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The Impact of Atmospheric Pollutants on the Prevalence of Atopic Eczema in 6-7-Year-Old Schoolchildren in Spain; ISAAC Phase III

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ABSTRACT

Atopic Eczema (AE) is a chronic inflammatory skin disease that affects children and adults, and alters quality of life with a high morbidity rate and severe economic burden. The objective of the present work was to analyse specific atmospheric pollutants (O_3, NO, PM10 and SO_2) affecting the prevalence of diagnosed AE and its symptoms among 6-7-year-old schoolchildren.

The participants included 21311 schoolchildren aged 6-7 years from 8 Spanish regions, whose parents completed the ISAAC Phase III questionnaire to ascertain AE diagnosis and symptoms. The mean levels (μg/m^3) of O_3, NO, PM10 (particles 10 micrometers or less in diameter) and SO_2 were determined in each geographical area participating in this study.

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According to these mean levels, three levels of exposure to each pollutant were considered: level 1 (percentiles 0-25); level 2 (percentiles 26-74); level 3 (percentiles 75-100). Exposure to O_3 was associated with increased prevalence of rashes (exposure level 2, Odds Ratio (OR): 1.22, 95% Confidence Interval (95%CI): 1.02-1.45; level 3 OR: 1.33, 95%CI: 1.10-1.61) and diagnosed AE (level 2, OR: 1.27, 95%CI: 1.17-1.39; level 3 OR: 1.27, 95%CI: 1.15-1.41). An association was found between the level of NO and a drop in the prevalence of diagnosed AE (exposure level 2, OR: 0.88, 95%CI: 0.81-0.95; level 3 OR: 0.85, 95%CI: 0.74-0.97). There was also an association between the highest exposure level to PM10 and a reduced prevalence of rashes (level 3 OR: 0.42, 95%CI: 0.22-0.81) and diagnosed AE (level 3 OR: 0.53, 95%CI: 0.38-0.75).

Future studies into exposure to O_3 and its relationship with allergic diseases may be conducted in order to prevent this association.

Keywords: Atmospheric Pollutants; Atopic Eczema; Phase III ISAAC Study

INTRODUCTION

Atopic Eczema (AE) is a chronic, pruriginous, inflammatory skin disease with acute phases that affects a large number of children and adults, alters their quality of life and that of their families, and causes a high morbidity rate and severe economic burden for both the family and the health system.[1,2] According to the latest results of the International Study of Asthma and Allergies in Childhood (Phase III ISAAC Study), AE prevalence is around 6-15% in children in industrialised countries and is lower in developing countries.[3] This disease appears in the first year of life in 60% of cases, and before the age of 5 in 80-90% of cases, and the atopic triad is the earliest sign.[1]

Regarding the aetiopathogeny of the disease, we know that immunologic, metabolic and vascular alterations are based on hereditary genetics.[4] Environmental factors (diet, pneumoallergens, climate, infections and atmospheric pollutants), including ozone (O_3), nitrogen monoxide (NO), particles of 10 micrometers or less in diameter (PM10) and sulphur dioxide (SO_2), could influence the way the disease develops.[5] These factors are thought to be related with the westernisation of ways of life, and they essentially act in the intrauterine stage and during early infancy.[6,7] As several studies have shown, both climate and pollution are important factors to consider when we talk about the prevalence of AE, its seriousness and the transiency of its symptoms.[8,9]

Recent studies have shown the influence of specific atmospheric pollutants on AE, but their results do not always coincide.[10,11] Along these lines, we carried out a previous research within the Phase III ISAAC Study for the purpose of analysing the association between AE prevalence and other allergic diseases, and some air pollutants such as sulphur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO) and total suspended particulate matter.[12] The findings from this study suggest that CO concentration increases the risk of diagnosed AE in schoolchildren in Spain. With these results, we thought about the need to study the possible association between other atmospheric pollutants and the risk of AE by focusing a study on not only the prevalence of diagnosed AE, but also on the prevalence of AE symptoms as another atopy measure. To this end, we proposed the present study, whose aim was to analyse whether specific atmospheric pollutants (O_3, NO, PM10 and SO_2) affect the prevalence of diagnosed AE and its symptoms among 6-7-year-old schoolchildren.

