

Impact of Environmental Air Pollutants on Disease Control in Asmathic Patients

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Abstract

Purpose Asthmatics are adversely affected by the presence of air pollutants, the concentrations of which can nowadays be measured. However, the utility of this information in clinical practice has not been defined in a group of asthmatics in stable condition. Our objective was to determine what impact the level of air pollutants had on the control of their asthma and the degree of airway inflammation.

Methods We performed a cross-sectional study of adult asthmatics in stable condition. From the regional environmental authority, we obtained the concentrations of ambient nitric oxide (NO₂), ozone (O₃), suspended particulate matter up to 10 micrometers in diameter (PM₁₀) and sulphur dioxide (SO₂) at fixed geographical points. Disease

control was assessed using asthma control test (ACT) scores, and airway inflammation using fraction of exhaled nitric oxide (FeNO) values. Correlation and linear regression studies were performed using ACT scores as the dependent variable.

Results The study included 99 asthmatics, aged 39 years (SD 8), 55 % women. Mean ACT value was 17.2 (SD 6.5), and FeNO 33.7 (SD 16). Of the pollutants studied, only NO₂ was correlated with ACT scores (CC = 0.45, $p < 0.001$). We found no relationship between pollutants and airway inflammation. Multivariate analysis showed that ACT score was predicted by ambient air NO₂ concentration and, to a lesser extent, mean FeNO.

Conclusions Information on the concentration of ambient NO₂ in our environment can help the clinician to interpret the evolution of asthmatic patients.

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Introduction

Asthma is an inflammatory disease of the airways in which periods of crisis alternate with symptom-free periods. Among the factors that may influence clinical course, the presence of pollutants in ambient air can trigger crises [1, 2] and even act as an etiologic factor in symptom onset [3].

Ambient air quality (AAQ) is clearly of great importance for the health of the general population, and commitment to its preservation should be a priority of Public Institutions [4]. For information on AAQ, air monitoring is required to analyze and measure the concentrations of different pollutants. This work is carried out by local authorities, with a network of monitoring sites located in

specific places. The data collected are then presented in a standardized way. The interpretation and potential usefulness of this information in clinical practice is not well established and few studies have addressed the relationship between disease control and chronic exposure to air pollutants.

Our hypothesis was that the incorporation of AAQ data into the assessment of asthma patients may provide the clinician with information that helps explain possible changes in the status of their patients and even be useful for preventive purposes.

In a group of asthmatics in stable condition, we aimed to determine the impact of air pollutant levels in the geographical area where they usually reside on the control of their disease.

Patients and Methods

This study was conducted in Oviedo, a non-industrialized city located in northern Spain with approximately 225,000 inhabitants. Between the months of May–July 2012 and June 2013, we recruited consecutive asthma patients attended at our lung function laboratory: their medical history suggested the presence of either: 1) spirometry-detected airflow limitation reversible with bronchodilators and/or steroid treatment or 2) positive methacholine test. Inclusion criteria were: age above 14 years, stable situation defined as the absence of exacerbations or need for therapeutic changes in the previous 4 weeks, and habitual place of residence within 10 km of an air pollution monitoring site. Exclusion criteria were: nearest monitoring site more than 10 km from home, cases of severe asthma (with daily symptoms, use of rescue medication several times a day, extremely limited functional activity and forced expiratory volume in 1 s (FEV1) less than 60 % of normal predicted value, or poor compliance with prescribed medication. For a confidence level of 95 % and a confidence interval of 10 %, the sample size required was 96 patients. The cross-sectional descriptive study design was approved by the research ethics committee of our hospital.

Clinical Measurements

From patients who met the inclusion criteria and gave their informed consent, we obtained the following data: age, sex, height, weight, body mass index, smoking status, presence of pollutants in the home (tobacco smoke, other sources of smoke, damp and fungi, and domestic animals), regular medication and allergen sensitization test results. The fraction of exhaled nitric oxide (FeNO) in parts per billion (ppb) was measured on-line by chemiluminescence using an 88 CL analyzer (ECO MEDICS). Spirometry was performed using a Breez Suite spirometer (Medgraphics)

according to standard methodology [5]. FEV1 percentage of the normal predicted value was taken as a parameter for the study. The level of asthma control was assessed using the validated Spanish version of the “asthma control test” (ACT) [6].

Measurements of Exposure

For all patients, homes or the places where they reported spending at least 12 h per day were geographically located by postal code. Pollutant values, measured by the nearest local government monitoring site were obtained: particulate matter (PM) over 10 micrometers in diameter (PM₁₀), and concentrations of ozone (O₃), nitrogen dioxide (NO₂) and sulfur dioxide (SO₂). For the purposes of the present study, mean monthly values were taken, except for O₃ where the mean 8-hour value was used.

