Air quality impacts mortality in acute medical admissions

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Summary

Background: Air quality degraded by black smoke (particulate matter, PM10), sulphur dioxide (SO2) and nitrogen oxide (NOx) affects human health. Improvements following national legislation have lowered death rates. Whether background air pollution levels continue to affect human health remains unclear.

Aim: To determine impact of air pollutant concentrations (PM10, SO2 and NOx) on in-hospital mortality for acute medical admissions to St James’s Hospital over a decade (2002–11).

Design: All emergency admissions (55,596 episodes in n = 32,581 patients) were tracked prospectively and mortality assessed. Daily levels of PM10, SO2 and NOx were obtained from monitoring stations in our catchment area.

Methods: Univariate and multivariate logistic regression was employed to examine relationships between pollutant concentration and odds ratio (OR) for death following adjustment for other mortality predictors.

Results: Mortality related to each pollutant variable assessed (as quintiles of increasing atmospheric concentration) was significantly predictive. For PM10 and SO2, mortality in the highest three quintile concentrations (compared with base quintile) was significantly increased (P < 0.001) with univariate ORs of 1.24, 1.36 and 1.25 for PM10 and 1.43, 1.54 and 1.58 for SO2, respectively. Mortality in all quintile concentrations (compared with base quintile) was significantly increased (P < 0.05) for NOx with univariate ORs of 1.14, 1.18, 1.28 and 1.35, respectively. Following adjustment for other mortality predictors such as acute illness severity, all three air pollutants were independently predictive of mortality.

Conclusion: Despite improvement to air quality in Dublin, the prevailing background pollutant concentrations continue to affect human health at levels considered safe and below that previously recognized.

Introduction

Prior work has shown clear association between particulate air pollution and daily mortality.1–3 This threat to public health led to tightening of air quality control standards by the World Health Organization (WHO). A study at our institution almost three decades ago linked increases in mortality to that in urban air pollution.4 Air quality in Dublin however continued to deteriorate necessitating legislation in 1990 banning the marketing, sale and distribution of bituminous coals. Further work by Clancy et al.5 assessed the effect of air pollution control legislation on death rates in Dublin. The study described that average black smoke concentration decreased ~35.6 μg/m³ following the legislative ban on coal sales. Adjusted non-trauma death rates also reduced by 5.7%, respiratory deaths by 15.5% and...
cardiovascular deaths by 10.3% providing solid evidence for the government’s intervention. Following this success, the legislation was then extended to 11 other urban communities within Ireland. Decreases in black smoke concentrations particularly after the heating season were seen after each successive ban but interestingly no decrease was observed in total gaseous acidity. A recent re-assessment of these improvements to air quality did not find a reduction in the total or cardiovascular mortality in contrast to that shown following the 1990 ban in Dublin. Interestingly, a significant decrease in respiratory mortality was recorded consistent with the magnitude of black smoke reduction.6

Although the beneficial effects of intervention in Ireland are clear, published evidence to date suggests that air pollution even below the accepted international standards still has detrimental effects on health.2,3,7,8 The effects of particulate matter and sulphur dioxide on mortality are independent.2 We sought to investigate whether accepted post-legislation levels of PM10, SO2 and NOx impacted upon mortality for acute medical admissions to our hospital over a decade.6

Methods

Background

St James’s Hospital operates a continuous sectorized acute general medical ‘take’ for emergency admissions in its catchment area of 270,000 adults. All unselected emergency medical admissions between 2002 and 2011 (10-year period) were prospectively recorded into an anonymised database maintained through the Acute Medical Admissions Unit (AMAU). The operation and outcome of the AMAU have been described elsewhere.9–11

Data collection

The information collated within the anonymised patient database prospectively assembles core information about each clinical episode including elements contained on the patient administration system, the national hospital in-patient enquiry (HIPE) scheme, the patient electronic record, the emergency room and other laboratory systems including microbiology, haematology and biochemistry. HIPE is a national database of coded discharge summaries from acute public hospitals in Ireland, run by the Economic and Social Research Institute.12

Specific data prospectively recorded on admission include the patients’ unique hospital number, admitting consultant, date of birth, gender, area of residence by county, principal diagnosis, up to nine additional secondary diagnoses, procedures (principal and up to nine additional secondary procedures) and admission and discharge dates. Additional information cross-linked and automatically uploaded to the database includes physiological, haematological and biochemical parameters. During and following the admission, HIPE data of all coded diseases at time of discharge/death together with procedures and investigations undertaken during the hospital stay are included.