MATERIALS AND METHODS

Study Subjects

The Spanish Phase III ISAAC Study was conducted in 2002-2003. The study population included 21,311 schoolchildren aged 6-7 years who lived in eight Spanish geographical areas: Cartagena, Barcelona, Bilbao, Valencia, Madrid, Asturias, San Sebastián and La Coruña.[13] Population groups were based on schoolchildren with a sample size of 3,000 per geographic region. Power calculations indicated that this represents a 90% statistical capacity rate to detect 2% prevalence differences among schools at the 0.01 level of significance.

Study Design

This is a cross-sectional survey based on the Phase III ISAAC methodology that assesses the prevalence of AE and other allergic diseases in a study population of 6-7 year-old schoolchildren. For reasons of operating capacity, the fieldwork was done in schools (the participating schools were chosen per clusters from a randomised school sample). In all the geographical areas, each ISAAC centre obtained authorisations from the corresponding academic institutions and from the participating schoolchildren' parents. This study was approved by the Hospital 12 de Octubre's Ethics Committee (Madrid, Spain).

Questionnaire

This work used the Phase III ISAAC questionnaire on AE prevalence and its symptoms, which has been previously validated and standardised.[14-16] The schoolchildren's parents completed the questionnaire at home. It basically included three questions: 1) Have you (has your child) ever had an itchy rash which has been coming and going for at least 6 months? (yes/no); 2) has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, the front of the ankles, under the buttocks, and around the neck, ears, or eyes? (yes/no); 3) Have you (has your child) ever had eczema or atopic dermatitis?" (yes/no). According to the ISAAC criteria questions, affirmative responses to Questions 1 and 2 were defined as presenting AE symptoms (itchy rashes). The schoolchildren whose parents answered affirmatively to Question 3 were defined as being diagnosed with AE by a medical specialist. In Spain, a diagnosis is usually made according to the Spanish Academy of Dermatology (SAD) criteria based on the diagnostic criteria scale developed by Hanifin and Rajka in 1980.[17]

A series of variables was added to the original questionnaire: mother's level of education, use of paracetamol in the first year of life and parental smoking habit.

Air Pollution

The data used in this study were obtained from the State Register of Emission and Pollutant Sources (Spanish Ministry of the Environment and Rural and Marine Means),[18,19] the European Air Quality database,[20] and various air quality monitoring and controlling networks. [21-24] In 2002-2003, we calculated the mean levels (µg/m^3) of O_3, NO, PM10 and SO_2 in each geographical area participating in this study. According to these mean annual levels, three levels of exposure to the each pollutant were considered: level 1 (percentiles 0-25); level 2 (percentiles 26-74); level 3 (percentiles 75-100).

Climate Data

The climate characteristics included in this study were mean annual temperature (ºC), mean annual precipitation (mm), mean relative humidity (%) and mean annual number of sunny hours (%) in 2002-2003. These data were obtained from the Spanish National Statistics Institute[25-28] (provided by the Spanish Agency of Meteorology).

Statistical Analysis

Prevalences of diagnosed AE and its symptoms (rashes) were estimated as a percentage of the schoolchildren diagnosed with diagnosed AE/rashes divided by the total of participants from each geographical area.

Then we did a logistic regression to determine its associations with exposure to O_3, NO, PM10 and SO_2 by adjusting for gender, mother's level of education, use of paracetamol in the first year of life, parental smoking, mean annual temperature (ºC), mean annual precipitation (mm), mean relative humidity (%) and mean annual number of sunny hours (%).

All the analyses were done with SPSS 15.0 (Copyright, SPSS, Inc, 1986-2006. Chicago, USA).

