Ann Dermatol Vol. 30, No. 6, 2018
pISSN 1013-9087 · eISSN 2005-3894
https://doi.org/10.5021/ad.2018.30.6.662

ORIGINAL ARTICLE

Increasing Prevalence of the Sensitization to Cat/Dog Allergens in Korea

Bok Won Park, Jun Yeong Park, Eun Byul Cho, Eun Joo Park, Kwang Ho Kim, Kwang Joong Kim

Department of Dermatology, Hallym University Sacred Heart Hospital, College of Medicine, Hallym University, Anyang, Korea

Background: Recently, the number of domestic pets has increased. As a consequence, sensitization to animal allergens, such as cat or dog allergens, has become a problem. **Objective:** We studied the annual trends of sensitization to cats or dogs, and the characteristics of the patients. **Methods:** We retrospectively analyzed the medical records of 7,469 patients who visited a dermatology clinic and underwent an allergic profile test, from January 2011 to December 2015. Specific immunoglobulin E (IgE) levels to cat or dog antibody greater than 3.50 IU/ml were regarded as positive results. **Results:** In all, 274 patients showed significant increase in levels of specific IgE antibody to dog, and 307 revealed increase in levels of of specific IgE antibody to cat. The prevalence of these specific IgEs increased from 2011 to 2015. Independent risks for sensitization to cat allergens were sensitization to dog, but not to house dust, *Dermatophagoides pteronyssinus*, and *D. farinae*. Independent risks for sensitization to dog allergens were sensitization to cat, but not to house dust, *D. pteronyssinus*, and *D. farinae*. Total IgE level was not related to specific IgE level against either cats or dogs. **Conclusion:** In conclusion, the prevalence of sensitization to cat or dog has increased. Sensitization to cat or dog is related to each other, but is irrelevant to the total IgE level. **(Ann Dermatol 30(6) 662～667, 2018)**

Received March 15, 2018, Revised June 28, 2018, Accepted for publication July 10, 2018

Corresponding author: Kwang Ho Kim, Department of Dermatology, Hallym University Sacred Heart Hospital, 22 Gwanpyeong-ro 170beon-gil, Dongan-gu, Anyang 14068, Korea. Tel: 82-31-380-3765, Fax: 82-31-386-3761, E-mail: dermakkh@naver.com
ORCID: https://orcid.org/0000-0001-5315-6031

-Keywords-
Atopic dermatitis, Cat, Dog, Specific immunoglobulin E

INTRODUCTION

The prevalence of allergic diseases has increased over recent decades[1,2]. As furry pet ownership, especially of cat or dog, increases in Korea, sensitization to pet allergens from domestic exposure is an increasingly important issue. Indirect exposure as well as direct pet ownership can lead to sensitization to pet allergens and allergic disease. The risk of sensitization to pet allergen may be increased in people who do not own pets in areas with a high proportion of pet owners[3].

In a survey performed by Seoul Development Institute in 2004[4], 17.2% of families had pets in their house, and the dog ownership (16.6%) was notably higher than cat ownership (0.8%). Another survey collected by Korea pet food association[5], 28.8% of adults replied that they were having pets in their house, and the proportion of dog ownership was 22.7%, which was higher than that of cat ownership (5.6%). In Korea, as the number of pets has increased, the possibility of more indirect exposure to pet allergens might have increased. This could lead to increased numbers of individuals who become sensitized to pet allergens. However, there are few studies about time trends of pet allergy. Thus, the purpose of this study was to investigate the trends of sensitization to pet allergens and characteristics of sensitized patients. For this purpose, we determined the annual sensitization rate to cat or dog allergens in Korea, and explored the associated independent risk factors.

