

Medication requirements and house dust mite exposure in mite-sensitive asthmatics

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To better understand the clinical consequences of exposure to house dust mites (HDM), we investigated the relationship between treatment requirements to control symptoms in mite-allergic asthmatic patients and HDM-allergenic levels in their mattresses. This study included 49 asthmatic subjects recruited from an outpatient clinic. The protocol consisted of a questionnaire about the number of asthma attacks and treatment requirements in the last 3 months. Patients provided a sample of house dust collected from their mattresses by a standardized vacuum cleaning procedure. Mean antigen P1 equivalent defined as the sum of major allergens Der pI and Der pII (Ag P1 Eq) level was 1.34 µg/g dust in patients who had no treatment, 5.4 µg/g dust in patients who took puffs of beta₂-agonists only when required and 17.3 µg/g dust in patients who required daily long-term treatment. Similar relationships were demonstrated between mean Ag P1 Eq levels and the number of asthma attacks. These data support the clinical role of allergenic exposure in HDM-allergic asthmatics.

Key words: asthma, environment, house-dust mites, risk factor

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Although most asthmatic patients have positive skin tests to house dust mites (HDM) in childhood and early adulthood (12), a causal relationship between HDM and asthma is difficult to establish for two reasons. The first is that a tenth to a third of the general population exhibits positive skin tests to HDM without ever developing allergic symptoms or asthma (1, 2, 3). The second is that identification of HDM-induced symptoms from a questionnaire is difficult (8). Nevertheless, to decide whether environmental measures should be implemented to control mite infestation, a better understanding of the role of HDM exposure in disease is necessary. Previous reports suggest that a level of antigen P1 equivalent (Ag P1 Eq), sum of Der pI and Der pII, higher than 10 µg/g house dust enhances the risk of allergic reactions in

mite-sensitive patients (10, 11, 12). Further work is needed to quantify the exact levels at which the major mite allergens trigger clinical symptoms in allergic patients. The amount of treatment required in sensitized asthmatics may be a reliable indicator of the clinical effects of mite exposure. To explore this possibility, we studied the relationship between the treatment needed to control symptoms in mite allergic asthmatics and the HDM-allergenic level (P1 Eq) in their mattresses.

METHODS

The study comprised 49 outpatients who came to our allergy clinic in Marseille, France, from October 1987 to April 1988. Marseille is located on the French Mediterranean coast where the

mean relative humidity between 1985 and 1989 was $79.0 \pm 8.3\%$. There were 28 males and 21 females with a mean age ($\pm$ SD) of 28.7 ± 14.9 years. In all patients asthma had been diagnosed by the subject's personal physician and confirmed by spirometry showing at least a 15% reversal of bronchial obstruction (Vitalograph Ltd, Birmingham, England) either spontaneously or after inhaled beta-agonists (200 μ g salbutamol). All patients had positive skin prick test to *Dermatophagoides pteronyssinus*. Skin prick tests were performed with the same batch of a standardized extract that gives a mean wheal diameter of 6 mm in an allergic population (100 reactivity units extract, Stallergènes, Paris, France). A test was considered positive if within 15 min it induced a wheal greater than half the diameter of the positive control test and larger than the negative control test. Positive control tests were done with codeine phosphate 9% which provides a mean wheal diameter equal to 6 mm. Negative control was obtained with a saline solution. Responses to other allergenic extracts (cat dander, dog dander, grass and Parietara pollens) were also recorded. Patients with a positive skin test to cat or dog dander were excluded if they had either pet at home. We also excluded patients who exhibited symptoms of upper or lower respiratory infections in the previous month.