To determine deprivation, we utilized the Irish National Deprivation Index for Health and Health Services Research, derived by the Small Area Health Research Unit (SAHRU) at Trinity College Dublin.13

To assess seasons, winter was taken as November to January inclusive and each successive 3-month interval classed as Spring, Summer and Autumn, respectively. Daily temperature was determined from the Automatic Weather Station, located at Dún Laoghaire Harbour. From weather records (at 10-min intervals) for each 24-h period, daily mean and minimum temperatures were calculated and cross-linked by date to each patient admission over the period assessed.

Air quality

Simultaneous measurement of the pollutants occurs daily at fixed monitoring sites nationwide (www.EPA.ie). For this study, data over the last decade (2002–11) from three stations within our hospital catchment area (Rathmines, Winetavern and Coleraine Street) were assessed and measurements for PM10 (recorded daily), SO2 and NOx (recorded hourly) according to methods described elsewhere.14 To acquire one reliable measure (for each pollutant) for each individual day, an average was taken where all three sites had recorded values. In some instances however, data from a particular station were missing. The systematic approach we adopted to such data was to select the value from the site typically recording the highest value for analysis and if unavailable, proceeding in descending order. Differences between sites were only relevant in terms of determining hierarchal order of selection.

Confounding factors

Acute illness severity predicts clinical outcome and must be accounted for when evaluating mortality in hospital admissions. Deranged hemodynamic and physiological admission parameters may be utilized to derive an Acute Illness Severity Score.15–17 Such aggregate score systems may be used to adjust univariate estimates of risk for other major outcome predictors as described by our group and others.18,19 The Acute Illness Severity Score, Charlson
Comorbidity Index,\textsuperscript{20} primary disease classification [major disease category (MDC)] of respiratory (MDC4), cardiovascular (MDC5) or neurological (MDC1) during the hospital admission have all been included in a stepwise logistic regression model as described using 30-day in-hospital mortality as the primary endpoint.

**Statistical methods**

Descriptive statistics were calculated for demographic data, including means/standard deviations (SD), medians/interquartile ranges (IQR), or percentages. We examined 30-day in-hospital mortality as the primary outcome. Comparisons between categorical variables and 30-day in-hospital mortality were made using chi-square tests; multiple comparisons were adjusted for multiplicity using Scheffe’s comparison statistic. Logistic regression analysis was used to examine all significant outcome predictors ($P<0.10$ from the univariate analysis) on 30-day in-hospital mortality. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated where appropriate for those predictors that significantly entered the model ($P<0.10$). A stepwise logistic regression analysis examined the association between 30-day mortality and the following predictor variables: acute illness severity (lab score on admission), the Charlson Comorbidity Index, MDCs of the primary diagnosis of respiratory (MDC4), cardiovascular (MDC45) or neurological type (MDC1), Deprivation Index according to the upper or lower half as represented by the SAHRU deprivation number, season of the year and mean daily temperature. We used the margins command in Stata 12.1 to estimate and interpret adjusted predictions for interactions of key predictors, while controlling for other variables such as illness severity, using computations of average marginal effects. Margins are statistics calculated from predictions of a previously fitted model at fixed values of some covariates and averaging or otherwise over the remaining covariates. Statistical significance was assumed at a $P$-value $<0.05$. Stata v.12.1 (Stata Corporation, College Station, TX, USA) software was used for analysis.

**Results**

**Patient characteristics by air quality distribution**

A total of 55,596 episodes were recorded in $n=32,581$ unique patients admitted as acute medical emergencies between January 2002 and December 2011 (10-year period) were included for analysis. These episodes included patients admitted directly into the intensive care unit (ICU) or high dependency unit (HDU). The proportion of males was 49.1%. Median (IQR) length of stay (LOS) was 5.0 (2.0, 9.8) days. The median (IQR) age was 61.8 (41.7, 76.8) years, with the upper 10% boundary at 84.2. The Charlson Comorbidity Score of 0, 1, or 2 was present in 45.4%, 26.9% and 27.7%, respectively. The MDCs were respiratory (26.1%), cardiovascular (16.3%), neurological (15.8%) and gastrointestinal (11.1%). There was little systematic difference in the distribution of major demographic features between patients, when considered by category of admission on a low or high day of air pollution (Table 1).

