Air Pollution and Sudden Infant Death Syndrome

Robert Dales, MD*‡; Richard T. Burnett, PhD*; Marc Smith-Doiron, Dipl Adm*; David M. Stieb, MD*; and Jeffrey R. Brook, PhD§

ABSTRACT. Background. Sudden infant death syndrome (SIDS) affects ~1 in 1000 live births and is the most common cause of infant death after the perinatal period.

Objective. To determine the influence of air pollution on the incidence of SIDS.

Methods. Time-series analyses were performed to compare the daily mortality rates for SIDS and the daily air pollution concentrations in each of 12 Canadian cities during the period of 1984-1999. Serial autocorrelation was controlled for by city, and then the city-specific estimates were pooled. Increased daily rates of SIDS were associated with increases, on the previous day, in the levels of sulfur dioxide (SO2), nitrogen dioxide (NO2), and carbon monoxide but not ozone or fine particles measured every sixth day. Effects persisted despite adjustments for season alone or the combination of daily mean temperature, relative humidity, and changes in barometric pressure for NO2 and SO2 but not carbon monoxide.

Results. Increases in both SO2 and NO2, equivalent to their interquartile ranges, were associated with a 17.72% increase in SIDS incidence.

Conclusion. Ambient SO2 and NO2 may be important risk factors for SIDS. Pediatrics 2004;113:e628–e631. URL: http://www.pediatrics.org/cgi/content/full/113/6/e628; air pollution, epidemiology, SIDS.

ABBREVIATIONS. SIDS, sudden infant death syndrome; PM10, particulate matter with a median aerodynamic diameter of <10 μm.

The rate of sudden infant death syndrome (SIDS) in the mid-1990s was ~1 in 1000 live births.1,2 In Canada, the incidence of SIDS decreased from 1.09 in 1000 live births in 1984 to 0.49 in 1000 live births in 1999. Many risk factors have been identified and publicized, including the winter season,2,3 lower social status of parents,4 environmental tobacco smoke,1,4 and the prone position.2 The role of ambient air pollution has received relatively little attention is related to the challenging methodologic issues involved. Similar to the studies that documented the currently accepted risk factors for SIDS, air pollution studies must be observational and not interventional. Large populations must be studied because of the relatively infrequent event rate and the expected modest effect size of air pollution. Administrative database studies comparing regional mortality statistics and regional air pollution concentrations and case-control designs are efficient for the study of infrequent events but are prone to confounding. If the rates of SIDS in areas with high levels of pollution were compared with the rates in areas with lower levels, then it would be necessary to control for the many other potential personal risk factors for SIDS that may differ according to region to avoid potential confounding.

To investigate the influence of ambient air pollution on SIDS, we conducted a time-series analysis comparing daily rates of SIDS and daily concentrations of air pollution during a 16-year period in Canada. A large, unbiased population sample was studied. Social status and the many other risk factors mentioned above required no adjustment, because we compared mortality rates on higher- and lower-air pollution days for the same population. To bias the results, a variable would need to be associated with daily changes in air pollution and also be a risk factor for SIDS, making confounding unlikely.

METHODS

The Canadian cities studied were Halifax, Saint John, Quebec, Montreal, Ottawa, Toronto, Hamilton, Windsor, Winnipeg, Edmonton, Calgary, and Vancouver. The total population for these 12 cities is 10,310,309 (1996 Census). These cities were chosen on the basis of the availability of air pollution data. SIDS data were extracted from Statistics Canada Vital Statistics, which records all births and deaths in Canada. SIDS is defined as a sudden, unexplained death of a child <1 year of age for which a clinical investigation and autopsy fail to reveal a cause of death. The offices of the Chief Coroner/Chief Medical Examiner must investigate every case. Autopsies have been mandatory since the 1990s, but whether this was the case in all jurisdictions in the 1980s could not be determined. Data were available for the period of January 1, 1984, to December 31, 1999.

