
Sensitization to cat allergens in non-cat owner patients with respiratory allergy

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Background: Cats represent one of the most important sources of indoor allergens. The sensitization rate can reach up to 60% in western countries. Keeping cats indoors is uncommon in big cities in Turkey, but cats living in the streets are common.

Objective: To investigate the prevalence of sensitization to cats in patients with respiratory allergy from Izmir, Turkey, and its relationship to home cat allergen levels.

Methods: A total of 387 patients (70.8% female; mean age, 34.3 years) with respiratory allergic diseases (rhinitis and/or asthma) were included in this study. Skin prick test to cat was performed. House dust samples were collected from the living room of 25 patients and 14 healthy subjects. The major cat allergen (Fel d 1) levels were measured by Dustscreen. Fel d 1 levels given by the manufacturer were as follows: 0.05, 0.13, 0.40, 1.1, and 6.2 mU/mL.

Results: The prevalence of cat sensitivity was 44.7% (n = 173). Only 6 patients (1.6%) had a history of feeding a cat in their houses. Thirty-six (92%) of 39 houses had detectable levels of cat allergen (mean Fel d 1 level, 2.24 ± 2.69 mU/mL). The mean Fel d 1 levels were 1.58 ± 2.51 mU/mL in the healthy group, 1.91 ± 2.61 mU/mL in the asthmatic group, and 3.26 ± 2.85 mU/mL in the group with allergic rhinitis ($P = 0.12$). The prevalence of cat sensitivity in patients who had 1.1 mU/mL of Fel d 1 in their homes was 57.1%. This rate was five times lower (11.1%) in patients who had the highest Fel d 1 level (6.2 mU/mL) in their homes.

Conclusions: The prevalence of cat sensitivity in Izmir, where cats are generally not kept within homes, is as high as in western countries. The sampled houses have measurable levels of Fel d 1 even in the absence of indoor cats. High prevalence of cat sensitivity in Izmir is probably due to indirect exposure.

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INTRODUCTION

Cat allergens represent an important risk factor for allergic respiratory diseases.^{1–4} It is estimated that 60% to 70% of houses in western countries have pets.¹ Exposure to cat allergen can cause sensitization in up to 60% of atopic individuals and is responsible for acute asthma attacks and bronchial hyperresponsiveness.^{5–9} Cat and dog allergens are commonly present in homes without pets, and it is possible that the exposure that occurs at home, even if no animal is present, may be sufficient to induce sensitization in susceptible individuals.¹⁰ It is not usual to keep pets in houses in big cities in Turkey, but cats living in the streets are common. Data on the prevalence of cat sensitivity in adults with respiratory allergy are not available from Izmir, Turkey. Therefore, we investigated the prevalence of sensitization to cats in patients with respiratory allergy and its relationship with home cat allergen levels.

MATERIALS AND METHODS

Participants

A total of 676 patients attending our outpatient clinic in Izmir, Turkey, between June 2000 and June 2001 were considered for the study. Of these patients, 387 (57.2%; 274

female [70.8%]) had allergic rhinitis and/or allergic asthma and also fulfilled the study criteria and were therefore included in the study. The mean age of the patients was 34.3 years (range, 14 to 59 years). After informed consent was obtained, the prevalence of positive skin test results to cat and other indoor allergens, such as house dust mite, dog dander, cockroach, and aspergillus, was determined in this population.

Subject Selection

Subjects were evaluated by a standard history, including cat presence in the home and physical examination. Subjects were included for the study if they met the following criteria: male or nonpregnant female older than 14 years, history of allergic rhinitis and/or allergic asthma for at least 12 months' duration, residence in Izmir for at least the past 2 years, the ability to withhold all antihistaminic medications for at least 5 days, and physical examination consistent with allergic rhinitis and/or asthma. Individuals were excluded from the study if they were receiving antihistamines, β -blockers, tricyclic antidepressants, or long-term high-dosage corticosteroids (more than 30 mg/d of prednisone or equivalent for longer than 2 weeks).

Skin Testing

Skin prick tests were performed with cat dander (Fel d 1) and other indoor allergens, such as *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, dog dander (Can f 1), cockroach (*Blattella germanica*), and aspergillus (Stallergenes, Antony Cedex, France). Histamine phosphate (10-

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mg/mL histamine base) was the positive control and glycerinated saline the negative control. To prevent cross-reactivity between cats and dogs due to albumin, we used albumin-free skin prick test solutions.

The prick puncture method used a lancet for epicutaneous testing with the forearm as a skin test site. Each test was separated by approximately 3 cm. Tests were interpreted at 20 minutes. A wheal diameter at least 3 mm greater than the negative control was considered a positive response.