**Impact of air pollutants on 30-day in-hospital mortality**

We divided patients by quintile of measured air pollutant, related to the three parameters of particulate matter ($PM_{10}$), sulphur dioxide ($SO_2$) and nitrogen oxides ($NO_x$). The data were the average daily level across all three stations; where a value was missing, we took the average of the remaining stations. The mortality related to each variable progressively increased, by $PM_{10}$ quintile. The median and IQR increased from 8.9 $\mu g/m^3$ (7.5, 10.0) to 33.8 $\mu g/m^3$ (28.4, 42.4) from quintiles 1 to 5. Mortality by quintile was 7.2%, 7.3%, 8.8%, 9.6% and 8.9%; mortality for the top three quintiles (compared with the base quintile) was significantly increased ($P<0.001$) with univariate OR of 1.24 (1.09, 1.41), 1.36 (1.20, 1.54) and 1.25 (1.09, 1.42), respectively (Table 2).

Similar trends of increasing mortality by quintile (Table 3) were observed for sulphur dioxide ($SO_2$). The median and IQR increased from 0.87 (0.62, 1.07) $\mu g/m^3$ to 7.23 (5.98, 10.5) $\mu g/m^3$; mortalities by $SO_2$ quintile were 6.6%, 7.0%, 9.1%, 9.7% and 10.0%. The mortality in the top three quintiles was increased significantly ($P<0.001$), compared with quintile 1 with univariate ORs of 1.43 (1.26, 1.62), 1.54 (1.36, 1.75) and 1.58 (1.39, 1.80), respectively.

For nitrogen oxides ($NO_x$) the median and IQR increased from 23.6 (19.5, 27.8) to 132.0 (106.4, 186.8) $\mu g/m^3$; mortalities by $NO_x$ quintile were 7.1%, 8.0%, 8.3%, 9.0% and 9.4%. The mortality in all quintiles was increased significantly, compared with quintile 1 with univariate ORs of 1.14 (1.00, 1.29: $P<0.05$), 1.18 (1.04, 1.34: $P<0.01$), 1.28 (1.13, 1.46: $P<0.001$) and 1.35 (1.20, 1.53: $P<0.001$) (Table 4).

**Risk estimates of air quality adjusted for major outcome predictors**

The major predictors of a poor outcome from admission (mortality) were the acute illness severity...
(biochemical laboratory score at admission), Charlson Comorbidity Index (20), Deprivation Index (SAHRU National Index),13 major diagnoses of cardiovascular, respiratory or neurological categories and air temperature (Table 5A–C). The full model predicted any in-hospital death by Day 30 with an AUROC of 0.88 (95% CI 0.87, 0.89). After adjustment for the above predictor variables, all three pollutants were independently predictive of mortality (Table 5A–C). The PM10 level, on the day of admission, remained predictive of an in-hospital death by Day 30 for the third and fourth PM10 quintiles, respectively, with adjusted ORs of 1.19 (95% CI: 1.04, 1.37) and 1.20 (95% CI: 1.05, 1.38) (P=0.013 and 0.009) (Table 5A). With respect to SO2, it was independently predictive of mortality

### Table 1
Patient characteristics (SJH: 2002–11) by air quality distribution

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lower</th>
<th>Upper</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13 673 (49.2%)</td>
<td>13 619 (49.0%)</td>
<td>&lt;0.69</td>
</tr>
<tr>
<td>Female</td>
<td>14 132 (50.8%)</td>
<td>14 172 (51.0%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>27 805 (100%)</td>
<td>27 791 (100%)</td>
<td></td>
</tr>
<tr>
<td>Age (years), median (IQR)</td>
<td>61.3 (41.4, 76.9)</td>
<td>62.4 (42.0, 76.7)</td>
<td>&lt;0.09</td>
</tr>
<tr>
<td>LOS (days), median (IQR)</td>
<td>5.0 (2.0, 9.7)</td>
<td>5.1 (2.0, 9.8)</td>
<td>&lt;0.11</td>
</tr>
<tr>
<td>Charlson Index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>12 842 (46.2%)</td>
<td>12 407 (44.6%)</td>
<td>&lt;0.25</td>
</tr>
<tr>
<td>1</td>
<td>7698 (27.7%)</td>
<td>7261 (26.1%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>7265 (26.1%)</td>
<td>8123 (29.2%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>MDC class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>7044 (48.5%)</td>
<td>7485 (51.5%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cardiac</td>
<td>4556 (50.1%)</td>
<td>4529 (49.9%)</td>
<td>&lt;0.78</td>
</tr>
<tr>
<td>Neurological</td>
<td>4573 (52.1%)</td>
<td>4208 (47.9%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>3023 (49.2%)</td>
<td>3119 (50.8%)</td>
<td>&lt;0.19</td>
</tr>
</tbody>
</table>

