



Cluster analysis of indoor environmental factors associated with symptoms of mite allergy



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ABSTRACT

Background: The clinical efficacy of controlling environmental allergens as a component of allergic asthma treatment remains controversial. Multifaceted allergen reductions appeared to be the most efficient methods. However, they require home visits with indoor technicians.

Objective: To examine the characteristics of indoor environments that might be related to symptoms of children and adult patients with mite allergic rhinitis and/or asthma.

Methods: We included 315 patients allergic to house dust mites with rhinitis and/or asthma who had been visited at home by 2 medical indoor environment counselors (MIECs) from the Strasbourg University Hospital between January 2007 and June 2015. In a cluster analysis, we analyzed 42 characteristics of respiratory symptoms, dwelling characteristics, and indoor pollutants in this population.

Results: Three clusters were defined among the patients. Cluster 1 included 55 patients, all with rhinitis, 32% with asthma, and all living in an urban area. Clusters 2 and 3 included 86 and 174 patients, respectively. The important factors in these 2 clusters were asthma incidence and exposure to different indoor pollutants, such as indoor perfumes, cleaning products, and tobacco smoke.

Conclusion: Our results underlined the variability of indoor environments and the importance of MIEC home visits to investigate individual patient environments and propose an appropriate avoidance management plan. Our results showed that sensitization to mite and exposure to indoor chemical pollutants were associated with severe asthma.

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Introduction

In some guidelines, environmental allergen control comprises an important treatment for allergic asthma.^{1,2} This recommendation has been discussed in other studies^{3,4} based on a meta-analysis by Gøtzsche.^{5,6} However, the most recent meta-analysis did not include 2 multifaceted allergen-reduction studies, as pointed out by several authors.^{7,8} In the 4 studies^{9–12} that were not included in the meta-analysis by Gøtzsche,^{5,6} global allergen reduction was demonstrated to be effective for reducing allergen exposure and for improving clinical outcomes of children with moderate to severe asthma. More recently, a new study confirmed the clinical efficacy of allergen reduction with mite-impermeable bedcovers for children with allergic asthma¹³ as underlined in a

recent review by Wilson and Platt-Mills.¹⁴ To perform multifaceted allergen reductions, indoor technicians are required. Recently, this new occupation has been recognized as cost-effective, and health insurance companies in the United States will reimburse patients for this service.¹⁵ In France, the effect of indoor technicians has been perceived as positive by patients and physicians.¹⁶ However, it remains difficult to define precisely the appropriate phenotypes of patients who are most likely to receive the greatest clinical benefit from global indoor pollutant reduction.¹⁷ We reasoned that candidate asthma phenotypes might be identified with a cluster analysis.^{18,19} In addition, we were interested in studying the indoor environments of adults and children with the same medical diagnosis. In the present study, we aimed to describe the characteristics of indoor environments of children and adult patients with mite allergy-related rhinitis and/or asthma and to determine the associations between these environmental characteristics and allergy symptoms. To that end, we performed a cluster analysis.

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Methods

Patients

We included patients allergic to house dust mites who had rhinitis and/or asthma and had received a home visit from 2 medical indoor environment counselors (MIECs) from Strasbourg University Hospital between January 2007 and June 2015. Dust mite sensitization was defined as a positive response to a skin prick test (Stallergenes or ALK) with a mean wheal diameter of 3 mm or greater compared with the negative control and/or a specific IgE response to *Dermatophagoides pteronyssinus* greater than 0.35 KU/L (Thermo Fisher, Upsala, Sweden). All common aeroallergen skin tests were performed with Stallergenes or ALK extracts.

The MIECs were from the Chest Diseases Department of the Strasbourg University Hospital. Physicians (general practitioners, allergists, pulmonologists, pediatricians) from all parts of the Alsace area referred patients to the MIECs. The MIECs performed a home visit and completed a standardized home exposure evaluation.²⁰ The MIECs carefully recorded different information concerning use of candles, incense, essential oils, and/or fragrance diffuser. Cleaning products were reported, especially if they contained quaternary ammoniums. Recent painting work (sometimes the paint was still visible MIEC could be obtained information on the COV's content). We also reported if new furniture was bought during the last 12 months. When necessary, indoor allergens were measured in the dust with a home test (Acarex-test or Acari-test) or with an enzyme-linked immunosorbent assay monoclonal antibody test specific to Der p 1 or Fel d 1 (Indoor Biotechnologies, Charlottesville, Virginia). The physicians who had requested the home visit provided the MIECs with medical information about the patients. After the visit, the MIECs sent a report to the patient's physician.