Air pollution data were obtained from the National Air Pollution Surveillance system for carbon monoxide (CO), nitrogen dioxide (NO2), ozone, sulfur dioxide (SO2), and particulate matter with a median aerodynamic diameter of <10 μm (PM10) or <2.5 μm. Daily data were available for pollutant gases, whereas particulate matter levels were measured every sixth day. When data were available from >1 monitoring site, they were averaged. Daily weather data obtained from the Environment Canada meteorology archive included 24-hour mean temperatures and relative humidity levels and changes in barometric pressure between 8 AM on the day of observation and 8 AM the preceding day.
Daily variations in the number of SIDS cases were correlated with daily variations in ambient concentrations of air pollutants by using a random-effects regression model for count data. A linear association between air pollution and the incidence of SIDS was assumed on the logarithmic scale, with the association varying at random among cities. The SIDS frequency is known to vary with time, with higher death rates in winter than in summer. Air pollution also varies seasonally. To adjust for temporal trends that might confound the SIDS-air pollution association, we used piecewise constant functions in time that varied by 3, 6, or 12 months throughout the study period. For each city, we selected the temporal model that maximized the evidence that the model residuals did not display any type of structure, including serial correlation, using Bartlett’s test for each city separately. Time lags of 0 to 5 days were examined in addition to multiple-day lags of 2 to 6 using Bartlett’s test for each city separately. Time lags of 0 to 5 did not display any type of structure, including serial correlation, for each city. The results for each city were pooled, and the estimates of the pooled effect size and the SE were calculated by using a fixed- or random-effects model. A random-effects model was used whenever the between-city variance was >0, even if the heterogeneity among effect-size estimates for individual cities was not statistically significant. The presence of statistical heterogeneity in effect size between cities was assessed by using the Q statistic. Several analyses were conducted to examine the sensitivity of the SIDS-air pollution association to a number of other variables including weather factors (daily mean temperature, daily mean relative humidity, and maximum change in barometric pressure, all measured on the day of death), length of time-period adjustment (all cities used 3 months), seasonal indicator variables, and size-fractionated particulate mass. Pooled estimates were expressed as the percentage increase in SIDS incidence associated with an increase in the concentration of air pollutants equivalent to the interquartile range among all cities.

RESULTS

The number of cases of SIDS in the 16 years was 1556, varying by city from 0 to 34 cases annually (Table 1). The 24-hour average pollutant concentrations, averaged for the period of observation (from 1984 to 1999), are presented in Table 2. Air-quality measures improved somewhat between 1984 and 1999, with the exception of ozone. The concentrations of air pollutants in 1984 and 1999 were as follows: 31 and 34 ppb for ozone, 23 and 19 ppb for NO2, 7 and 5 ppb for SO2, 1.1 and 0.7 ppm for CO, and 30 and 21 µg/m³ for PM10, respectively.

On the basis of Bartlett’s test, the time factor selected was 12 months for Toronto and Quebec and 6 months for all other cities except Edmonton, for which no time was used. On the basis of the Q statistic, heterogeneity among the 11 cities was not statistically significant for any of the pollutants (SO2, P = .41; NO2, P = .67; CO, P = .45).

With adjustment for time, the strongest association between SO2 levels and SIDS incidence was found with the SO2 concentration on the previous day (Table 3). There was an 8.49% increase (95% confidence interval: 2.15%–15.22%) in SIDS incidence for an interquartile increase in SO2 levels (P = .0079). The strongest associations for NO2 and CO were with the average levels in the 3 days preceding the death. For an interquartile increase in NO2 levels, there was a 15.23% increase (95% confidence interval: 6.74%–24.39%) in SIDS incidence (P = .003); for CO, the increase was 10.73% (95% confidence interval: 5.02%–16.75%) (P = .0002). No significant effect was observed for ozone or particulate air pollution.

To assess the influence of the analytic techniques on the findings, the relationship between air pollution and SIDS incidence was tested with several different models (Table 4). CO effects were not robust. They remained significant when results were adjusted for each climate variable individually but not when all climate variables were entered simultaneously in the model and not when a 3-month factor or season was included in the model. In contrast, SO2 and NO2 effects remained significant in the model using a 3-month factor and also in the full model adjusting for time, temperature, relative humidity, and barometric pressure. There was no significant effect modification according to season for NO2, CO, or SO2.

The combined effects of pollutants, adjusted for time, are presented in Table 5. Ozone effects were negatively correlated with CO, NO2, and SO2 effects. Pearson correlations with NO2 were 0.22 for SO2 and 0.55 for CO. The correlation between SO2 and CO effects was 0.21. All correlations were significant at P < .0001. SO2 and NO2 had independent effects, but the effects of CO disappeared when either SO2 or NO2 was considered.