*aBaseline demographic and clinical data comparing all patients, related to the bottom or top half of PM10 distribution on day of admission.*

### Table 2
Particulate matter (PM10 μg/m³) by quintile and 30-day mortality

<table>
<thead>
<tr>
<th>Quintile</th>
<th>Median (IQR)</th>
<th>Mortality, %</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.9 (7.5, 10.0)</td>
<td>7.2</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>12.5 (11.8, 13.2)</td>
<td>7.3</td>
<td>1.01 (0.89, 1.15)</td>
<td>0.19</td>
</tr>
<tr>
<td>3</td>
<td>16.0 (15.0, 17.1)</td>
<td>8.8</td>
<td>1.24 (1.09, 1.41)</td>
<td>0.001</td>
</tr>
<tr>
<td>4</td>
<td>20.9 (19.3, 22.7)</td>
<td>9.6</td>
<td>1.36 (1.20, 1.54)</td>
<td>0.001</td>
</tr>
<tr>
<td>5</td>
<td>33.8 (28.4, 42.4)</td>
<td>8.9</td>
<td>1.25 (1.09, 1.42)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Univariate analysis for prediction of in-hospital death by Day 30 stratified by PM10 quintile on day of admission with ORs and 95% CIs.

### Table 3
Sulphur dioxide (SO2 μg/m³) by quintile and 30-day mortality

<table>
<thead>
<tr>
<th>Quintile</th>
<th>Median (IQR)</th>
<th>Mortality, %</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.87 (0.62, 1.07)</td>
<td>6.6</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.59 (1.41, 1.79)</td>
<td>7.0</td>
<td>1.07 (0.94, 1.22)</td>
<td>0.3</td>
</tr>
<tr>
<td>3</td>
<td>2.52 (2.27, 2.84)</td>
<td>9.1</td>
<td>1.43 (1.26, 1.62)</td>
<td>0.001</td>
</tr>
<tr>
<td>4</td>
<td>4.11 (3.59, 4.76)</td>
<td>9.7</td>
<td>1.54 (1.36, 1.75)</td>
<td>0.001</td>
</tr>
<tr>
<td>5</td>
<td>7.23 (5.98, 10.5)</td>
<td>10.0</td>
<td>1.58 (1.39, 1.80)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Univariate analysis for prediction of an in-hospital death by day 30 stratified by SO2 quintile on day of admission with ORs and 95% CIs.
for the top three quintiles with adjusted ORs of 1.46 (95% CI: 1.27, 1.68), 1.58 (95% CI: 1.38, 1.82) and 1.38 (95% CI: 1.20, 1.59), respectively (all \(P<0.001\)) (Table 5B). \(\text{NO}_x\) was independently predictive in respect of the highest two quintiles compared with quintile 1, with fully adjusted ORs of 1.23 (95% CI: 1.07, 1.41; \(P=0.004\)) and 1.17 (95% CI: 1.10, 1.35) (both \(P<0.05\)) (Table 5C).

### Discussion

We have shown that major urban air pollutants PM_{10}, \(\text{SO}_2\) and \(\text{NO}_x\) all have independent effects on all-cause mortality following an emergency medical admission. The study was conducted over a prolonged time period in a large population. The levels at which effects were observed were interestingly far below that previously described within the literature.
suggesting that air quality continues to impact upon human health despite attainment of EU standards and introduction of successful legislation in Ireland.

Particulate matter and gas pollutants remain the most important air quality determinants in urban areas that affect human health. WHO air quality guidelines (Air Quality Guidelines Global Update 2005) recommend annual mean levels of PM$_{10}$ and PM$_{2.5}$ to be <20 and 10 $\mu$g/m$^3$, respectively. Furthermore, annual mean nitrogen dioxide concentrations are recommended to be <40 $\mu$g/m$^3$ with daily mean sulphur dioxide levels <20 $\mu$g/m$^3$. Measurements at the three local centres in Dublin within our hospital catchment area fell well below the recommended guidelines suggesting good air quality. However, despite this we detected clear effects on mortality of low to moderate levels of PM$_{10}$, SO$_2$ and NO$_2$. The effects of each pollutant were independent. On days where PM$_{10}$ was in the higher range a statistically significant increase in respiratory and neurological admissions was observed; however, we did not find a statistically significant increase in cardiovascular admissions observed in early work.$^5$ An important reason for this is our measured levels of air pollutants were well within European standards and below that which was assessed in prior studies.