MATERIALS AND METHODS

Study subjects

The medical records of patients who underwent the ImmunoCAP® specific immunoglobulin E (IgE) test (Pharmacia Diagnostics, Uppsala, Sweden) for evaluation of various allergic skin diseases from January 2011 to December 2015 were reviewed retrospectively. The ImmunoCAP® Specific IgE test is an *in vitro* test that detects serum specific IgE antibody to specific antigen. It detects 45 common inhalant and food allergens, including house dust, *Dermatophagoides pteronyssinus* (D1), *D. farina* (D2), cat epithelium, and dog epithelium. It is less painful than the *in vivo* skin prick test (SPT) and has similar sensitivity[6,7].
In the ImmunoCAP® Specific IgE test, there are six classes of results according to antibody level. Class 0 is a specific IgE level of 0.00～0.34 IU/ml. Classes 1, 2, 3, 4, 5, and 6 are respective antibody levels of 0.35～0.69, 0.70～3.49, 3.50～17.49, 17.50～49.99, 50.00～99.99, and greater than 100.00 IU/ml. A result of class 3 or greater was considered positive for sensitization to the specific antigen[8].
We focused on cat and dog allergens and reviewed the records of patients with positive results for cat or dog allergens. Demographic data, pet ownership, and mode of exposure to each animal were reviewed, and additional information was gained through a phone call with each patient. Data concerning house dust, D1, and D2 were included to compare with cat or dog sensitization, because they are common sensitizing antigens.

Statistical analyses

Prevalence is expressed as a percentage and continuous variables are expressed as the mean±standard deviation. Chi-square tests was performed to analyze annual rates of sensitization of each antigen between each year. Independent risk factors for sensitization to each animal allergen were evaluated by chi-square tests, with results expressed as odds ratio (OR) with 95% confidence intervals (CIs). To evaluate the relationship between IgE level and specific cat or dog IgE, Spearman correlation analysis was performed. A *p*-value <0.05 was considered as statistically significant. All statistical analyses were performed using SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). The study was approved by the Institutional Review Board of the Hallym University Sacred Heart Hospital (IRB no. 2017-I138).

RESULTS

In total, 7,469 patients who underwent allergic profile testing from 2011 to 2015 were enrolled. Of these, 274 (3.67%) were sensitized to dog allergen and 307 (4.11%) were sensitized to cat allergen. We analyzed the annual trends of patients who were positive for cats, dogs, house dust, D1, or D2 among the patients who underwent allergic profile testing from 2011 to 2015 (Fig. 1). The most common clinical manifestation of cat group was atopic dermatitis (30.3%), followed by allergic urticarial (26.4%), prurigo (18.2%), allergic contact dermatitis (3.6%). The most common clinical manifestation of dog group was atopic dermatitis (40%), followed by allergic urticarial (18.7%), prurigo (7%), allergic contact dermatitis (16%).

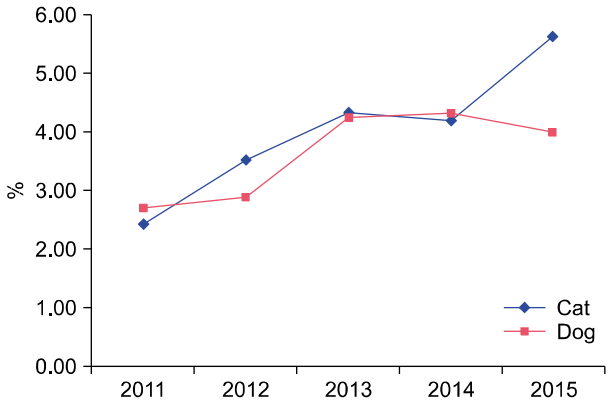

Fig. 1. Annual rates of the sensitization to cat and dog from 2011 to 2015.

Table 1. Annual rates of sensitization to cats and dogs

Variable	2011 (n=1,437)	2012 (n=1,384)	2013 (n=1,237)	2014 (n=1,640)	2015 (n=1,771)	Total (n=7,469)	*p*-value
Dog	39 (2.71)	40 (2.89)	53 (4.28)	71 (4.33)	71 (4.01)	274 (3.67)	0.04*
Cat	35 (2.44)	49 (3.54)	54 (4.37)	69 (4.21)	100 (5.65)	307 (4.11)	<0.001*
House dust	201 (13.99)	186 (13.44)	210 (16.98)	287 (17.5)	351 (19.82)	1,235 (16.54)	0.04*
D1	395 (27.49)	474 (34.25)	395 (31.93)	516 (31.46)	541 (30.55)	2,318 (31.03)	0.003*
D2	392 (27.28)	427 (30.85)	381 (30.8)	533 (32.5)	522 (29.47)	2,150 (28.79)	0.028*

Values are presented as number (%).
D1: *Dermatophagoides pteronyssinus*, D2: *D. farina*.
Annual rates are compared by chi-squre test, showing significant difference between each year *$p<0.05$.

