

The relative importance of socio-economic status, parental smoking and air pollution (SO₂) on asthma symptoms, spirometry and bronchodilator response in 11-year-old children

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The aim of this study was to evaluate the relative contribution of several risk factors to the prevalence of allergic respiratory symptoms, and the positivity of the bronchodilator test with fenoterol, and to establish the relative importance of these factors on the variability of FVC, FEV₁, PEF, MEF₂₅, MEF₅₀ and MEF₇₅. A total of 340 11-year-old children attending school in polluted and non-polluted areas of the city of Cartagena, Spain, were studied. The polluted area had had an annual mean of 75 µg/m³ of SO₂ over the last 10 years and the non-polluted area had < 20 µg/m³ during this period. A questionnaire about allergic respiratory symptoms was completed by the parents. Specific questions about parental smoking habits and socio-economic level were included. Each child's performance in spirometry before and after administration of 0.2 mg of inhaled fenoterol was evaluated. The only significant predictive variables in the logistic regression (for suffering any symptom or a positive bronchodilator response) were male sex for nasal symptoms (RR 1.37; *p* = 0.04) and housing near heavy traffic for eye symptoms (RR 1.45; *p* = 0.01). Living in the polluted area reduced the risk of a positive bronchodilator response (RR 0.61; *p* = 0.004). Maternal smoking, even though not statistically significant, tended to increased the risk of suffering any symptom (RR 1.26; *p* = 0.07) or of having a positive bronchodilator response (RR 1.23; *p* = 0.1). None of the risk factors studied was of significant importance in explaining the variability of spirometry results. Although none of the risk factors were specifically determinant to the symptom questions, bronchodilator test or spirometric measurements, having a mother who smokes seems more important than living in a polluted area if statistically non-significant trends are considered.

Luis García-Marcos¹, José J. Guillén², Robert Dinwiddie³, Agustín Guillén² and Paloma Barbero⁴

¹Department of Pediatrics, Murcia School of Medicine and Pediatric Research Unit, Cartagena, Spain, ²Regional Health Authority, Area II, Cartagena, Spain, ³Respiratory Unit, Great Ormond Street Hospital for Children, London, UK, ⁴Practiser Medical Center, Cartagena, Spain

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Luis García-Marcos, Unidad de Investigación, Dirección de Salud del Area II, Pza. San Agustín 3, 30201 Cartagena, Spain.

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One of the most extensively studied risk factors for asthma is air pollution. Sulphur dioxide is one of the components of chemical air pollution and its relationship with asthma symptoms is controversial, especially when asthma prevalence is compared between countries with very different

levels of pollution. Sometimes these differences could be explained only in part by the different composition of air pollution of each area or country (1–8). Some authors have supported the idea that a Western lifestyle on its own is a risk factor for development of asthma (8–10). When

the two factors are considered together, some discrepancies arise (7,11,12). Asthma emergencies seem to be slightly higher when the levels of SO_2 are greater, but this does not mean that the underlying prevalence of asthma itself is greater.

Parental smoking has also been related to respiratory symptoms and asthma occurrences, especially in infants (13–15). Most studies have focused on one of the risk factors, or when several have been reviewed the analysis has not been multi-factorial.

In this paper, we try to establish the relative contribution of a number of factors to asthma symptoms, spirometry and bronchodilator response in 11-year-old school children.

Materials and methods

The study was carried out in winter 1992. Children aged 10–11 years, living and attending schools within a polluted and a relatively non-polluted area, were studied. A total of 140 children were eligible from schools in the polluted area and twice this number from the non-polluted area. Polluted and non-polluted areas were defined according to the 1988 report from Environment and Systems Co., which established each zone of the city as high or low in SO_2 concentrations. Although SO_2 levels were controlled from the late 1970s, children born in 1982 have suffered a level of about $75 \mu\text{g}/\text{m}^3$ in the polluted area and $< 20 \mu\text{g}/\text{m}^3$ in the non-polluted area. These values refer to annual means.

Daily peaks and troughs are frequent, and mean values of over $200 \mu\text{g}/\text{m}^3$ in the polluted area have not been infrequent. For example, on 3 December 1991, the mean level over 24 h was $553 \mu\text{g}/\text{m}^3$.

