Respiratory effects of sulphur dioxide: a hierarchical multicity analysis in the APHEA 2 study


Background: Sulphur dioxide (SO₂) was associated with hospital admissions for asthma in children in the original APHEA study, but not with other respiratory admissions.

Aims: To assess the association between daily levels of SO₂ and daily levels of respiratory admissions in a larger and more recent study.

Methods: Time series of daily counts of hospital emergency admissions were constructed for asthma at ages 0–14 years and 15–64 years, COPD and asthma, and all respiratory admissions at ages 65+ years in the cities of Birmingham, London, Milan, Paris, Rome, Stockholm, and in the Netherlands for periods of varying duration between the years 1988 and 1997. A two stage hierarchical modelling approach was used. In the first stage generalised additive Poisson regression models were fitted in each city controlling for weather and season. These results were then combined across cities in a second stage ecological regression that looked at potential effect modifiers.

Results: For an increase of 10 µg/m³ of SO₂, the daily number of admissions for asthma in children increased 1.3% (95% CI 0.4% to 2.2%). Effect modification among cities by levels of other air pollutants or temperature was not found. The SO₂ effect disappeared after controlling for PM₁₀ or CO, but correlation among these pollutants was very high. Other respiratory admissions were not associated with SO₂.

Conclusion: SO₂ is associated with asthma admissions in children, indicating that reduction in current air pollution levels could lead to a decrease in the number of asthma admissions in children in Europe.
Table 1  SO2 and hospital admissions daily averages (SD) by diagnosis, age group, and city; APHEA 2 study

<table>
<thead>
<tr>
<th>City (years)</th>
<th>SO2 (µg/m³)</th>
<th>Asthma</th>
<th>COPD + asthma</th>
<th>All respiratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milan (1990-97)</td>
<td>32.5 [37.5]</td>
<td>0.7 [1.0]</td>
<td>0.5 [0.7]</td>
<td>2.9 [2.2]</td>
</tr>
</tbody>
</table>

Table 2  Percentage increase (95% CI) in respiratory emergency room admissions (RERA) per each increase in 10 µg/m³ of sulphur dioxide, according to the regression model

<table>
<thead>
<tr>
<th>RERA</th>
<th>Age</th>
<th>Fixed effects</th>
<th>Random effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>0-14</td>
<td>1.3 (0.4 to 2.2)</td>
<td>1.3 (0.4 to 2.2)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1-64</td>
<td>0.0 (-0.9 to 1.0)</td>
<td>0.0 (-0.9 to 1.0)</td>
</tr>
<tr>
<td>COPD + asthma</td>
<td>&gt;64</td>
<td>0.6 (0.0 to 1.2)</td>
<td>0.4 (-0.6 to 1.2)</td>
</tr>
<tr>
<td>All respiratory</td>
<td>&gt;64</td>
<td>0.5 (0.1 to 0.9)</td>
<td>0.4 (-0.4 to 1.2)</td>
</tr>
</tbody>
</table>

the remaining short term serial correlation in the residuals. Temperature and humidity on the day of admission were included in all models and the smoothing parameter that minimised Akaike's Information Criterion, a likelihood based measure of goodness of fit, was chosen. This criterion was used to determine if, in addition, there were delayed effects of weather variables (up to three days before the admission) by testing whether such variables improved the model fit. Further details of this approach to model selection have been published previously. In every city, the air pollution indicator (that is, SO2) was introduced as a linear term of arithmetic averages of the same day (as admission) and the previous day measures. Finally, two pollutant models were fitted to assess the changes in the SO2 estimates after the inclusion of the other pollutants in the regression model.

In the second stage the results were combined using a meta-regression approach. This consists of an ecological regression where the estimated effect of SO2 in each city was regressed on possible explanatory factors that vary across the cities. These included climatic variables, population differences, and levels of other air pollutants. If no factors explained any differences across the cities the regression with only an intercept term gave the inverse variance weighted average. An iterative maximum likelihood based approach was used to estimate a random variance component in these regressions. It reflects any unexplained variance in the results by city that do not appear to be due to chance; the significance of the random variance component was tested using a χ² test for heterogeneity.