Annual trends of the number of sensitized patients are shown in Table 1. The number of patients sensitized to cats was 35 (2.44%) in 2011, 49 (3.54%) in 2012, 54 (4.37%) in 2013, 69 (4.21%) in 2014, 100 (5.65%) in 2015. The number of patients sensitized to dogs was 39 (2.71%) in 2011, 40 (2.89%) in 2012, 53 (4.28%) in 2013, 71 (4.33%) in 2014, 71 (4.01%) in 2015. The number of cat-sensitized patients increased steadily until 2015. The number of dog-sensitized patients increased until 2014 and decreased slightly in 2015. There were 1,235 (16.54%) patients sensitized to house dust. Their numbers increased steadily and gradually from 2011 to 2015. Positive results for D1 and D2 were given by 2,318 (31.03%) and 2,150 (28.79%) patients, respectively, with no evident annual trends. By using chi-square test, annual rates of all antigens are showing significant differences between each year (Cat, $p=0.04$; Dog, $p=0.001$; House dust, $p=0.04$; D1, $p=0.003$; D2, $p=0.028$).

The clinical characteristics of the patients sensitized to cat or dog allergen are shown in Table 2. The mean age was 24.6 ± 16.5 years in the cat-sensitized group and 25.84 ± 17.4 years in the dog-sensitized group. In the cat- and dog-sensitized group, 127 (41.4%) and 117 (45.5%) patients, respectively, had a family history of allergic disease. Most of the patients were urban residents (97.0% for cat, 95.6% for dog). The most common clinical diagnosis of both groups was atopic dermatitis, followed by allergic urticaria, prurigo, and allergic contact dermatitis.

The proportion of direct exposure to the causative antigen was 48.9% in the dog-sensitized group, whereas 12% in the cat-sensitized group (Table 3). A 'no exposure' result to the causative antigen was 78.8% in the cat-sensitized group, whereas 37.6% in the dog-sensitized group. Through the period of study, dogs were pets of 44.5% and 45.5% of patients sensitized to cat and dog respectively.

Independent risk factors for sensitization to each animal allergen were determined (Table 4). Risk factors for sensitization to the cat allergen including sensitization to dog (OR=1.443, $p=0.015$), but not to house dust (OR=1.076, $p=0.61$), D1 (OR=1.017, $p=0.906$), and D2 (OR=1.250, $p=0.128$). Risk factors for sensitization to the dog allergen included sensitization to cat (OR=1.443, $p=0.015$), house dust (OR=0.937, $p=0.659$), D1 (OR=0.928, $p=0.611$), and D2 (OR=0.869, $p=0.347$). Spearman correlation analysis conducted to evaluate the association between specific IgE level to each animal allergen and total IgE level did not reveal any significant relationship (rho=-0.019, $p=0.705$ for cat group and rho=-0.064, $p=0.194$ for dog group).

Table 2. Clinical characteristics of subjects sensitized to cats or dogs

Variable	Cat (n=307)	Dog (n=274)
Sex		
Male	145 (47.2)	118 (43.1)
Female	162 (57.8)	156 (56.9)
Age (y)	24.6±16.5	25.84±17.4
Age<10	45 (14.7)	44 (16.1)
10≤Age<20	84 (27.4)	77 (28.1)
20≤Age<30	78 (25.4)	60 (21.9)
30≤Age<40	38 (12.4)	38 (13.9)
40≤Age<50	23 (7.5)	17 (6.2)
50≤Age<60	26 (8.5)	24 (8.8)
Age≥60	13 (4.2)	14 (5.1)
Family history of allergic disease	127 (41.4)	117 (45.5)
Place of residence		
Urban	298 (97.0)	262 (95.6)
Rural	9 (3.0)	12 (4.4)
Clinical diagnosis		
Atopic dermatitis	93 (30.3)	103 (40.0)
Allergic urticaria	81 (26.4)	48 (18.7)
Prurigo	56 (18.2)	18 (7.0)
Allergic contact dermatitis	11 (3.6)	41 (16.0)
Others	66 (21.5)	64 (23.4)

Values are presented as number (%) or mean±standard deviation.