DISCUSSION

In the largest cities in Canada, we found that SIDS was associated with air pollution, with the effects of SO2 and NO2 seeming to be independent of sociodemographic factors, temporal trends, and weather.

<table>
<thead>
<tr>
<th>TABLE 1.</th>
<th>Number of SIDS Cases in Canada, According to City and Year, 1984–1999</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calgary</td>
<td>24</td>
</tr>
<tr>
<td>Edmonton</td>
<td>26</td>
</tr>
<tr>
<td>Halifax</td>
<td>8</td>
</tr>
<tr>
<td>Hamilton</td>
<td>10</td>
</tr>
<tr>
<td>Montreal</td>
<td>13</td>
</tr>
<tr>
<td>Ottawa/Hull</td>
<td>16</td>
</tr>
<tr>
<td>Quebec</td>
<td>4</td>
</tr>
<tr>
<td>Saint John</td>
<td>4</td>
</tr>
<tr>
<td>Toronto</td>
<td>51</td>
</tr>
<tr>
<td>Vancouver</td>
<td>33</td>
</tr>
<tr>
<td>Windsor</td>
<td>6</td>
</tr>
<tr>
<td>Winnipeg</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>206</td>
</tr>
</tbody>
</table>
The effects of CO disappeared when climate effects were considered, whereas the effects of ozone and particles were not significant. The latter finding might have been attributable in part to the reduction in observations, with measurements being available every sixth day.

Woodruff et al.10 studied the cross-sectional association between elevated PM10 levels and SIDS incidence among 4 million infants born between 1989 and 1991. The unit of observation was a metropolitan statistical area. Among normal birth weight infants, levels of air pollution in 86 metropolitan statistical areas, with an odds ratio of 1.26 (95% confidence interval: 1.14%–1.39) between the areas of highest and lowest exposure, estimated as the mean for the first 2 months of life (44.5 and 23.6 μg/m³, respectively). The odds ratio was adjusted for maternal ethnicity, education, smoking during pregnancy, marital status, month of birth, and average ambient temperature during the first 2 months of life. SIDS rates were not adjusted for birth weight or income, and gaseous pollutants were not considered in the study. Another cross-sectional study, by Lippert et al.,5 found an association between levels of particulates, but not gases, and SIDS incidence, with an unadjusted odds ratio of 1.42 (no confidence interval given) between metropolitan statistical areas with low versus high levels of PM10 pollution (27.5 and 50.9 μg/m³, respectively). This association persisted after adjustment for several factors including gender, ethnic background, birth weight, mother’s aid, adequacy of prenatal care, smoking, and education. The database cohort included all infants born in the United States in 1990. Air pollution exposure was estimated at the county level and included PM10, CO, sulfate oxide, and sulfate. Positive associations were found also with non-sulfate PM10 and negative mortality associations were observed for sulfates. SIDS incidences were higher in the winter, in the northern and western areas of the United States, and outside large cities. One earlier study, which lacked modern statistical techniques for time-series analyses, reported increased visibility and decreased PM10 levels before the occurrence of SIDS.11 A second study found no increase in daily SO2 levels on days of SIDS, compared with 1 and 2 weeks before and after,12 whereas a third study reported a correlation between SIDS and elevated levels of gas pollutants (SO2, NO2, CO, and hydrocarbons) 7 weeks before the event.13

Lippert et al.5 in reviewing their results and those of others, cautioned against attributing differences in SIDS rates to air pollution when there may be other observable but as yet unexplained differences between regions that influence mortality rates. The present report makes a significant contribution by confirming an adverse effect of air pollution in a large population study using a study design that is not confounded by differences among populations or geographic areas (a potential weakness of previous studies that compared regions). One weakness of the present study is the lack of daily data on particulate material of <2.5 μm, which reduces the power to detect an effect. However, the observed SO2 and NO2 effects were unlikely to be confounded by particulate material, because no independent effect was observed. Another weakness is the lack of data on personal exposure to air pollution. However, personal exposure monitoring would necessitate a prospective study, which is not feasible given that the incidence of SIDS is only 1 per 1000 live births. Furthermore, the inaccuracy of area exposure data, through random misclassification, would be expected to reduce the observed effect estimate, suggesting that the observed SO2 and NO2 effects might be even larger than reported.