Children were studied at school during the same time of day, their weight and height was measured and pulmonary function (FVC, FEV_1 , PEF_R, MEF₂₅, MEF₅₀ and MEF₇₅) were determined by spirometry (Datospir-100) according to American Thoracic Society (ATS) standards. Those with documented upper or lower respiratory tract infection during the previous 15 days or known to have respiratory problems other than asthma were rejected, as the study was only focused on asthma.

Inhaled fenoterol 0.2 mg was delivered by a metered dose inhaler (MDI) and spacer. The spirometry was repeated before and 10 min after administration. A bronchodilator response (BD) test was considered positive if the FVC after fenoterol increased by at least 10% or PEF_R by 12%, according to Mueller & Eigen (16).

A researcher visited each child and their parents at home and completed a questionnaire comprising the following items:

1. Symptoms. Has your child ever sounded wheezy in his/her chest? Has your child ever suffered from watery discharge or itching in his/her nose, or sneezing? Has your child ever suffered from redness or itching in her/his eyes?

2. Situation of housing in relation to heavy traffic locally.

3. Standard questions to establish the socio-economic level of the family by the Graffar method (17), and

4. Current smoking habits of the parents.

The qualitative variables were grouped into risk factors and signs or symptoms of disease. Risk factors were: living in a polluted area (yes/no), maternal smoking at the time of questionnaire (yes/no), paternal smoking at the time of questionnaire (yes/no), number of people living in the house, proximity to heavy traffic roads (within 50 m). Signs or symptoms of disease were: chest symptoms (wheezing), nasal or eye symptoms, and bronchodilator test (positive or negative). Outcome variables were: signs and symptoms of disease and spirometric results.

Statistical methods

These comprised the χ^2 expression in terms of relative risk and its 95% confidence interval for qualitative variables, and Student's *t* test for the difference of means in the case of quantitative variables. The relative 'weight' of each risk factor on individual symptoms or signs of disease was established by logistic regression including as independent variables all risk factors and as dependent variables each sign or symptom of illness. The relative contribution of each studied variable (risk factor or disease sign or symptom) to the variability of spirometry was calculated by the sum of squares in the analysis of variance.

Results

The participation rate was higher in the polluted area than in the non-polluted area (84% versus 70%). The number of children included were 118 (60% males) in the polluted area and 222 (55% males) in the non-polluted area. No statistical association existed between sex and zone. Of the children in the polluted area, 79% had lived there for at least 10 years, as had 75% of those in the non-polluted area (difference not significant). There were no significant differences between zones in terms of age (11.1 ± 0.8 versus 11.0 ± 0.7 years), height (142.4 ± 7.5 versus

144.4 $\pm$ 7.5 cm) or weight (39.1 $\pm$ 10.1 versus 40.7 $\pm$ 10.2 kg).

The sample allowed for the detection of a relative risk (RR) of 2 between groups for a positive answer to 'wheezing in the chest' with a power of 80% and a confidence level of 95% for a 15% prevalence in the non-exposed group.

Although the RR must be relatively high to detect significant differences between groups, it is enough for the analysis performed here, as we did not intend to discover differences but to investigate the different 'weights' of several risk factors. In this case, it is assumed as a rough index that the number of the sample, for a multivariate analysis, must be at least 10 times higher than the number of variables in the equation. The total number of children (340) allows for a reliable analysis.

There were no major differences between the groups with regard to the mean spirometric values before or after the bronchodilator, but the MEF 25% after bronchodilator was higher in the children from the polluted area than in the non-polluted area (2.1 $\pm$ 0.6 l/min versus 1.9 $\pm$ 0.5 l/min, $p < 0.05$). Socio-economic status was also greater in the non-polluted area (3.7 $\pm$ 0.6 versus 4.2 $\pm$ 0.3, $p < 0.001$).

Significant or near-significant univariate associations of risk factors and outcome variables were found between proximity to heavy traffic and eye symptoms (RR = 1.68; 95% CI 1.1–2.59), male sex and nasal symptoms (RR = 1.62; 95% CI 0.99–2.64), and non-pollution and a positive bronchodilator test (RR = 1.69; 95% CI 1.08–2.63). Positive associations were also found between living in a polluted area and maternal smoking (RR = 1.65; 95% CI 1.21–2.26), and between a polluted area and housing near heavy traffic (RR = 1.51; 95% CI 1.07–2.13) (Table 1).