Dust Samples

Due to the economic limitations, we could only collect a limited number of dust samples. We called back every 11th patient regardless of his or her status of cat sensitivity. Twenty-five (71%) of 35 patients agreed and collected dust samples from July 2001 to September 2001. We also obtained dust samples from 14 healthy subjects without allergic disorder. In 36 of these homes, cats had never been kept, but cats were kept in 3 of 39 homes. House dust samples were collected using a standardized technique from an area of 1 m² of the living room with a 1200-W, filtered vacuum cleaner. The allergen was extracted from the filter by introducing 10 mL of extraction buffer. After incubation for 15 minutes at room temperature, 1 mL of clean dust solution was removed for the test. The major cat allergen (Fel d 1) levels were determined by Dustscreen (CMG-Heska, Fribourg, Switzerland). Dustscreen uses a nitrocellulose-polyvinyl chloride strip with a positive and negative control and dot areas for the major cat allergen (Fel d 1) and other indoor allergens. The test strip was incubated in an incubation chamber for 1 hour with 1 mL of the supernatant of dust extraction, which was prepared according to the manufacturer's directions. After the washing procedure, 1 mL of the second horseradish peroxidase-labeled antibody was added, and the mixtures were incubated for 2 hours. After washing, 15 drops of chromogen and two drops of enzyme substrate were added, and the mixture was incubated for 15 minutes. After a washing procedure and 30 minutes of drying, a colored spot appeared, with the intensity of color reflecting the amount of allergen as determined by a comparison table (batch no. 991117/10). Fel d 1 levels given by the manufacturer were as follow: 0.05, 0.13, 0.40, 1.1, and 6.2 mU/mL (1 mU = 2 ng).

Analysis of Data

Results are given as mean $\pm$ SD for demographic data. All statistical analyses were performed using SPSS statistical software for Windows 9.05 (SPSS Inc, Chicago, IL). Pearson χ^2 test was used for comparison of frequencies between groups (eg, cat sensitive and insensitive). Odds ratios (ORs) with 95% confidence intervals (CIs) are also presented. The mean levels of Fel d 1 in houses of patients with or without respiratory allergies were compared by Kruskal-Wallis H test. Nonparametric tests (Mann-Whitney) were used for comparisons between cat-sensitive and -insensitive patients for mean Fel d 1 levels. $P < 0.05$ was considered statistically significant.

RESULTS

Only six patients (1.6%) had a history of feeding a cat in the house. These allergic cat owners were sensitive to cats. However, a group of 167 patients (96.5% of the cat-sensitive group) with no history of interaction with cats also had positive skin prick test results to cat antigen. The prevalence of cat sensitivity in this allergic population was 44.7% ($n = 173$). Characteristics of the patients are given in Table 1.

Asthma prevalence was 38.7% ($n = 67$) in cat-sensitive and 33.6% ($n = 72$) in cat-insensitive patients. Sensitivity to cat allergen was not associated with the risk of being asthmatic ($P = 0.34$; OR, 1.247; 95% CI, 0.821 to 1.892).

Sensitization to other indoor allergens was more frequently found among cat-sensitized subjects. More than half of the cat-sensitized patients were also sensitized to dog dander (61%), cockroach (54.8%), and *D. pteronyssinus* (53.8%) (Table 2).

Thirty-six (92%) of 39 houses had detectable levels of cat allergen (mean Fel d 1 level, 2.24 ± 2.69 mU/mL). The mean Fel d 1 levels were 1.58 ± 2.51 mU/mL in the healthy group, 1.92 ± 2.61 mU/mL in the asthmatic group, and 3.26 ± 2.85 mU/mL in the group with allergic rhinitis (Fig 1; $P = 0.12$).

Only 3 patients (1 with allergic rhinitis, 2 with allergic asthma) were keeping cats at home (8.8% of the patient group). The Fel d 1 level exceeded the maximum measurable concentration in the 2 samples measured, and both of these subjects were cat insensitive and asymptomatic during cat exposure. The other cat owner had 1.1 mU/mL of Fel d 1 in her house dust and a positive skin prick test result to cat. She experienced asthma when in the presence of a cat. Other patients reported that they had no contacts with cats. The mean Fel d 1 levels in houses with cats were higher than houses without cats (4.5 ± 2.94 mU/mL vs 2.12 ± 2.62 mU/mL). The statistical analysis was not performed because the number of patients having cats was not sufficient.

In the allergic population, the mean Fel d 1 level in houses of the cat-insensitive group ($n = 19$) was slightly higher than the cat-sensitive group ($n = 6$; 2.86 ± 2.94 vs mU/mL 1.83 ± 2.15 mU/mL, $P = .87$). The prevalence of cat sensitivity in patients who had 1.1 mU/mL of Fel d 1 in home was 57.1%. This rate was five times lower (11.1%) in patients who had 6.2 mU/mL of Fel d 1 in their homes (Fig 2).