It can be argued that air pollution may be a causal factor in SIDS.
Values are adjusted for time.

* Individual air pollutant effects are adjusted for copollutants.

SO2 and CO, but not particulates, have been associ-

TABLE 5.

TABLE 4. Association Between SIDS and Gaseous Air Pollutants (SO2, NO2, and CO) With Different Statistical Models to Adjust for Time, Climate, and Particulate Air Pollution

<table>
<thead>
<tr>
<th>Covariates in Model with Air Pollution</th>
<th>CO (3-d Average)</th>
<th>NO2 (3-d Average)</th>
<th>SO2 (1-d Average)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β P Value</td>
<td>β P Value</td>
<td>β P Value</td>
</tr>
<tr>
<td>None</td>
<td>.27552 &lt;.0001</td>
<td>.01581 &lt;.0001</td>
<td>.0147 &lt;.1276</td>
</tr>
<tr>
<td>3-mo time factor for all cities</td>
<td>.02236 .7922</td>
<td>.01020 .0121</td>
<td>.01263 .0018</td>
</tr>
<tr>
<td>Time factor + season (summer/winter)</td>
<td>.12102 .0784</td>
<td>.00905 .0608</td>
<td>.01259 .0043</td>
</tr>
<tr>
<td>Time factor + temperature + relative</td>
<td>.11367 .1603</td>
<td>.01011 .0144</td>
<td>.01371 .0136</td>
</tr>
<tr>
<td>humidity + barometric pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time factor + PM10</td>
<td>.20454 .2247</td>
<td>.01268 .3789</td>
<td>.04041 .3628</td>
</tr>
<tr>
<td>Time factor + PM2.5*</td>
<td>-.25694 .1251</td>
<td>-.01060 .4635</td>
<td>-.01452 .3212</td>
</tr>
<tr>
<td>Time factor + PM2.5* + PM10</td>
<td>-.09669 .6549</td>
<td>-.00858 .4685</td>
<td>-.03028 .4474</td>
</tr>
</tbody>
</table>

* PM2.5 particulate matter with a diameter of <2.5 μm.

risk factor for SIDS. First, the association is consistent with the following observations: air pollution has been associated with increased morbidity and mortality rates for both cardiac and respiratory diseases, and SIDS manifests as a cardiopulmonary arrest. Second, one indoor air pollutant, namely, environmental tobacco smoke, has been associated with an increased risk of SIDS.1,4 The gaseous air pollutants SO2 and CO, but not particulates, have been associated with low birth weight, which is in turn a risk factor for infant death.5,14,15 Finally, there is a biologically plausible explanation for the findings, at least for SO2. SO2 is a highly water-soluble gas that is absorbed into and irritates the upper respiratory tract. At 0.5 ppm, it can provoke bronchoconstriction among individuals with asthma.16 The acute effects of NO2, an oxidant, are more controversial, but NO2 may increase respiratory symptoms and bronchial responsiveness.17–19 Irritation and edema of the nasal mucosa or pharynx would increase total pulmonary resistance and the work of breathing, which may be particularly detrimental for infants, who have been said to be oblate nose breathers20 and at least have a preference for the nasal airflow.21 Irritation of the larynx also may provoke vagally mediated apnea among infants.22 SIDS is thought to occur among infants with impaired ventilatory control. It can be speculated that gaseous air pollutants may predispose subjects to episodes of apnea and/or increase the work of breathing, which may be particularly dangerous for infants with disordered ventilatory control, who may be unable to generate a sufficient compensatory response.

REFERENCES


http://www.pediatrics.org/cgi/content/full/113/6/e628
Air Pollution and Sudden Infant Death Syndrome
Robert Dales, Richard T. Burnett, Marc Smith-Doiron, David M. Stieb and Jeffrey R. Brook

Pediatrics 2004;113:e628
DOI: 10.1542/peds.113.6.e628
Air Pollution and Sudden Infant Death Syndrome
Robert Dales, Richard T. Burnett, Marc Smith-Doiron, David M. Stieb and Jeffrey R. Brook

Pediatrics 2004;113;e628
DOI: 10.1542/peds.113.6.e628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/113/6/e628