Cluster Analysis Variables

To identify clustering in this population, we analyzed 42 characteristics, including age, sex, number of rooms in the house, number of residents, dwelling location (urban areas ≥ 5000 inhabitants and rural areas < 5000 inhabitants), type of housing (apartment, house, public housing), type of heating (wood, gas, electric, central heating, supplementary heating), ventilation, and house and environment exposure factors (cockroach, rodent, pet, mold, plants, indoor perfume, candles, essential oils, cleaning products, passive and active smokers, insecticide, dog, cat, stuffed animals, carpet, and new furniture). The asthma diagnosis and severity were based on the Global Initiative for Asthma (GINA) guidelines 2016⁴ and the presence or absence of rhinitis; rhinitis severity was based on the Allergic Rhinitis and Its Impact on Asthma guidelines.³ Polysensitization was defined as positive skin test results to more than 3 common aeroallergens. All clinical information was reviewed by a single physician to avoid discrepancies in the diagnosis and evaluations of asthma and/or rhinitis severity.

Statistical Analysis

Data were described and analyzed with R, version 3.2.2 (R Core Team; www.R-project.org/). The demographic, clinical, and environmental characteristics of patients were analyzed with a multiple correspondence analysis (FactoMineR package). Incomplete continuous and categorical data were imputed based on a factorial analysis for mixed data (missMDA package). Hierarchical clustering analysis was then performed with factorial analysis for mixed data transformed data. Intercluster comparisons were performed with nonparametric statistics; we used the Wilcoxon test for continuous variables and the Fisher exact test for categorical variables.

Table 1
Patient Characteristics^a

Characteristic	Children	Adults	All participants
Total	137 (43.5)	178 (56.5)	315 (100)
Age, mean (range), y	9.6 (2–17)	39.3 (18–78)	26.3 (2–78)
Male	83 (60.6)	78 (43.8)	161 (51.1)
Rhinitis	89 (64.9)	100 (56.2)	189 (60.0)
Asthma and rhinitis	50 (36.4)	61 (34.2)	111 (35.2)
Asthma	98 (71.5)	136 (76.4)	234 (74.2)
Step 1 ^b	20 (14.6)	16 (8.9)	36 (11.4)
Step 2 ^b	18 (13.1)	18 (10.1)	36 (11.4)
Step 3 ^b	28 (20.4)	22 (12.3)	50 (15.9)
Step 4 ^b	28 (20.4)	69 (38.8)	97 (30.8)
Step 5 ^b	0 (0)	7 (3.9)	7 (0.2)

^aData are presented as number (percentage) of patients unless otherwise indicated.

^bAccording to the 2016 Global Initiative for Asthma guidelines.

Results

Patient Characteristics

A total of 1307 MIEC visits were performed during the study period. On the basis of those visits, we identified 698 patients who were allergic to house dust mites. Among those patients, 315 had complete clinical and environmental information for the analysis, and they were included in the study. All these patients were allergic to house dust mites and had asthma, rhinitis, or both. A total of 126 patients (40%) only had asthma. Patient characteristics are given in Table 1.

Cluster Analysis

We used a cluster analysis approach to identify distinct clusters of patients with dust mite allergies. A dendrogram was generated based on the different variables described above. Three distinct clusters were identified that centered on allergic symptoms, house conditions, and allergen exposure (Table 2, Table 3, and Table 4).

Cluster 1: Urban Patients With Rhinitis

Cluster 1 included 55 patients. All had rhinitis, and 32% had asthma. All lived in an urban area. Among these patients, rhinitis was significantly more severe and polysensitization was less prevalent than among patients in other clusters. In the indoor environments, these patients were less frequently exposed to indoor chemicals and allergens (rodents, pets, dogs) than patients in other clusters. Among the 32% with asthma, the asthma was less severe than among patients in other clusters.

Cluster 2: Patients in Rural Areas

Cluster 2 included 86 patients. Of these, 65% lived in rural areas and 87% lived in a house with mostly natural ventilation and wood heating. A total of 60% were polysensitized, 80% had asthma, and,

Table 2
Patients Characteristics According to Domestic Environment^a

Characteristic	Cluster 1	Cluster 2	Cluster 3	Total	P value
Patients	55	86	174	315	
Men	26 (47.3)	48 (55.8)	87 (50)	161	.54
Mean age, y	25.7	26.5	26.5	26.4	.95
Asthma	18 (32.7)	69 (80.2)	150 (86.2)	237 (75.2)	<.001
Asthma step 1 ^b	9 (16.3)	7 (8.1)	23 (13.2)	39 (12.4)	
Asthma step 2 ^b	5 (9.1)	8 (9.3)	24 (13.8)	37 (11.7)	
Asthma step 3 ^b	3 (5.4)	23 (26.7)	26 (14.9)	52 (16.5)	
Asthma step 4 ^b	1 (1.8)	30 (34.9)	71 (40.8)	102 (32.4)	
Asthma step 5 ^b	0 (0)	1 (1.2)	6 (3.4)	7 (2.2)	
Rhinitis	55 (100)	62 (72.1%)	72 (41.4%)	174 (55%)	.0005
Polysensitization	20 (36.4)	52 (60.5%)	94 (54%)	166 (52%)	.02

^aData are presented as number (percentage) of patients unless otherwise indicated.