The measurement of air contaminants is performed at air pollution monitoring sites by initial capture using absorbent tubes. O₃ levels were determined by gas chromatography, SO₂ by ultraviolet fluorescence, NO₂ by chemiluminescence and PM₁₀ by a gravimetric method, in accordance with current legislation (BOE 24/01/2011).

Statistical Analysis

Data are presented as means and standard deviation for quantitative variables and percentages for qualitative variables. Statistical analysis was performed by a comparison of means (*t* test) after ensuring a normal distribution of the variables (Kolmogorov-Smirnov test) and correlation coefficients (CC) for quantitative variables. Qualitative variables were analyzed using χ^2 test.

Multivariate linear regression analysis was applied, taking ACT questionnaire scores as the dependent variable, and those variables showing significant differences in the bivariate analysis as predictors.

Results

Of 110 cases eligible for inclusion in the study, six were excluded because their nearest monitoring site was over 10 km from home and another five patients were excluded for self-confessed poor adherence to prescribed medication. The final sample included 99 patients, mean age 39 years (SD 8), 55 % women, and mean BMI 26.4 (SD 6). All were receiving anti-inflammatory treatment (82 % inhaled steroids, 24 % Montelukast); 13 % were active smokers and 64 % had positive skin tests for aeroallergens (mites and pollen). Mean FEV1 was 86 % (SD 14) compared to the reference value. Mean FeNO was 33.7 ppb (SD 16) and mean ACT score 17.2 (SD 6.5).

Nearly half (49 %) the patients reported the presence of an air contaminant in the home: 18 % pets (dogs and/or cats), 8 % passive smoking, 9 % other sources of smoke, and 9 % damp and fungi. There were no statistically significant differences between patients recruited in 2012 and those recruited in 2013 in age, sex, BMI, positive skin tests, presence of contaminants at home, FEV1 or anti-inflammatory treatment.

We found a significant correlation between ACT score, age, NO₂ concentration and FeNO value (Table 1). The value of FeNO was not related to any of the ambient air or household pollutants. Active smoking, atopy, rhinitis, FEV1 and BMI showed no correlation with ACT score.

The average distance of air pollution monitoring sites from patient homes was 3.5 km (SD 2.0). For the first recruitment period (May–July 2012: 68 patients), AAQ information was obtained from ten different monitoring sites; 75 % of the sample resided in four districts. Mean temperature for that period was 21.3 °C. In the second recruitment period (June 2013: 31 patients) AAQ information was obtained from the same 10 monitoring sites; 77 % of these patients resided in the same 4 districts as the 2012 sample. Mean temperature for this period was 19 °C. There were significant differences between NO₂ and SO₂ concentrations measured in 2012 and 2013, as well as mean ACT scores (Table 2).

Multivariate linear regression analysis was performed using ACT score as the dependent variable and the following as independent variables: age, NO₂ and SO₂ concentrations, FeNO value and the inclusion period (2012 or 2013). In our model, ACT score was explained by NO₂ concentration and FeNO value using the following equation: $ACT = 25 - 0.22 [NO_2] - 0.046 [FeNO]$.

Table 1 Correlation of ACT score with patient characteristics and ambient air pollutants

variable	ACT scores	
	Pearson's correlation coefficient	P
Age	0.33	0.001
Body mass index	0.15	NS
FEV1 (% of NPV)	−0.081	NS
FeNO ppb	−0.23	0.021
SO ₂ µg/m ³	−0.16	NS
PM ₁₀ µg/m ³	−0.03	NS
NO ₂ µg/m ³	−0.45	<0.001
O ₃ µg/m ³	0.041	NS

FeV1 forced expiratory volume in 1 s, NPV normal predicted value, FeNO fraction of exhaled nitric oxide, ppb parts per billion, SO₂ sulfur dioxide, PM₁₀ particulate matter of up to 10 micrometers in diameter, NO₂ nitric oxide, O₃ ozone

Table 2 Air pollutants and ACT score comparison between 2012 and 2013

	Mean (standard deviation)		P
	June 2013	May–July 2012	
NO ₂ µg/m ³ monthly mean	21.1 (6.2)	29.7 (12.7)	0.001
SO ₂ µg/m ³ monthly mean	8.0 (3.9)	11.2 (7.5)	0.07
PM ₁₀ µg/m ³ monthly mean	27.6 (5.3)	25.8 (9.5)	NS
O ₃ µg/m ³ monthly mean	58.8 (5.7)	58.2 (12.7)	NS
ACT score	19.5 (4.1)	16.1 (7.2)	0.01

NO₂ nitric oxide, SO₂ sulfur dioxide, PM₁₀ particulate matter of up to 10 micrometers in diameter, O₃ ozone, ACT Asthma control test

Discussion

The most important finding of our work with a group of moderate asthmatics in stable clinical condition was that the concentration of air pollutants was not related to the state of their lung function or degree of airway inflammation assessed by FeNO. Only the high concentration of NO₂ may partially explain clinical deterioration reflected by ACT scores.