DISCUSSION

In this study, we investigated the prevalence of sensitization to cat dander in adult allergic patients who attended our

Table 1. Patient Characteristics

Characteristic	Cat-sensitive patients (n = 173)	Cat-insensitive patients (n = 214)
Male, No. (%)	50 (28.9)	63 (29.4)
Female, No. (%)	123 (71.1)	151 (70.6)
Age, mean $\pm$ SD, y	33.3 $\pm$ 11.2	34.8 $\pm$ 9.9

Table 2. Patients with Positive Skin Prick Test Results to Indoor Allergens (n = 387)

Allergens	No. (%) of patients		P value*	OR (95% CI)
	Positive skin prick test result (n = 173)	Negative skin prick test result (n = 214)		
Mites†	98 (56.6)	91 (42.5)	0.006	1.766 (1.178–2.647)
<i>Dermatophagoides farinae</i>	72 (41.6)	76 (35.5)	0.25	1.294 (0.857–1.954)
<i>Dermatophagoides pteronyssinus</i>	93 (53.8)	84 (39.3)	0.006	1.799 (1.199–2.699)
Dog dander	105 (61)	21 (9.8)	<0.001	14.403 (8.354–24.833)
Cockroach	91 (54.8)	41 (20.1)	<0.001	4.824 (3.048–7.634)
Aspergillus	51 (29.5)	45 (21)	0.06	1.570 (0.988–2.496)

Abbreviations: CI, confidence interval; OR, odds ratio.

* Pearson χ^2 .

† Sensitivity to *D. farinae* and/or *D. pteronyssinus*.

outpatient clinic in Izmir, Turkey. The prevalence of sensitization to cat was 44.7%. Cat sensitivity rates are reported between 15 and 60% of atopic individuals in western countries,^{5–9} where it is estimated that 60 to 70% of households have pets.¹ In big cities in Turkey, indoor cats are not as common as in western countries. In our cohort, only 1.6% of 387 patients had cats in their houses. Although indoor cats are uncommon, cats living in the streets are common, and this may be the main cause of this high prevalence of cat sensitivity.

To investigate the cause of this relatively high prevalence of cat sensitivity, we collected dust samples from the houses of allergic and nonallergic subjects, with or without cats in their homes, and measured Fel d 1 levels with the Dustscreen assay, a method easier to perform and as satisfactory as enzyme-linked immunosorbent assay.¹¹ We found that 92.3% of houses had detectable cat allergens; this finding was independent of having an indoor cat. The small particle size of squamous cell fragments can explain why cat allergen can be

found almost everywhere, even in the absence of an indoor cat.¹² Many cat-allergic patients do not keep cats but nonetheless become sensitized through environmental exposure to cat allergen. Bollinger et al¹³ found detectable levels of Fel d 1 in all 37 homes with cats and in 38 of the 40 homes without cats. Ichikawa et al¹⁴ reported a 34% sensitization prevalence to cats in 394 patients who had never kept cats, a rate slightly lower than ours. Interestingly, sensitization to cat allergen occurred in Tristan da Cunha, an island where there are no cats.¹⁵ All these findings, including ours, suggest that indirect exposure to cat allergen in many homes without cats may be sufficient to sensitize atopic people and may be capable of inducing allergic symptoms.¹³ Our cat-sensitive patients who did not have indoor cats did not report past regular contacts with cats. So we do not know if these patients would have developed symptoms if they had contact with cats.

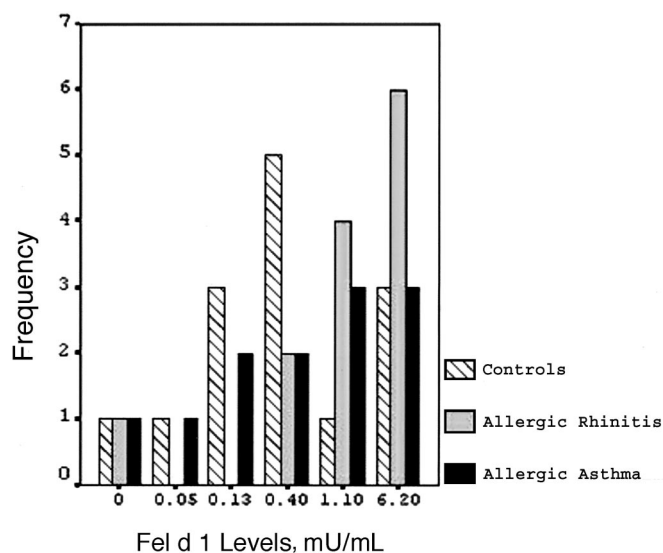


Figure 1. Fel d 1 levels in the houses of healthy controls and patients with allergic rhinitis and asthma. Home Fel d 1 levels in each group were comparable ($P = 0.12$).