^bAccording to the 2016 Global Initiative for Asthma guidelines.

Table 3
Results of Cluster Analysis According to Housing Characteristics^a

Characteristic	Cluster 1	Cluster 2	Cluster 3	Total	P value
Country	0 (0)	56 (65.1)	22 (12.6)	78 (24.8)	<.001
Urban	55 (100)	30 (34.9)	152 (87.4)	237 (75.2)	<.001
House	2 (3.6)	75 (87.2)	31 (17.8)	108 (34.3)	<.001
Flat	37 (67.3)	11 (12.8)	102 (58.6)	150 (47.6)	<.001
Social housing	17 (30.9)	1 (1.2)	41 (23.6)	59 (18.7)	<.001
No. of rooms	3.5	5.2	3.5	4	<.001
No. of occupants	3.6	3.9	3.2	3.5	<.001
Mechanical ventilation	33 (60)	30 (34.9)	92 (52.9)	155 (49.2)	.006
Natural ventilation	22 (40)	56 (65.1)	81 (46.5)	159 (50.5)	.006
Wood heating	1 (1.8)	36 (41.9)	3 (1.7)	40 (12.7)	<.001
Gas heating	30 (54.5)	30 (34.9)	88 (50.6)	148 (47)	.03
Electric heating	16 (29.1)	16 (18.6)	34 (19.5)	66 (20.9)	.26
Central heating	47 (85.5)	79 (91.9)	155 (89.1)	281 (89.2)	.53
Extra heating	0 (0)	0 (0)	7 (4)	7 (2.2)	.07

^aData are presented as number (percentage) of patients unless otherwise indicated.

among these patients, 36.1% had severe asthma (36.1% GINA step 4 or 5). These patients were more exposed to plants, stuffed animals, and essential oils than patients in other clusters.

Cluster 3: Urban Patients With Asthma

Cluster 3 was the largest group, with 174 patients. Of these, 86% had asthma and 54% were polysensitized. Asthma was particularly severe in this group (44.2% GINA step 4 or 5) and 87% lived in urban areas. Compared with patients in other clusters, they were more exposed to indoor chemical pollutants, such as indoor perfumes, cleaning products, insecticides, and tobacco smoke (active or passive).

Discussion

Indoor Allergen Exposure

Our study found that, among patients with the same medical diagnosis (mite allergy with rhinitis and/or asthma), different indoor environments could be distinguished that were related to phenotypic traits. Asthma was more frequent and more severe in clusters 2 and 3, which was particularly interesting because it highlighted a group of patients with more severe asthma who appeared to be more frequently exposed to indoor allergens. These results were consistent with those from studies on severe asthma.²¹ Indeed, mite sensitization was identified as a risk factor for asthma and asthma severity,^{22,23} in addition to exposure to cockroach allergen^{24,25} and dog or mold allergens.²⁶

Cluster 3 represented a group of urban patients who were particularly frequently exposed to indoor perfumes, cleaning products, and tobacco smoke (active or passive). These patients might have belonged to a population with low incomes, a condition known to be a risk factor.^{27,28} Indoor chemicals were more common in clusters 2 and 3. It was previously demonstrated that volatile organic compounds (VOCs) could have an adjuvant effect on mite-related symptoms. A previous experimental human study found that exposure to low levels of formaldehyde significantly enhanced bronchial responsiveness to mite allergen in patients with asthma who were sensitized to mites.²⁹ In epidemiologic studies,^{30,31} exposure to VOCs may cause asthma-like symptoms and increase the risk of childhood asthma. However, a meta-analysis that investigated the direct role of VOCs on the occurrence of asthma did not provide conclusive results.³² In a recent study of inner-city children with asthma, concomitant exposure to allergen, chemicals (nitrogen dioxide, nicotine), and endotoxin had different effects, according to their indoor concentrations. That study emphasized the cocktail effect of these pollutants on asthma severity.³³ Interestingly, the present study found that patients more