RESULTS

There was a wide range in the SO2 daily averages among the seven participating areas, from 6.8 µg/m³ in Stockholm to 32.5 µg/m³ in Milan (table 1). There was also considerable variability in potential effect modifiers such as levels of co-pollutants, mean wintertime temperature, and standardised mortality rates as shown elsewhere. Daily admissions for respiratory illness also varied substantially between the seven cities. Among the four groups of respiratory admissions studied, only daily admissions for asthma in children were associated with daily values of SO2 (table 2). The associations with asthma in children were homogeneous among the seven centres (p = 0.7); thus the fixed and the random effects models gave very similar results (at 2 significant figures). We did not find evidence for effect modification with climatic variables or pollutant levels in the second stage analysis. The association of SO2 with childhood asthma admissions was sensitive to inclusion of a second pollutant in the models (percentage increase due to SO2: −3.7% and −0.7% after controlling for particulate matter (PM10) and carbon monoxide (CO) respectively; p > 0.1). However, the correlation between SO2 and both pollutants was very strong in all areas (the median correlation coefficient among the seven cities was 0.64 for PM10 and 0.53 for CO). Control for other pollutants in models for the other respiratory admissions did not change the lack of association found in the single pollutant models.

DISCUSSION

We found daily variations in SO2 were related to daily number of asthma admissions in children, but not with other respiratory diseases in other age groups. These findings agree with the results of the original APHEA study. The analysis for SO2 in the original APHEA study only included the cities of Helsinki, London, and Paris. The present study shows a very similar magnitude of the association with asthma in children after studying seven cities. Previous studies carried out during the 1960s with higher urban levels reported an increase in respiratory infections in relation to SO2 in children and in children with asthma, but SO2 has not been shown to be related to asthma admissions in adults, even at high values of exposure. The pattern of association (with childhood asthma but not other respiratory admissions) may be related to exposure factors. Asthmatic reactions can occur in response to a short term exposure, whereas exacerbations of other respiratory conditions, for example pneumonia, are more likely to be in response to a longer term insult. The nature of SO2 exposure...
makes it more likely that high pollution days result in peak exposure to a subpopulation of children who play outside during the day than in a substantial multi-hour or day exposure of relevance for the other outcomes. This is because SO₂ is a highly reactive gas whose concentration is very seasonal, peaking in the winter. Because of this reactivity, indoor concentrations of SO₂ are usually much lower than outdoor concentrations. Since people spend most of their time indoors in western society, particularly in the winter, exposures indoors remain low, even when levels are raised outdoors. Hence it may be less likely that the elderly will receive exposures high enough to exacerbate infection, and more likely that children may receive short term exposures high enough to trigger asthma attacks.

SO₂ is a gas produced by fuel combustion. Currently, the major source of combustion pollution in most cities is traffic. Hence, SO₂ might be a surrogate of the traffic pollution mixture. The high correlations between SO₂, PM₁₀, and CO did not allow the effects of these pollutants to be separated in the multi-pollutant regression models. However, two recent studies in eastern European countries suggested that SO₂ by itself might be related to respiratory diseases in children. In the Czech Republic and Poland, among 6959 children from 130 different sites, the winter concentrations of SO₂ were associated with asthma prevalence diagnosed by a doctor. In three areas of eastern Germany, decreases in levels of SO₂ were associated with a decrease of respiratory symptoms among 7632 children.

We did not find evidence of effect modification by levels of other air pollutants or temperature. While our study had limited power to detect such associations, with only seven cities examined, we note that previous analyses of hospital admissions in the eight APHEA 2 cities did find indications of effect modification for PM₁₀ on the same outcomes.

We conclude that daily values of SO₂ were associated with increases in the number of daily emergency admissions for asthma in children in European cities. However, our study cannot differentiate as to whether these associations were due to SO₂ itself or to other pollutants emitted from the fuel combustion processes. Nevertheless, this study suggests that a reduction in current outdoor SO₂ levels could lead to a decrease in the number of admissions for asthma among children in Europe. We failed to find evidence for an association between SO₂ and other respiratory conditions in adults.

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REFERENCES
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