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ORIGINAL ARTICLE

Air pollution positively correlates with daily stroke admission and in hospital mortality: a study in the urban area of Como, Italy

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Abstract Some current evidences suggest that stroke incidence and mortality may be higher in elevated air pollution areas. Our study examined the hypothesis of a correlation between air pollution level and ischemic stroke admission and in Hospital mortality in an urban population. Data on a total of 759 stroke admissions and 180 deaths have been obtained over a 4-year period (2000–2003). Five air ambient particles have been studied. A general additive model estimating Poisson distribution has been used, adding meteorological variables as covariates. NO_2 and PM_{10} were significantly associated with admission and mortality (P value < 0.05) and with estimated RR of 1.039 (95% CI 1.066–1.013) and 1.078 (95% CI 1.104–1.052) for hospital admission at 2- and 4-day lags, respectively. In conclusion, this study suggests an association between short-term outdoor air pollution exposure and ischemic stroke admission and mortality.

Keywords Ischemic stroke · Risk factor · Air pollution

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Introduction

Epidemiological studies demonstrated that high level of outdoor air pollution can increase the incidence and the mortality risk for cardiovascular diseases [1, 2]. Based on these findings, some studies tried to demonstrate an association between elevated short-term outdoor air pollution and cerebrovascular diseases. The evidence suggests that stroke hospital admissions are higher in areas with elevated levels of outdoor air pollutants. This is due to the combined acute and chronic effects of the exposure to air pollution on stroke risk. There is an increasing interest in using hospital admission data and air pollutant short-term effects. Time series studies show a statistically significant positive association between daily levels of particulate matter and other gaseous pollutants and hospitalization for cerebrovascular events.

Studies conducted in Seoul, Korea, in Taiwan, and in Europe have shown a significant association between some air pollutants and stroke hospital admissions and mortality [3–7]. On the other hand, some works reported lack of association [8, 9].

We investigate the association between short-term outdoor air pollutant levels and ischemic stroke hospital admissions and mortality in Como urban area citizens, over a 4-year period (2000–2003) and before the setting of the two Stroke Units now existing in the town.

Materials and methods

Como is situated in the North-West of Italy and its population is about 85,000 people. Como downtown is near the lake and it is surrounded by not very high mountains causing a poor ambient-air circulation and persistent high

level of air pollutants. Data about hospital admissions for ischemic stroke and mortality-related are obtained from the Stroke Registry of the two principal City Hospitals. To identify some other cases, we analyzed computerized records of daily clinic hospital admissions, using the codes 433 and 434 of the International Classification of Disease, 9th revision (ICD-9). For these cases we have no data about vascular risk factors and stroke severity. Two air-quality monitoring stations were established in Como and controlled by the Regional Agency for the Ambient Protection (ARPA). These monitoring stations are automated and can provide daily reading and saving of SO_2, NO_2, CO, O_3 and PM_{10}. We obtained daily data about ambient temperature, atmospheric pressure, wind speed, and precipitation level from two meteorological stations.

The associations between daily stroke admissions and mortality in Como and air pollutions, as well as weather variables, were analyzed with a general additive model (GAM) estimating Poisson distribution (the dependent variable was rare and was assumed to be Poisson distributed) [10]. First, GAM was used to study associations between stroke admission and air pollution covariates (SO_2, NO_2, CO, O_3 and PM_{10}) with different time-delay (1–5 days). Second, meteorological covariates were introduced in the model with different time-delay. The final model was determined using a backward selection process in which model covariates were examined for their statistical significance and no interactions were considered in order to avoid estimating too many parameters.

The odds ratio and the estimate relative risk for admission were calculated for each air pollutant considering exposed days and not-exposed days and the number of days with registered events [11]. In the analysis we considered alarm levels of each pollutant as reported in the actual European laws. Using a χ^2 test, a different lag time between 0 and 5 days was considered.

Results

There were a total of 759 ischemic stroke admissions and 180 deaths during hospitalization. On average, there were 2.2 ischemic strokes every 1,000 Como citizens/year, with 23.6% mortality year-rate. Mean age was 68 ± 13 years, with a prevalence of male (56.7%). Analyzing air pollutant levels, a cyclical trend was found, with higher levels during autumn and winter, except for the ozone which showed the pick in the summer time.

Analyzing hospital stroke admissions and each data, higher ischemic event rate was found in cool days than in the warm ones. The statistical model showed an inverse association ($P < 0.05$).

Using the statistical model, we observed a significant association between ischemic stroke admissions and the trend of values of NO_2, CO, and O_3 ($P < 0.001$). After meteorological data inclusion in the statistical model, among these pollutants, NO_2 remained the only agent with a positive association ($P < 0.05$). Besides that PM_{10} was associated with ischemic stroke hospital admissions ($P < 0.05$).

Using the same statistical model, a positive association was observed between daily mortality and NO_2 level ($P < 0.01$) with 1-day delay after pollutant exposure and with PM_{10} levels ($P < 0.05$) with 5-day delay. No other air pollutant was associated with daily mortality. Contour analysis of PM_{10} and NO_2 with daily stroke admission with 1-day lag was showed in the generalized additive model plot (Fig. 1).

We observed estimated relative risks of 1.057 (95% CI 1.083–1.031) and 1.039 (95% CI 1.065–1.013) for hospital admission for PM_{10} and SO_2 concentrations, respectively, on the same day. We found the maximum estimated relative risk of 1.078 (95% CI 1.104–1.052) for PM_{10} with a 4-day lag. We observed statistically significant association between hospital ischemic stroke admission and NO_2 with a 2-day lag (RR 1.039, 95% CI 1.066–1.013). At the same time lag, we found the best estimated relative risk for SO_2 with 1.058 (95% CI 1.085–1.032).