RESULTS

Participation Rate

As Table 1 shows, 21311 schoolchildren aged 6-7 years participated in our study. The response rate was higher than 70.0% in all the geographical areas, except San Sebastián and Valencia, with a response rate of 62.0% and 53.4% respectively. In terms of sample distribution per gender, the sample included 10630 boys and 10681 girls.

Prevalence of Rashes/ Diagnosed AE

Table 2 shows the prevalence of rashes and diagnosed AE per geographical area and gender. Both total prevalence of rashes and diagnosed AE were slightly higher among boys than among girls (5.7% vs. 6.3%; 31.7% vs. 31.8%). The highest prevalence of both rashes

Table 1. The participating Spanish geographic regions. Number of 6-7-year-old schoolchildren studied. Participation rate and sample size according to gender.

Regions	Boys	Girls	No. participating schoolchildren	Participation rate(%)
Cartagena	1359	1358	2717	71.7
Barcelona	1533	1357	2890	82.2
Bilbao	1469	1570	3039	82.2
Valencia	1665	1721	3386	53.4
Madrid	1162	1176	2338	89.0
Asturias	1505	1522	3027	86.5
San Sebastián	465	432	897	62.0
La Coruña	1472	1545	3017	73.8
Total	10630	10681	21311	75.1

and diagnosed AE was found in San Sebastián (8.2% and 38.6%, respectively).

Distribution of Atmospheric Pollutants

Table 3 presents the mean of the pollutants studied (O_3, NO, PM10 and SO_2) in the Spanish geographic regions. Table 4 offers the means, standard deviations (SD), medians, minimums, maximums, and the 25th and 75th percentiles of the pollutants studied (O_3, NO, PM10 and SO_2) in the eight studied geographical areas. Important differences were found among geographic regions, principally for PM10, with a minimum of 6.00 $\mu g/m^3$ and a maximum of 46.64 $\mu g/m^3$. We also found a significant negative correlation (p<0.05) between NO and O_3 and between NO and SO_2.

Table 2. Prevalence of rashes and diagnosed Atopic Eczema (AE) in the participating Spanish geographic regions arranged per gender in schoolchildren aged 6-7.

Regions	Boys (n=14256)		Girls (n=14148)		Total (n=28404)	
	Rashes	Diagnosed AE	Rashes	Diagnosed AE	Rashes	Diagnosed AE
	AF prevalence*	AF prevalence*	AF prevalence*	AF prevalence*	AF prevalence*	AF prevalence*
Cartagena	71	415	57	350	128	765
	5.2	32.1	4.2	27.2	4.7	29.6
Barcelona	53	376	60	341	113	717
	3.5	24.9	4.4	25.6	3.9	25.2
Bilbao	102	458	100	511	202	969
	6.9	32.1	6.4	33.6	6.6	32.8
Valencia	91	496	108	522	199	1018
	5.5	31.6	6.3	32.3	5.9	31.9
Madrid	62	356	79	375	141	731
	5.3	32.3	6.7	33.0	6.0	32.7
Asturias	100	472	98	461	198	933
	6.6	32.4	6.4	31.4	6.5	31.9
San Sebastián	30	169	44	168	74	337
	6.5	37.3	10.2	39.9	8.2	38.6
La Coruña	99	536	121	538	220	1074
	6.7	37.6	7.8	35.9	7.3	36.7
Total	817	4369	889	4337	1706	8706
	5.7	31.7	6.3	31.8	6.0	31.8

AF, Absolute Frequency *Prevalence per 100 schoolchildren 95% CI, 95% Confidence Interval †p≤ 0.05 Chi-square Test.

Table 3. Annual means of atmospheric contaminants (μg/m^3) in the ISAAC Phase III centres.