Table 4
Results of Cluster Analysis According to Indoor Pollutants

Pollutant	No. (%) of patients				P value
	Cluster 1	Cluster 2	Cluster 3	Total	
Cockroach	0 (0)	0 (0)	10 (5.8)	10 (3.2)	.01
Rodents	0 (0)	13 (15.1)	22 (12.6)	35 (11.1)	.004
Pets	6 (10.9)	45 (52.3)	57 (32.8)	108 (34.3)	<.001
Stuffed animals	6 (10.9)	28 (32.6)	30 (17.2)	64 (20.3)	.003
Carpet	49 (89.1)	70 (81.4)	157 (90.2)	276 (87.6)	.12
Plants	23 (41.8)	57 (66.3)	71 (40.8)	151 (47.9)	<.001
Indoor perfume	4 (7.3)	7 (8.1)	31 (17.8)	42 (13.3)	.04
Essential oil	3 (5.4)	18 (20.9)	7 (4)	28 (8.9)	<.001
Candles	7 (12.7)	16 (18.6)	26 (14.9)	49 (15.6)	.63
Cleaning products	0 (0)	1 (1.2)	14 (8.1)	15 (4.8)	.009
Current smoker	3 (5.4)	0 (0)	20 (11.5)	23 (7.3)	.001
Passive smoker	8 (14.6)	11 (12.8)	58 (33.3)	77 (24.4)	.001
Insecticides	0 (0)	1 (1.2)	14 (8.1)	15 (4.8)	.008
Painting housework	12 (21.8)	26 (30.2)	38 (21.8)	76 (24.1)	.29
New furniture	1 (1.8)	7 (8.1)	17 (9.8)	25 (7.9)	.14
Mold	3 (5.4)	12 (13.9)	14 (8.1)	29 (9.2)	.21
Dog	3 (5.4)	17 (19.8)	40 (23)	60 (19.1)	.01
Cat	7 (12.7)	23 (26.7)	48 (27.6)	78 (24.8)	.07
Pollen	0 (0)	2 (2.3)	13 (7.5)	15 (4.8)	.03

exposed to cleaning products, perfumes, or essential oils (clusters 2 and 3) had a higher prevalence of asthma. We recently found that the use of a spray of multiple essential oils increased the total VOC levels to 25 mg/m³ in a standard room, which was far above the European norms.³⁴

Home Visit

Our study demonstrated the importance of home visits for patients with allergies who were sensitized to mites. Among patients with the same medical diagnosis (dust mite allergy), we found different categories of indoor environments. This finding suggested that recommendations for reducing indoor pollution given by an allergist during an outpatient visit could not provide sufficiently precise advice for patients. However, several years ago, a published study stated that American allergists were not able to perform visits at patient dwellings.³⁵ Moreover, although allergen avoidance is an intuitive strategy, it has not been easy to obtain evidence of strong efficacy in adults; thus, this strategy remains a subject of controversy.^{5,6,36} However, home visits with indoor technicians could inform patients about ways to reduce allergens globally. Indeed, several studies in children with allergic asthma found that a multifaceted home-based intervention aimed at reducing allergen exposure had beneficial effects on asthma.^{9–12} Moreover, the efficacy of allergen reduction in children with asthma appeared to be confirmed in recent studies.^{13,37} Thus, recently, emerging payment approaches by insurance companies in some places of the United States offer new potential for coverage of home-based environmental intervention costs.¹⁵

Limitations

The main limitations of this study were its monocentric, retrospective nature and the fact that we could not include 50% of patients with known mite allergies. The major reason for patient exclusion was the lack of complete clinical information (particularly an asthma classification). We confirmed that there was no center or specialist effect. Accordingly, we assumed that it was unlikely that the patient characteristics were significantly different between those excluded and those studied. Another limitation was that the exposure data were obtained only with a questionnaire, not through direct quantification of VOCs or other chemicals exposure. However, the 2 MIECs that collected data had specific qualifications for performing home visits. They were well-trained professionals

with more than 10 years of experience, which gave credibility to the information. Moreover, it would have been interesting to obtain information about exposure at school for children because it has been demonstrated that the school environment could also be an important contributor to childhood asthma morbidity.³⁸

Conclusion

The results of this study demonstrated the importance of home visits with an indoor technician in identifying allergens for patients with mite allergies. Our findings emphasized that different patients with the same medical diagnosis of mite allergy might live in different indoor environments. Our results suggested that a mite sensitization combined with chemical exposure was highly associated with severe asthma. In contrast, rhinitis was more frequently associated with mite sensitization combined with mite exposure and less frequently associated with cofactors. These findings suggest that, among patients with asthma who are sensitized to mites, it is important to take into account indoor chemicals in the environment, such as VOC.

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