The results of the logistic regression show that none or only one of the variables entered into each equation (Table 1) was significant for

predicting a positive answer to questions relating to chest, eye, nasal or any other symptoms or positive bronchodilator test. The significant predictor variables were: male sex for nasal symptoms, housing near heavy traffic for eye symptoms, living in a non-polluted area for a positive bronchodilator test. The main contributor for the variability for spirometric values was height. Risk factors were much less important (Table 2).

Discussion

In a recent review by Zhong (1), air pollution including SO₂ was found to be one of the contributing factors to the increase in asthma prevalence in the Asia Pacific region. It is well established that, in the laboratory setting, provocation with levels of SO₂ of around 750 $\mu\text{g}/\text{m}^3$ (18) can cause bronchospasm in asthmatics. Although the SO₂ concentrations in the atmosphere in our polluted area, in terms of annual means, are far lower, some daily peaks have almost reached these concentrations. Chronic low-level exposure may have very different effects than acute high-level exposure: in fact we did not find SO₂ concentrations in the atmosphere to be a risk factor for wheezing in our questionnaire despite the fact that the polluted zone had an annual mean of 75 $\mu\text{g}/\text{m}^3$ and the non-polluted area a mean $< 20 \mu\text{g}/\text{m}^3$. Similar concentrations have been found in Barcelona, Helsinki, Paris and London, and have been related to an increase in asthma admissions with an RR of 1.075 for an increase of 50 $\mu\text{g}/\text{m}^3$ of SO₂ (2). Although significant, the risk is very low and large numbers are needed to detect it. Also, more acute admissions do not necessarily mean increased prevalence.

In this study, 11.7% (95% CI 7.9–16.8) responded positively to the question on wheezing

Table 1. Relative risks of each factor in relation to a positive answer to symptoms questionnaire or bronchodilator test (logistic regression)

Factor	Nose symptoms	Eye symptoms	Chest symptoms	Any symptom	Positive BD test
House near heavy traffic roads	0.93	1.45*	1.16	1.22	0.87
Age†	1.21	1.09	1.01	1.17	0.83
Smoker father	0.92	0.96	1.23	1.01	1.01
Smoker mother	1.23	1.23	1.23	1.26	1.23
Graffar score‡	0.79	1.24	0.88	1.14	1.56
Number of people at home†	0.87	0.82	0.86	0.87	1.01
Male sex	1.37*	1.05	0.88	1.07	1.12
Height†	0.99	0.98	0.96	0.97	0.99
Polluted area	0.79	0.96	1.09	0.98	0.61*

* $p < 0.05$.

†For numerical variables, the risk denotes the probability of the event when the variable increases one unit.

‡Graffar score is higher when socio-economic level is lower.

Table 2. Percentage contribution of the different risk factors to the total explained variability§ of the spirometric variables studied*

	FVC	FEV ₁	PEFR	MEF ₂₅	MEF ₅₀	MEF ₇₅
House near/far from main roads	0.46	0.12	0.10	1.10	1.16	0.24
Age	2.18‡	1.71	0.34	4.99	0.71	0.17
Smoker/non-smoker father	0.41	0.34	0.34	0.30	0.37	0.53
Smoker/non-smoker mother	0.46	0.37	0.68	4.80	2.92	1.75
Graffar score	0.03	0.01	3.05	0.11	0.16	4.72
Number of people at home	0.27	0.53	0.05	1.00	1.25	0.55
Sex	0.64	0.42	1.20	2.74	0.33	0.28
Height	81.59†	86.74†	86.77†	60.61†	75.66†	81.47†
Polluted/non-polluted area	1.81‡	1.64‡	2.27	1.24	1.52	2.31
Interactions	12.14	7.91	5.16	23.06	15.89	7.94

*Percentage of the total explained variability according to the sum of squares in the ANOVA analysis.

§Of the total variability, total *explained* variability was 41.8% for FVC; 43.33% for FEV₁; 21.46% for PEFR; 12.18% for MEF₂₅; 14.32% for MEF₅₀; 26.21% for MEF₇₅.