Regions	O_3	NO	PM10	SO_2
Cartagena	49.3	14.9	6.0	15.7
Barcelona	30.5	44.6	46.7	3.0
Bilbao	29.3	28.8	37.0	9.3
Valencia	29.2	38.2	30.8	5.3
Madrid	42.6	33.7	34.0	9.6
Asturias	38.8	21.5	44.5	20.5
San Sebastián	33.5	31.0	28.5	5.0
La Coruña	60.5	12.7	18.9	12.4

Association between Prevalence of Rashes/Diagnosed AE and Exposure to Atmospheric Pollutants

Table 5 provides the logistic regression model with estimations for odds ratios (OR) and their 95% confidence intervals (95%CI) for rashes and diagnosed AE per exposure to each atmospheric pollutants level. Exposure to O_3 was associated with increased prevalence of both rashes (exposure level 2, OR: 1.22, 95%CI: 1.02-1.45; level 3 OR: 1.33, 95%CI: 1.10-1.61) and diagnosed AE (level 2, OR: 1.27, 95%CI: 1.17-1.39; level 3 OR: 1.27, 95%CI: 1.15-1.41).

There was no association between level of NO and prevalence of rashes, although an association was found with decreased prevalence of diagnosed AE (exposure level 2, OR: 0.88, 95%CI: 0.81-0.95; level 3 OR: 0.85, 95%CI: 0.74-0.97). The results were similar when using PM10, but in this case, the association was only between the highest exposure level and reduced prevalence of both rashes (level 3 OR: 0.42, 95%CI: 0.22-0.81) and diagnosed AE (level 3 OR: 0.53, 95%CI: 0.38-0.75).

Finally, no associations were found between level of SO_2 and prevalence of rashes and diagnosed AE.

DISCUSSION

The literature includes studies whose results are similar to our own. The association found between exposure to O_3 and rashes/diagnosed AE coincides with the results of similar studies done in France and Brazil. These studies found that O_3 may modulate the immune response by inducing inflammatory changes in the respiratory tract and allergy/sensitivity phenomena through oxidation reactions.[4,29,31-33]

On the other hand, some studies found a positive association between prevalence of allergic diseases and NO,[34] PM10[35-36] and SO_2.[37] We could think that the negative association we found between exposure to NO and prevalence of diagnosed AE could be due to the negative correlations between the levels of NO and O_3.

In relation to the interaction among the environmental variables, it is necessary to take into account that our results have been adjusted for climatic conditions. Some studies have pointed out the need for this adjustment.

Table 4. Annual means, standard deviations, medians, minimums, maximums, and the 25th and 75th percentiles of atmospheric contaminants (μg/m^3) in the ISAAC Phase III centres.

	O_3	NO	PM10	SO_2
Mean (SD)	39.2 (11.2)	28.2 (11.1)	30.8 (13.4)	10.1 (5.9)
Median	36.1	29.9	32.4	9.4
Minimum	29.2	12.7	6.0	3.0
Maximum	60.5	44.6	46.7	20.5
25th percentile	29.6	16.6	21.3	5.1
75th percentile	47.6	37.0	42.6	14.9

SD, standard deviation.

O_3, ozone; NO, nitrogen monoxide; PM10, particles of 10 micrometres in diameter or less; SO_2, sulphur dioxide.

Table 5. Logistic regression models: odds ratios (OR) estimations for rashes and diagnosed Atopic Eczema (AE).