The study protocol consisted of a standardized questionnaire and a sampling of house dust from the mattress. In the questionnaire, the patient was asked to evaluate the number of asthmatic episodes and the treatment required in the last 3 months. The score was 0 if the patient had no attacks during the 3 months, 1 if he had less than one attack/month, 2 if he had less than one attack/week and more than one/month and 3 if he had more than one attack/week. Treatment was classified into 3 categories, i.e.: "no treatment", "inhalation of a β_2 -agonist spray as needed" and "long-term daily treatment" using any one or combination of the following: bronchodilators, local corticosteroids, cromoglycate sprays, ketotifen or corticosteroid tablets. House dust samples were obtained by a standardized (2 min/m² of surface area) vacuum cleaning of the whole upper sur-

face of the mattress. Samples containing less than 100 mg of house dust were discarded. All samples were sieved through a 0.3 mm mesh screen to obtain fine dust and stored in sealed paper bags at 4°C until processing by a slightly modified version of the two-site ELISA technique described by Luczynska et al. (7).

Microtiter plates coated with Der pI- and Der fI-specific monoclonal antibodies were incubated with house dust extracts and bound antigen was detected with a second biotinylated monoclonal antibody recognizing another epitope common to Der pI and Der fI. The monoclonal antibodies were provided by MD Chapman and TAE Platts-Mills (Charlottesville, VA, USA). Their production and characterization have been previously described (9, 11). After addition of an enzyme-substrate system (streptavidine peroxidase plus ortho-phenyl-diamine), the concentration of Der pI and Der fI was obtained by comparison of the optical density read at 492 nm on samples and a standard curve. The results were expressed in terms of micrograms (μ g) of antigen P1 equivalent (Ag P1 Eq), defined as the sum of major allergens Der pI and Der fI, per gram of house dust (g house dust). Evaluation of severity on the basis of treatment and incidence of asthma attacks was done before analysis of house dust samples.

For statistical analysis ELISA results were transformed into their decimal logarithm counterparts in order to normalize distribution. Mean values and their standard deviation were computed from these transformed values. Comparison of mean values was achieved by analysis of variance and comparison of groups by the Newman-Keuls procedure (6). For the sake of clarity, mean Ag P1 Eq values provided in Results are geometric means, i.e. means of logarithmic values retransformed into standard values.

RESULTS

Ag P1 Eq in mattresses and occurrence of asthma attacks

In the 12 patients reporting no attack in the last 3 months (score 0), the geometric mean of Ag

P1 Eq was 1.4 µg/g, i.e. less than 2 µg/g house dust. In 15 patients reporting occasional asthma attacks (score 1), the mean level was 9 µg/g. In the 22 patients reporting more than one attack per month (scores 2 and 3), the mean level of P1 Eq was high, over 10 µg/g house dust. The difference in mean Ag P1 Eq level between score 0 and score 1 and between score 1 and score 2 was significant ($P < 0.01$). No significant difference was found between score 2 and score 3 (Table 1). The season during which the dust mite samples were obtained was comparable in the four subgroups.

Ag P1 Eq in mattresses and treatment scores

As shown in Fig. 1 there were large individual differences in each subgroup. However, in 11 of the 12 patients who used no treatment, the concentration of Ag P1 Eq was < 10 µg/g. In eight of these patients, Ag P1 Eq values were < 2 µg/g. In 18 of the 22 patients requiring long-term daily treatment, the concentrations of P1 Eq were > 10 µg/g. Only two of these patients had values < 2 µg/g. Wide variation in Ag P1 Eq concentrations were observed in the 15 patients who occasionally used a beta₂-agonist spray. As shown in Table 2, the geometric means of P1 Eq concentration were statistically different among all three groups. Mean values were < 2 µg/g in the "no treatment" group, between 2 and 10 µg/g in "occasional beta₂" group and > 10 µg/g in the "long-term treatment" group.

Table 1.

Relationship between symptoms and P1 Eq level (sum of Der p1 and Der p2) in mattresses

Symptom score	Ag P1 Eq (µg/g house dust) Geometric means (95% confidence interval)
0 ($n = 12$)	1.4 (0.58-3.39) **
1 ($n = 15$)	9.06 (4.06-20.4) **
2 ($n = 12$)	14.09 (5.9-33.11) NS
3 ($n = 10$)	13.49 (4.3-45.6)

(** $P \leq 0.01$; *** $P \leq 0.001$)

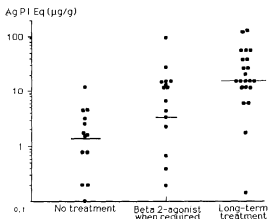


Fig. 1. Distribution of individual Ag P1 Eq levels (defined as the sum of major allergens Der p1 and Der p2) in house dust from mattresses according to the treatment required. Each patient is represented by a single dot. The horizontal bars represent the mean level computed in each group.