The negative impact of exposure to air pollutants on the clinical course of asthma and chronic respiratory diseases has been studied by different authors [5, 7–9]. The pollutant most commonly associated with respiratory symptoms and exacerbations is NO₂. The major source of NO₂ in ambient air is road traffic and this variable could be used as a surrogate measure [3]. In our sample, most patients resided in an urban area and the high concentrations of ambient NO₂ in those areas were most likely attributable to this source.

Taking the threshold values of pollutants recommended by the World Health Organization as reference values, we found few examples exceeding those values in our setting, but other authors have shown that although the concentration of NO₂ is below that threshold, there may still be negative effects for asthma control [3].

On comparing NO₂ levels found in our study (21.3–29.7 µg/m³) with those reported by other authors, large differences were found, and there were significant differences between the 32.1 µg/m³ reported by Jackemin et al. [10] in France and the 15.2 µg/m³ documented in Portugal by Martins et al. Surprisingly, despite the higher values of NO₂ found in the Jacquemin study, asthma symptoms/exacerbations were associated with elevated levels of PM₁₀ and O₃ (Table 3). In this regard, our study provides information on the most important pollutant in our area; although NO₂ seems consistently associated with asthma, there is some geographical variation in the concentration of air pollutants [3] and their possible impact on asthmatics. Thus, knowledge about the main pollutant can be very

Table 3 Major air pollutant values

Pollutants	WHO guideline values	A	B	C
NO ₂ (µg/m ³)	40 annual mean 200 µg/m ³ 1-h mean	21.1–29.7	7.7–50.2	6.0–28.0
SO ₂ (µg/m ³)	20 24-h mean 500 µg/m ³ 10-min mean	8.0–11.2		
PM ₁₀ (µg/m ³)	20 annual mean 50 24-h mean	25.8–27.6	12.2–27.6	17.4–92.7
O ₃ (µg/m ³) ^a	100	58.2–58.8	35.7–74.1	9.0–95.0

Comparison of World Health Organization guideline values with those found in the present study and others

A range of values in the present study, B range of values reported by Jackemin et al. (10), C range of values reported by Martins et al. (11)

^a 8-h mean

helpful in decision-making for AAQ control in a given area.

For the present study, patients were recruited during two different periods of time with a gap of one year. We detected changes in the concentrations of pollutants between the two periods, due to various circumstances (changes in emission levels, weather conditions, etc.). In the two groups of patients with similar characteristics, our results showed that variations in the concentration of NO₂ coincided with changes in disease control assessed by ACT scores. This finding is consistent with that of a recent study showing that asthma symptoms were more frequent in patients residing in areas with greater truck [9].

We found no association between the concentration of pollutants and the intensity of inflammation as measured by FeNO or functional impairment measured by FEV1. Previous studies have reported that FeNO was not altered by exposure to road traffic-related pollutants [12]. With respect to FEV1, our study participants were in “stable” condition with over 80 % of the normal value, which may explain why we detected no significant changes in this parameter.

Our results showed no significant association between the presence of pollutants in the home and lower ACT questionnaire scores. This coincides with the findings of other authors using a similar questionnaire [11]. However, home pollutants were not directly measured and this factor may have been underestimated.

The limitations of the present study include the fact that the air pollutant values used were obtained from our local government network of monitoring sites, as in other studies, but these values may not accurately reflect the degree of exposure of a particular individual [13]. In addition, a fundamental parameter of asthma control is patient adherence to prescribed medication, and this was not objectively investigated.

In conclusion, among the variables considered by the clinician in the assessment of patients with asthma, information on air pollutants, especially NO₂ in our setting, may help explain the clinical course in some of these patients. Improving the quality of air we breathe improves the condition of patients with a disease as prevalent as asthma.

When ambient air pollutant levels are below or even well below guidelines values, disease control in stable asthma patients may still be negatively affected.

Conflict of interest The authors declare that they have no conflict of interest.

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