Table 3. Type of exposure to cat or dog

Variable	Cat (n=307)	Dog (n=274)
Direct exposure	37 (12)	134 (48.9)
Past ownership	10 (3.3)	73 (26.6)
Present ownership	20 (6.5)	52 (19)
Occupational	7 (2.3)	9 (3.3)
Indirect exposure	28 (9.1)	37 (13.5)
No exposure	242 (78.8)	103 (37.6)

Values are presented as number (%).

Table 4. Risk factors for sensitization to dog or cat

Variable	Cat OR (95% CI)	Dog OR (95% CI)
Sensitization to		
Cat	-	1.443 (1.074~1.939)*
Dog	1.443 (1.074~1.939)*	-
House dust	1.076 (0.812~1.426)	0.937 (0.700~1.253)
D. pteronyssinus	1.017 (0.768~1.346)	0.928 (0.696~1.238)
D. farinae	1.250 (0.937~1.667)	0.869 (0.649~1.164)

OR: odds ratio, CI: confidence interval.
*Indicates $p=0.015$ chi-square tests were performed.

DISCUSSION

The prevalence of allergic disease like atopic dermatitis has been increasing worldwide, including Korea[2]. Avoidance of the causative allergen is important in allergic diseases. In this regard, the increasing interest in pet ownership in Korea, especially for cats and dogs, is germane. The increased popularity of dogs and cats as domestic pets has led to an increase in animal allergens in society.

The results of this study revealed that the number of patients positive for dog and cat allergens has steadily increased since 2011. The most likely explanation is the increased number of cats and dogs in the community. In one survey performed in Korea[5], the number of cat ownership has been sharply increased since 2010 compared to that of dog ownership. The number of cat ownership had been increased consistently since 2000 and showed steep increase since 2010, whereas that of the dog ownership showed plateau between 2000 and 2009, and showed mild increase since 2010 compared to that of cat ownership. Most of people who owned cat replied that they started cat ownership after 2010 (73.5%). That explains the increasing trends of pet sensitization and the result that cat sensitization kept increasing since 2011, whereas dog sensitization showed plateau since 2013 in our study. One study reported that the proportion of sensitization in pet shop workers was not increased compared to that in the control group[9]. Several studies revealed that sensitization to cats was reduced with low or high exposure to the Fel d 1 cat antigen, whereas the sensitization was highest with moderate exposure to Fel d 1[10,11]. In contrast, sensitization was increased in linear correlation in people exposed to house dust, cockroach, and rats[11].

Therefore, the overall increase in sensitization to cats or dogs seems to be due to the indirect moderate exposure, rather than direct and frequent exposure. The Fel d 1 cat antigen is considered a ubiquitous allergen. It has been found in many cat-free indoor private/public places, such as offices, hospitals, and schools[12]. Other studies revealed that cat allergens found in cat-free indoor environments were passively carried, mainly on the clothing of cat owners[13,14]. Consequently, the increased number of cats in society has led to increased indirect antigen transmission from cat owners and the ubiquity of the antigens, resulting in the rise of sensitization to cats[12,15-17]. Several studies described that the clothing of cat owners was the main contributor to the dispersal of cat allergen in cat-free places, indicating that a prevention strategy for allergies should include the avoidance of direct cat exposure and also indirect cat exposure from cat owners[12,18]. This indirect transmission concerns mainly the Fel d 1 antigen, because cat allergens are relatively light particles that can be easily carried on clothing[13,14,18].

This study was conducted with patients an overwhelming number of whom lived in urban areas (97.0%, 95.6% for cat and dog group, respectively). Pets in the city live in spaces where allergens can be readily present in insulation, carpets, and other household locations. Therefore, it may be easier to increase the ubiquity of antigens, leading to higher sensitization rates. A study conducted in a rural setting could yield different findings.

In this study, the proportion of patients sensitized to cat or dog was 4.11% and 3.67%, respectively, which is lower than the recent sensitization rate of 9.1% for cat and 8.6% for dogs reported in Korea[19]. The subjects of this study were confined to allergic patients who visited one dermatology clinic. Patients with these allergic diseases tend to avoid pets[20], which may explain this relatively lower sensitization rate.