‡p < 0.05; †p < 0.001.

in the non-polluted area, compared with 16.8% (95% CI 10.4–25.8) in the polluted area. Although wheezing appeared to be more prevalent in the polluted area, the difference was not statistically significant although the sample size may have been too small to detect such a difference. A study in Scandinavia (3) found that air pollution was not a risk factor for asthma prevalence in four different cities, but other studies have found more respiratory symptoms when SO₂ levels increase well above the WHO limits (4,5); However, more symptoms during peak levels do not necessarily indicate increased prevalence. In any case, as stated before, the purpose of this study was not to detect differences but look at the relative influence of several risk factors.

Apart from air pollution itself, there are other risk factors which could be involved in asthma. For example, Walters et al. (6) found that SO₂ and smoking were not associated with hospital admissions for asthma in the West Midlands (UK), but the Townsend deprivation score was a predictor for asthma admissions. In our case, the Graffar score showed a significant relationship between lower socio-economic level and living in a higher polluted area.

Although there was not an association between this score and chest symptoms, risk for wheezing in the logistic regression tended to be lower in the non-polluted area; however, this did not reach statistical significance.

The concept of recurrent chest infections as protective factors for asthma is supported by some authors (11,12,15), and lower socio-economic status would favor more infection. We have found that an increased number of people living in a house seems to offer protection against wheezing and also allergic nasal and eye symptoms (Table 1). However, this was only a

trend and was not statistically significant. Maternal smoking is consistently associated with an increased risk of nose, eye or chest symptoms (RR 1.23, p = 0.2 for each one of them; RR 1.26, p = 0.07, for having any of the three). This is in concordance with other studies (13–15). Paternal smoking was not statistically related to symptoms.

The bronchodilator test was more often positive in those from the non-polluted area: the risk of having a positive test was almost half in the polluted zone (RR = 0.61; p < 0.005). Considering only the non-polluted area, there is a highly significant association between no wheezing on the questionnaire but having a positive bronchodilator test (RR of a positive test for a negative answer 4.3; 95% CI 1.2–16.5). This may indicate that the parents living within these non-polluted areas are less aware of wheezing symptoms in their children. Alternatively, parents in the polluted areas are more sensitized to respiratory symptoms because of their awareness of the changes in the atmosphere. This may mean that wheezing is underestimated in the non-polluted areas and that the true prevalence between the two areas studied would be closer. This is supported by the results of the logistic regression (Table 1) indicating that risk of wheezing is not influenced by area of pollution (RR = 1.09; not significant).

Apart from this relationship to wheezing, it seems that the difference for a positive bronchodilator test in regard to the two zones of pollution is real. This finding is consistent with a recent study (7) which found bronchial hyper-responsiveness to be significantly more frequent in a less SO₂-polluted city (Hamburg, Germany) than in a more polluted one (Erfurt, Germany). Could SO₂ pollution thus provoke rigid and less physiologically responsive bronchi? As socio-

economic status is lower in the polluted area, could this result be justified by a greater number of infections in the children of this zone? A chance effect must be kept in mind as well. Also, the drop-out rate – which was higher in the polluted area – could account for the differences.

The use of the sum of squares as a method of establishing the relative contribution of several variables in spirometry could be controversial. In Table 2, only a few variables contributed significantly. The figures represent the percentage contribution of each variable to the sum of all of those included. This variability was highest with FEV₁ (43%) and lowest with MEF₂₅ (12.2%). As expected, the most important factor in variability was the height of the child.

It is remarkable however that pollution areas seem to be important in all the spirometric values. This does not mean that the FEV₁ is higher or lower in the polluted area, but it does suggest that the area in which the child lives is contributing in some way to his or her FEV₁ value. As interaction effects are high, it is not easy to determine whether this is a direct effect or whether it is influenced by other factors, such as maternal smoking. Maternal smoking appeared to be important in relation to MEF₂₅, MEF₅₀ and MEF₇₅.

In summary, we did not find any of the risk factors studied to be important enough to elicit statistically significant differences in the prevalence of symptoms or the results of the bronchodilator test or spirometric values. However, these results allow us to conclude that maternal smoking is a more important determinant than living in a polluted area.

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