Air pollution is a complex mixture of solid particles and gaseous pollutants. Determining the effect of each pollutant and at which concentrations adverse effects on human health occur is challenging but helps to determine local and national environmental policies. Several studies show the effects of PM and SO$_2$ concentrations on mortality. For instance, work by Katsouyanni et al.$^2$ investigated effects of ambient SO$_2$ and PM on mortality in 12 European cities.$^2$ In Western European cities, a 50 $\mu$g/m$^3$ increase in SO$_2$ or black smoke was associated with a 3.0% increase in daily mortality with the corresponding figure for PM$_{10}$ of 2.0%.$^2$ In the USA however, studies by Dockery and Pope$^3$ and Samet et al.$^1$ found that each increase in PM$_{10}$ level of 10 $\mu$g/m$^3$ increased the relative rate of death from all causes by 1.0% and 0.5%, respectively. Keary et al.$^{14}$ have shown a statistically significant correlation between PM$_{10}$ levels and traffic volumes in Dublin suggesting that new strategies to reduce traffic related air pollution are required.

Our work illustrates statistically significant increases in mortality when related to PM$_{10}$ and SO$_2$ concentrations. In terms of NO$_2$, increased mortality was noted at the second quintile (mean concentration = 38 $\mu$g/m$^3$) levels below the WHO recommended guidelines. Work performed in Canada,$^21$ Europe$^{22}$ and Asia$^{23}$ has all similarly shown an increased total, cardiovascular and respiratory mortality rate associated with increasing NO$_2$ concentrations. In the study of European cities, a 10 $\mu$g/m$^3$ increase in NO$_2$ was associated with a 0.3% increase in total mortality. It was further noted that the effect of increasing NO$_2$ on respiratory mortality was higher in cities with a larger population of elderly people.$^2$ The median age in our study was 62 that may have contributed to the increased mortality seen at lower quintiles of NO$_2$ compared with the other pollutants examined.

Oxidative stress by means of production of reactive oxygen species (ROS) and resultant inflammation have been proposed as major mechanisms by which air pollution impacts upon the pulmonary and cardiovascular systems.$^{24-27}$ Although each environmental pollutant has its own mechanism of toxicity, most pollutants are potent oxidants and capable of ROS production. Inflammation and the production of ROS are initially designed as a protective mechanism for the human body aiding removal of noxious stimuli. ROS are able to induce cell death. In vivo, this effect is counterbalanced by up-regulation of stress defence genes including antioxidants protecting cells from ROS-induced damage. However, if the protective effects fail or are inadequate pro-inflammatory responses are initiated mediated by mitogen-activated protein kinase and nuclear factor-kappaB cascades.$^{28}$ Air pollution is one mechanism by which such defences may be overwhelmed.

Although our study findings are novel and interesting, it is important to recognize its limitations. These include the lack of data on infectious disease pandemics. Consequently, we have not corrected for influenza pandemics that occurred during the study period. Importantly, correction for major confounding factors that affect mortality in acute medical admissions including the acute illness severity, co-morbidities, MDC, deprivation, ambient air temperature and season of the year has been accounted for. Only two of the three monitoring stations in our catchment area had recorded PM$_{10}$ levels and monitoring was limited to one value per day for this pollutant. Although our database includes patients admitted directly into the HDU or ICU from presentation into the emergency department, such groups are not separately stratified during data collection and the numbers too small to perform any meaningful analysis to compare effects of air quality on admission location (i.e. main floor vs. HDU or ICU admission). Although our study included a large population, it was single centred and conducted only in Dublin; therefore, translating its findings globally should be interpreted accordingly.

In summary, our study highlights the impact of relatively low levels of air pollution, which are within the limits of the WHO guidelines for human
health, on mortality. Despite the huge and successful impact of the Irish government ban on coal, current levels of air pollution still pose significant threats to public health and further strategies to reduce air pollution are indicated. Potential avenues for targeted strategies should focus on major sources nationally namely vehicle emissions and traffic congestion particularly in urban settings.

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Conflict of interest: None declared.

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