Concerning the exposure modality, exposure to dog allergen was mostly direct, whereas sensitization to cat allergen tended to be indirect, without specific contact. This is consistent with the knowledge that the prevalence of sensitization to cats is relatively high in the Korean population although cat ownership is very low[4,5,19,21]. The high number of stray cats and their high reproduction rate could explain the ubiquity of the cat allergen[22].

In this study, sensitization to cat was a risk factor for sensitization to dog, and vice versa. Dog and cat allergens share a major epitope, and these major proteins exhibit cross-reactivity[23,24]. This cross-reactivity may explain the association of the clinical and clinical symptoms between dog and cat allergies. This possibility should be explained to patients who are clinically sensitized to dogs or cats. However, house dust, D1, and D2 were not risk factors of cat or dog sensitization. Linneberg et al.[25] reported that atopic dermatitis itself could be a risk factor for sensitization to cats. House dust, D1, and D2 are usually positive in atopic dermatitis patients, but no association was uncovered in this study.

The association of total IgE with specific IgE antibody titer to dogs or cats was not statistically significant in both groups. The specific IgE level for dogs or cats was relatively small when compared to total IgE level, so specific IgE level for dogs or cats did not affect total IgE level. Erwin et al.[26] investigated the association between total IgE and specific IgE levels, and reported that cats did not show any association with total IgE levels, whereas dust mites showed an association with total IgE levels. The proportion of mite-specific IgE level to total IgE is typically high; the major allergen of dust mites could be a potential enzyme that has a non-specific effect on IgE antibody

production. In addition, immunologic desensitization of pet allergen can cause this discordance. High exposure to cat antigen can cause desensitization, therefore the sensitization can be highest with modest exposure to antigen[10,11].

Our study has several limitations. It is a retrospective study and the modality of pet exposure was only studied in people sensitized to cats or dogs. Nearly all subjects were urban dwellers, which could cause bias. In addition, since a practical survey on pets and an accurate sample survey have not been done in Korea, it is difficult to know the actual number of domestic pets in Korea. Therefore, the relationship between the number of actual pets and the sensitization rate cannot be investigated.

In conclusion, allergies to animal allergens play an increasingly important role in allergic diseases. In industrialized countries, such as Korea, the number of pets is increasing, which will increase the amount of pet allergens in public places and in pet-free settings. Increased exposure to direct and indirect antigens has led to an increase in the number of patients sensitized to dogs or cats annually since 2011. Since dog and cat antigens are cross-reactive, even if a patient is sensitized to one animal, attention should be paid to other species. However, specific IgE to dog and cat allergen is not associated with total IgE.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