Pollutants	Rash & AE	Rashes			Diagnosed AE		
		ORc (95%CI)	ORa_1 (95%CI)	ORa_2 (95%CI)	OR (95%CI)	ORa_1 (95%CI)	ORa_2 (95%CI)
O_3	Level 1	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
	Level 2	1.05 (0.93-1.19)	1.09 (0.94-1.26)	1.22 (1.02-1.45)	1.10 (1.04-1.17)	1.19 (1.10-1.28)	1.27 (1.17-1.39)
	Level 3	1.24 (1.10-1.39)	1.19 (1.04-1.37)	1.33 (1.10-1.61)	1.14 (1.07-1.22)	1.15 (1.08-1.24)	1.27 (1.15-1.41)
NO	Level 1	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
	Level 2	0.81 (0.71-0.92)	0.88 (0-76-1.03)	0.96 (0.81-1.13)	0.86 (0.80-0.92)	0.84 (0.77-0.90)	0.88 (0.81-0.95)
	Level 3	0.98 (0.87-1.10)	1.13 (0.97-1.31)	0.90 (0.70-1.17)	0.96 (0.90-1.02)	0.96 (0.89-1.04)	0.85 (0.74-0.97)
PM10	Level 1	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
	Level 2	0.82 (0.72-0.94)	0.84 (0.72-0.99)	1.08 (0.75-1.55)	0.80 (0.75-0.86)	0.77 (0.71-0.84)	0.92 (0.75-1.12)
	Level 3	1.04 (0.91-1.18)	1.02 (0.88-1.19)	0.42 (0.22-0.81)	0.94 (0.88-1.01)	0.94 (0.87-1.02)	0.53 (0.38-0.75)
SO_2	Level 1	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
	Level 2	1.17 (1.03-1.34)	1.16 (1.01-1.34)	0.97 (0.68-1.39)	1.14 (1.07-1.22)	1.17 (1.09-1.26)	1.12 (0.93-1.36)
	Level 3	1.17 (1.03-1.32)	1..20 (1.02-1.40)	0.70 (0.27-1.81)	1.10 (1.03-1.17)	1.16 (1.07-1.26)	0.89 (0.53-1.48)

O_3, ozone; NO, nitrogen monoxide; PM10, particles of 10 micrometres in diameter or less; SO_2, sulphur dioxide.
95%CI, 95% Confidence Interval. ORc, crude Odds Ratio. Ref, reference value
$ORa_{1,}$ Odds Ratio adjusted for gender, mother's level of education, use of paracetamol in the first year of life and parental smoking.
$ORa_{2,}$ Odds Ratio adjusted by for gender, mother's level of education, use of paracetamol in the first year of life, parental smoking, mean annual temperature (ºC), mean annual precipitation (mm), mean relative humidity (%) and mean annual number of sunny hours (%) (data from the Spanish National Institute of Meteorology). Level 1, percentiles 0-25; level 2, percentiles 26-74; level 3, percentiles 75-100.

For example, a study carried out by Marco et al (2002) into asthma showed how climate intervened in the association between asthma and pollution.[38] In other studies, the annual number of hours of sunshine appeared to be a protector factor against AE, which corroborated the need to take this variable into account .[39] Different studies have analysed the relationship between climate and AE, and shown that even the month of a child's birth may influence the appearance of AE.[6] Other studies have shown how AE patients' symptoms improved when they moved to a different climate area.[40] Finally, a recent study has shown an association between AE prevalence and relative humidity.[13]

One of the strong points of this study is that it offers good statistical power and high participation rates.[13] The ISAAC Study questionnaires used in our research have been validated in several countries and in various languages, which eliminates problems when making comparisons with other regions.[14,15]

However, limitations with ecological studies are well-known; in particular, an association at the geographical area level may be due to complex biases and it may not be possible to apply it individually.[30] Therefore, this study is limited by lack of accurate exposure estimations and we should deduce the relationships carefully.

In conclusion, this work shows that exposure to NO, PM10 and SO_2 does not seem to increase the overall prevalence of diagnosed AE and its symptoms (rashes). Nonetheless, exposure to O_3 might be related to an increased prevalence in both diagnosed AE and its symptoms. Future studies of exposure to O_3 and its relationship with allergic diseases should be conducted in an attempt to prevent it. As our sample is homogeneous in population, lifestyles and other environmental factors terms, and because we have included several climate variables, this work could prove to be a good model to continue research on a matter that not only affects a considerable number of schoolchildren, but also leads to high morbidity.

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