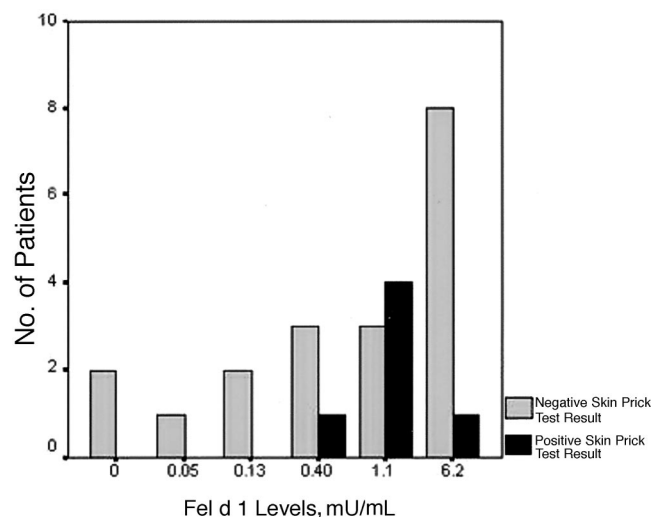


Figure 2. Home Fel d 1 levels in cat-sensitive and cat-insensitive patients. In allergic patients, Fel d 1 levels below 0.13 mU/mL were not associated with sensitization to cat. Most of the sensitized patients had 1.1 mU/mL of Fel d 1 in their homes. The sensitization rate was relatively lower in patients who had highest Fel d 1 levels in their homes.

Measures to reduce airborne allergen exposure for atopic patients (ie, removing cats from homes, washing them weekly, and minimizing surface areas such as carpeting and upholstered furniture to which cat allergen could attach)¹⁶ are recommended in homes with indoor pets. However, in a community where cats are not allowed indoors, the precautions that should be undertaken to reduce allergen level are unknown.

Dust mite allergens are associated in a dose-dependent manner with sensitization and respiratory symptoms such as rhinitis and asthma.^{17–19} However, subsequent studies suggest that, in contradistinction to what has previously been published, the avoidance of cat exposure in infancy does not prevent allergy in children, and early contact with cats may prevent allergy more effectively than avoidance.^{20–23} In our study, we found that the cat sensitization rate was the lowest in patients whose home Fel d 1 levels were below 0.40 mU/mL. The sensitization rate was also relatively low in patients who had highest Fel d 1 level in their homes (Fig 2). Two patients who had indoor cats with the highest level of Fel d 1 in their homes had neither symptoms with exposure to cats nor positive skin prick test results. Due to the small number of patients and inadequate information concerning exposure, we do not argue that cat exposure could lead to tolerance. Custovic et al²⁴ reported that the prevalence of sensitization to cats was decreased in the lowest and highest cat allergen exposure groups, and values in the midrange were associated with maximum prevalence of sensitization to cat. Indeed, extended and high-dose exposure to allergens can induce an increase in IgG4 antibodies with a decrease in IgE antibodies.^{25,26} Children exposed to greater than 20 µg of Fel d 1 per gram of house dust made an IgG and IgG4 antibody response to Fel d 1 without IgE antibody.²⁷ Because the expression of the gene for IgG4 can be induced by the Th₂ cytokine interleukin 4,²⁸ this modified Th₂ response could be regarded as a form of immunologic tolerance.²⁷

In our cohort, patients who tested positive for cat allergens did not have an increased risk for asthma. We also showed that sensitivity to cat allergens was associated with other indoor allergen sensitivities, such as dog, cockroach, and mite sensitivity, which might also contribute to the development of asthma (Table 1). Of all cat-sensitive patients, 61% were also positive for dogs. High rates of additional dog sensitivity in cat-sensitive patients may suggest the presence of cross-reactivity between these two allergenic sources. Albumin has been recognized as a relevant cross-reactive allergen between cats and dogs.²⁹ There are common and species-restricted IgE epitopes of the major cat and dog allergens that can be demonstrated by IgE inhibition studies.³⁰ Our skin prick test solutions do not contain albumin. However, we cannot rule out the effect of shared epitopes. On the other hand, dog allergens might be present in the dust samples from pet-free homes due to passive transfer from the outside and cat allergens.¹⁰ A sizable dog population is found on the streets of Izmir. Thus, both cross-reactivity and the generalized presence of dog allergens in the environment may explain the

increased prevalence of cosensitization in this group of Turkish patients with allergic respiratory disease.

In conclusion, the prevalence of cat sensitivity in Izmir, where cats are generally not kept within homes, is as high as in western countries. Most sampled houses have measurable levels of Fel d 1 even in the absence of indoor cats. The increased prevalence of cat sensitivity in Izmir is probably due to indirect exposure.

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