REFERENCES

1. Odhiambo JA, Williams HC, Clayton TO, Robertson CF, Asher MI. Global variations in prevalence of eczema symptoms in children from ISAAC phase three. J Allergy Clin Immunol 2009;124:1251-1258.
2. Lee JH, Han KD, Kim KM, Park YG, Lee JY, Park YM. Prevalence of atopic dermatitis in Korean children based on data from the 2008-2011 Korean national health and nutrition examination survey. Allergy Asthma Immunol Res 2016;8:79-83.
3. Plaschke P, Janson C, Norrman E, Björnsson E, Ellbjär S, Järvholm B. Association between atopic sensitization and asthma and bronchial hyperresponsiveness in Swedish adults: pets, and not mites, are the most important allergens. J Allergy Clinl Immunol 1999;104:58-65.
4. Yoo KY, Cho SH, Gin Y, Lee YJ. Strategic guidelines to protect and manage pet animals in Seoul (SDI 04-R-21). Seoul: The Seoul Institute, 2004.
5. Korean gallup. Pet ownership status and awareness survey in Korea. Seoul: Korea Pet Food Association; 2017. 58 p.
6. Calabria CW, Dietrich J, Hagan L. Comparison of serum-specific IgE (ImmunoCAP) and skin-prick test results for 53 inhalant allergens in patients with chronic rhinitis. Allergy Asthma Proc 2009;30:386-396.
7. Jung YG, Cho HJ, Park GY, Min JY, Kim HY, Dhong HJ, et al. Comparison of the skin-prick test and Phadia ImmunoCAP as tools to diagnose house-dust mite allergy. Am J Rhinol Allergy 2010;24:226-229.
8. Koh HS, Lee KS, Han DH, Rah YH, Choi SH. Relationship between serum total IgE, specific IgE, and peripheral blood eosinophil count according to specific allergic diseases. Allergy Asthma Respir Dis 2013;1:123-128.
9. Yilmaz I, Oner Erkekol F, Secil D, Misirligil Z, Mungan D. Cat and dog sensitization in pet shop workers. Occup Med 2013;63:563-567.
10. Custovic A, Hallam CL, Simpson BM, Craven M, Simpson A, Woodcock A. Decreased prevalence of sensitization to cats with high exposure to cat allergen. J Allergy Clin Immunol 2001;108:537-539.
11. Custovic A, Simpson BM, Simpson A, Hallam CL, Marolia H, Walsh D, et al. Current mite, cat, and dog allergen exposure, pet ownership, and sensitization to inhalant allergens in adults. J Allergy Clin Immunol 2003;111:402-407.
12. Enberg RN, Shamie SM, McCullough J, Ownby DR. Ubiquitous presence of cat allergen in cat-free buildings: probable dispersal from human clothing. Ann Allergy 1993;70:471-474.
13. D'Amato G, Liccardi G, Russo M, Barber D, D'Amato M, Carreira J. Clothing is a carrier of cat allergens. J of Allergy Clin Immunol 1997;99:577-578.
14. Patchett K, Lewis S, Crane J, Fitzharris P. Cat allergen (Fel d 1) levels on school children's clothing and in primary school classrooms in Wellington, New Zealand. J Allergy Clin Immunol 1997;100:755-759.
15. Almqvist C, Larsson PH, Egmar AC, Hedrén M, Malmberg P, Wickman M. School as a risk environment for children allergic to cats and a site for transfer of cat allergen to homes. J Allergy Clin Immunol 1999;103:1012-1017.
16. Custovic A, Simpson A, Chapman MD, Woodcock A. Allergen avoidance in the treatment of asthma and atopic disorders. Thorax 1998;53:63-72.
17. Partti-Pellinen K, Marttila O, Mäkinen-Kiljunen S, Haahtela T. Occurrence of dog, cat, and mite allergens in public transport vehicles. Allergy 2000;55:65-68.
18. Chan-Yeung M, McClean PA, Sandell PR, Slutsky AS, Zamel N. Sensitization to cat without direct exposure to cats. Clin Exp Allergy 1999;29:762-765.
19. Kim TB, Kim KM, Kim SH, Kang HR, Chang YS, Kim CW, et el. Sensitization rates for inhalant allergens in Korea; a multi-center study. J Asthma Allergy Clin Immunol 2003;23:483-493.
20. Svanes C, Zock JP, Antó J, Dharmage S, Norbäck D, Wjst M, et al. Do asthma and allergy influence subsequent pet keeping? An analysis of childhood and adulthood. J Allergy Clin Immunol 2006;118:691-698.
21. Kim J, Hahm MI, Lee SY, Kim WK, Chae Y, Park YM, et al. Sensitization to aeroallergens in Korean children: a population-based study in 2010. J Korean Med Sci 2011;26:1165-1172.

22. Lee SE, Kim JY, Kim YA, Cho SH, Ahn HJ, Woo HM, et al. Prevalence of Toxoplasma gondii infection in stray and household cats in regions of Seoul, Korea. Korean J Parasitol 2010;48:267-270.
23. Spitzauer S, Pandjaitan B, Mühl S, Ebner C, Kraft D, Valenta R, et al. Major cat and dog allergens share IgE epitopes. J Allergy Clin Immunol 1997;99:100-106.
24. Madhurantakam C, Nilsson OB, Uchtenhagen H, Konradsen J, Saarne T, Högbom E, et al. Crystal structure of the dog lipocalin allergen can f 2: implications for cross-reactivity to the cat allergen Fel d 4. J Mol Biol 2010;401:68-83.
25. Linneberg A, Nielsen NH, Madsen F, Frølund L, Dirksen A, Jørgensen T. Pets in the home and the development of pet allergy in adulthood. The Copenhagen allergy study. Allergy 2003;58:21-26.
26. Erwin EA, Rönmark E, Wickens K, Perzanowski MS, Barry D, Lundbäck B, et al. Contribution of dust mite and cat specific IgE to total IgE: relevance to asthma prevalence. J Allergy Clin Immunol 2007;119:359-365.