02% for an IQR increase of 7.3 µg/m³) (7). Ambient average daily PM_{2.5} levels were lower in both studies with 15.5 µg/m³ in Boston and 9.5 µg/m³ in Montreal, compared to 19.7 µg/m³ in Steubenville. While the main source of PM_{2.5} and sulfate in Steubenville is fossil fuel combustion (16) the dominant source of pollution in Boston is traffic (17).

As expected, subjects with cardiovascular conditions, ascertained by self-reported diagnoses and medication intake, had lower mean oxygen saturation than healthy subjects. While other studies have found that air pollution effects were more evident in certain subgroups defined by health status or medication intake, we did not see any significant effect modification by these factors. For example, DeMeo et al. reported a greater pollution-related decrease in oxygen saturation at rest in participants taking beta-blockers than in participants not on beta-blockers (6). In another study healthy subjects appeared to be more susceptible to air pollution exposure than subjects with COPD (8), suggesting that the respiratory effect may be related to efficient penetration and deposition of inhaled toxic particles into the airways.

Modification of particle effects on oxygen saturation by certain medications may be plausible, as medication intake may influence blood oxygenation. Beta blocker use was associated with lower oxygen saturation in hypertensive mountaineers at moderate altitude compared to a control group without medication (18), and in a randomized study on healthy, normotensive subjects during high altitude hypoxia compared to placebos (19). Calcium

channel blockers and ACE inhibitors may dilate pulmonary as well as peripheral vasculature and influence the ventilation perfusion ratio (20).

In this study, we were not able to disentangle the possible effect modification by medication intake from that due to specific diagnoses. The observed modification of effects by beta blocker, calcium channel blocker and statins (which are unlikely to directly influence oxygenation) probably reflects the disease process for which the participants were receiving the treatment.

In a large multicenter sleep study short-term elevation in PM_{10} was associated with the risk of sleep-disordered breathing and nocturnal hypoxemia (defined by percentage of sleep time at less than 90% oxygen saturation) which in turn is a risk factor for cardiovascular diseases and mortality (21). The current study adds to the limited previous studies of air pollution and oxygen saturation and provides another piece of evidence for the mechanistic pathway of particle induced respiratory and cardiovascular damage, with hypoxemia as a possible link. The small day time signals that we are observing in our analysis may be important indicators of more profound and clinically significant pollution effects on nighttime saturation.

We previously reported elevated levels of $PM_{2.5}$ and/or its sulfur component SO_4^{2-} were associated with decreased heart rate variability (10), and increased exhaled NO (12) in this Steubenville cohort study. Correlations between oxygen saturation and heart rate variability or exhaled NO were very weak, and including heart rate variability measures or exhaled NO levels in the models with oxygen saturation as our main outcome did not change the associations of air pollution exposures with oxygen saturation. We therefore conclude that the exposure effects on these different endpoints are independent.

Our greatest limitation is the size of the population, limiting power to detect significant associations. Small numbers and a predominantly female study population may also limit generalizability of study findings.

In summary, this study suggests that short-term increases in non-traffic particle exposure is linked to decreased oxygen saturation and thus may increase the risk of respiratory and cardiovascular morbidity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Estimated changes in percent oxygen saturation [95% Confidence intervals] during each protocol part associated with an IQR range increase in exposure ($13.4 \mu\text{g}/\text{m}^3$ for $\text{PM}_{2.5}$ and $5.1 \mu\text{g}/\text{m}^3$ for SO_4^{2-}).

(first rest: five minutes of rest in a supine position; bp: three supine blood pressure (bp) measurements; standing: five minutes of standing with three standing bp measurements taken after two minutes; exercise: five minutes of exercise (walking); second rest: five minutes of rest in a supine position and; breathing: two minutes and 20 seconds of paced breathing.)

Figure 2.

Estimated changes in percent oxygen saturation [95% Confidence intervals] during rest period associated with diagnoses (Angina, Myocardial Infarction, Coronary Artery Disease, Congestive Heart Failure, Hypertension, Diabetes, Chronic Obstructive Pulmonary Disease) and medication intake (Beta Blockers, Calcium Channel Blockers, Statin, Angiotensin Converting Enzyme Inhibitors, Digoxin).

Figure 3. Estimated changes in percent oxygen saturation [95% Confidence intervals] during rest period associated with an 13.4 $\mu\text{g}/\text{m}^3$ IQR range increase in $\text{PM}_{2.5}$ exposure by diagnoses and medication therapies (interaction models).