DISCUSSION

Up to now the clinical consequences of mite allergens in sensitized asthmatics have been assessed by studying the relationship between household Ag P1 and respiratory symptoms. Traditionally, mite-allergen levels in house dust have been determined by counting mite bodies under light microscopy. Voorhorst et al. (15), who performed numerous mite counts in Holland, considered counts of > 500 mites/g to be associated with a high risk of developing allergic symptoms. In 1983, Korsgaard (4) showed that

Table 2.

Relationship between treatment score and P1 Eq level (sum of Der p1 and Der p2) in mattresses

Treatment for asthma	Ag P1 Eq (µg/g house dust) Geometric mean (95% confidence interval)
No treatment ($n = 12$)	1.34 (0.59-3.05) **
β ₂ -agonist spray when required ($n = 15$)	5.37 (2.35-12.27) **
Long-term treatment ($n = 22$)	17.8 (10.38-30.48)

(** $P \leq 0.01$; *** $P \leq 0.001$)

mite counts in the homes (mattress surfaces and floors in bedrooms and living room) of 25 patients with newly-diagnosed house dust mite asthma were much greater than that in the homes of 75 randomly selected matched control subjects. He reported the relative risk of asthma associated with at least 100 mites/g of house dust (i.e. approx 2 µg Ag P1 Eq/g) to be 6.8.

In vitro assays of the allergen content of house dust extract provide a more practical and meaningful method of assessing mite-allergen exposure. Using this approach, a number of authors have presented strong evidence implicating mite allergens in the onset of asthma. The Charlottesville group has suggested that 2 µg of Ag P1 Eq/g of dust carries a risk of sensitization (presence of serum specific IgE against HDM) and that 10 µg increases the risk of asthma attacks in sensitized asthmatics (5, 10, 11, 13, 14). Platts-Mills (10) et al. demonstrated that 16 of 23 HDM-sensitive asthmatics requiring emergency room treatment had Ag P1 Eq levels over 10 µg/g of dust in their bedrooms and living rooms. In another report, Platts-Mills (11) studied seven asthmatics with allergy to HDM and perennial symptoms necessitating emergency room treatment 18 times during the course of study. On 16 of 18 of these occasions, allergenic dust evaluation demonstrated Ag P1 levels above 10 µg/g dust. Rowntree et al. (13) evaluated a group of 92 atopic children and showed that all children with specific serum IgE against HDM had mite concentrations above 2 µg/g dust on their bedroom floors. Similarly, Smith et al. (14) studied 20 asthmatic children allergic to HDM and showed that 17 of them had at least 10 µg/g of dust in either beds, bedroom floor or television room. Recently, Lau et al. (5) claimed that a P1 Eq level > 2 µg/g dust significantly increases the risk for sensitization in atopic children and that a level > 10 µg/g dust constitutes a very high risk.

Our results (Tables 1, 2 and Fig. 1) confirm these previous data. The degree of indoor pollution, i.e. the level of natural allergenic exposure in sensitized patients seems a particularly important factor. We excluded dander-sensitive asthmatics with pets and performed the study outside the grass pollen season in order to mini-

mize the possible role of other main aero-allergens. In our study most sensitized patients with no symptoms (score 0) and no treatment had P1 Eq levels below 10 µg/g house dust, with a geometric mean < 2 µg/g. Most patients with frequent asthma attacks and daily treatment had P1 Eq values over 10 µg/g with a geometric mean around 15 µg/g.

Several other factors could influence the severity of asthma, such as individual specific and non-specific bronchial hyperreactivity, degree of sensitization, compliance and efficacy of treatment. It is nevertheless interesting to observe how closely our data fit with previous findings. This may indicate that a level above 10 µg/g house dust in mattresses constitutes a serious risk factor for sustaining asthma symptoms in HDM-sensitive patients.

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