For CO, we observed a significant relative risk only with 1-day lag (RR 1.060, 95% CI 1.087–1.034).

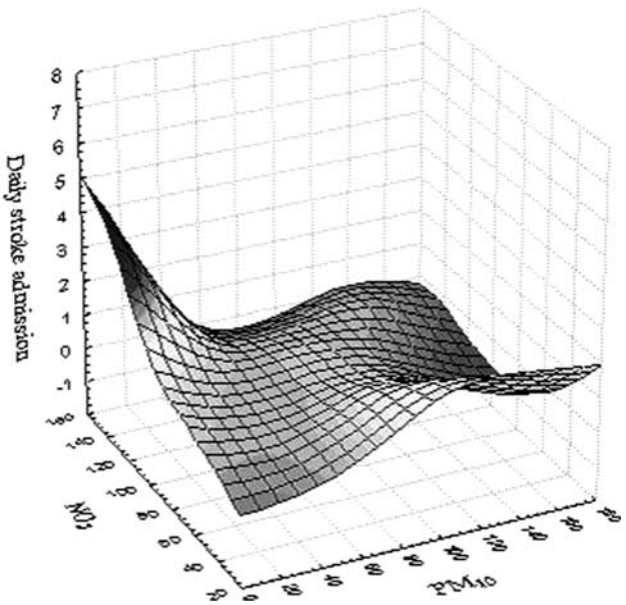

Fig. 1 Contour analysis of PM_{10} and NO_2 with daily stroke admission at different lag days

Table 1 Estimated relative risk and 95% confidence interval of hospital admission for ischemic stroke in exposed and not-exposed days in PM_{10}, NO_2, SO_2, CO and O_3 in single-pollutant model

Lag	PM_{10}		NO_2		SO_2		CO		O_3	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
0	1.057	1.083–1.031	0.990	1.015–0.963	1.039	1.065–1.013	0.976	1.003–0.950	0.920	0.947–0.894
1	1.010	1.036–0.98	1.010	1.035–0.983	1.031	1.057–1.004	1.060	1.087–1.034	0.881	0.907–0.855
2	0.990	1.016–0.96	1.039	1.066–1.013	1.058	1.085–1.032	0.969	0.995–0.942	0.936	0.962–0.910
3	1.044	1.07–0.98	0.981	1.007–0.955	1.041	1.068–1.015	1.005	1.031–0.979	0.870	0.896–0.844
4	1.078	1.10–1.052	0.985	1.012–0.959	1.042	1.069–1.016	1.021	1.048–0.995	0.911	0.937–0.887
5	1.000	1.02–0.96	1.017	1.043–0.991	1.017	1.044–0.991	1.005	1.032–0.979	0.867	0.893–0.841

No significant estimated relative risk was observed for O_3 (Table 1).

Discussion

To the best of our knowledge, this is the first Italian study to report a specific association between daily ischemic stroke hospital admissions and mortality, and air pollution. In fact, the previous meta-analysis of Italian studies was published without specific references to cerebrovascular disease [12].

As reported in several studies conducted in other countries, in the present work, a positive association between NO_2 and PM_{10} levels and ischemic stroke hospital admissions and mortality was observed. As reported in the analysis of the two air pollutants (PM_{10} and NO_2), the 2-day lag seems important to evaluate the short-term accumulated dose of air pollutants and to avoid other confounding factors in the hospital admission. It is interesting to note that meteorological data are very important for a correct analysis of the association and the most important variable seems to be the temperature. Differently from published studies in the South-East of Asia, we observed a negative association with the temperature because the number of stroke hospital admissions was higher during cool months, in particular, December, January and February. This evidence is not described by other similar studies in European or North-American countries [5–7]. In the urban area of Como, it is possible to observe higher levels of air pollutants during this period because of the turning on heat and the increasing car traffic. The increase in relative risk of hospital admission for ischemic stroke with air pollutant rising is in the order of 3–5%.

In the past, there have been many epidemiological and toxicological studies concerned with the potential mechanism linking air pollution and cardiovascular diseases, including stroke. Frampton et al. [13] hypothesized a systemic inflammation and vasoconstriction with an expression of leukocytes, endothelial adhesion molecules, oxidants and interleukins, induced by changes in vascular function due by particle acidity or particles with transition metals or ultrafine particles.

As other published studies, this work has some limitations. First, there is a potential selection bias due to clinically unrecognized stroke cases or stroke treated in other hospitals. Second, epidemic diseases were not included in the statistical model because data were not available. However, we observed an increased level of hospital stroke admissions before the classical beginning of epidemic influenza or getting worse again of other upper and lower respiratory diseases. Some recent studies have suggested the role of acute infections as trigger factor for cerebrovascular accident, but the relationship is not clear. However, other studies are actually ongoing to search a direct association between cerebral ischemic event and inflammation related to infections. Third, there are ecological biases which cannot be ruled out. Fourth, individual exposure was assigned as air pollutant level from fixed outdoor monitoring stations. Measurement errors resulting from differences between population-average exposure and ambient levels cannot be avoided. However, this kind of measurement error is known to cause a bias toward null and underestimates the pollution effects (Berkson type error) [4]. Finally, we have no data available on hypertension prevalence or other stroke risk factors that could potentially have mislead the associations observed. However, many individual vascular risk factors do not vary significantly over time or vary very slowly and they are unlikely to be confounding factors in time series study [4].

The present study shows the positive association between some air pollutants and ischemic stroke. Although this population is not large, these results suggest that air pollution could be a potentially modifiable risk factor for stroke. By focusing on the targeting policy interventions at high pollution areas, we could reduce stroke-related health problems more significantly.

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