Allergology International. 2014;63:227-233
DOI: 10.2332/allergolint.13-OA-0588

ORIGINAL ARTICLE

Is There a Need for Repetition of Skin Test in Childhood Allergic Diseases? Repetition of Skin Test and Allergic Diseases

Mahmut Dogru[1], Ilknur Bostanci[2], Serap Ozmen[2], Tayfur Ginis[2] and Handan Duman[2]

ABSTRACT

Background: Skin prick tests are widely used to determine sensitivity in allergic diseases. There is limited information about the natural history of skin sensitization tests and factors that affect them. It was aimed to determine the changes in skin test results and the factors affecting the reactivity of skin tests after a period of approximately four years in children with allergic disease.

Methods: SPT of 170 patients among 2485 children with asthma and/or allergic rhinitis and/or atopic dermatitis, who underwent SPT between 2005 and 2007, were repeated after an interval of at least 3 years.

Results: The mean age was 10.7 ± 3.1 (5-18) years and 70% of the patients were male. In total 66 (39.0% of the study population) had a different skin tests result in follow-up. Alterations: loss of sensitivity in 18 (11%) patients, the formation of a new sensitivity in 37 (22%) patients, and 11 (6%) both gained and lost sensitization. The presence of atopy in the family, the presence of allergic rhinitis and IgE elevation significantly predicted the incidence of new sensitization. The presence of sensitization to multiple allergens significantly predicted the incidence of loss of sensitization.

Conclusions: It is found that there was an alteration of sensitization in 4/10 children at the end of the average 4-year period. The presence of family atopy, the presence of allergic rhinitis and serum total IgE elevation were risk factors for the development of new sensitization. On the other hand sensitization to multiple allergens was risk factors for the loss of sensitization.

KEY WORDS

allergen, allergic asthma, house dust mites, seasonal allergic rhinitis, skin prick test

INTRODUCTION

Skin prick test (SPT) is commonly used to investigate type 1 hypersensitivity to a specific allergen. Skin prick test is a method that is simple, easy, comfortable, inexpensive, safe, rapid and can be applied at any age. It is recommended as the allergological "test of choice" in clinical practice and clinical-epidemiological research.[1,2] Response to histamine and allergens are affected by various factors such as time, immunotherapy and certain drugs. New sensitizations and the natural course of sensitization might be understood by repeated SPT. Various studies have been carried out to assess the natural course of sensitization in children and adults. In these studies, factors affecting SPT response were determined according to time, gender, exposure to tobacco smoke in childhood, high IgE levels, the presence of new allergic symptoms, family history of atopy, having siblings, having ever had one or more cats at home, rural living, having ever lived on a farm, and heavy traffic road within 200 m distance.[3-12]

It was aimed to determine the changes in SPT results and factors affecting the reactivity of skin tests

[1]Department of Pediatric Immunology Allergy and [2]Department of Pediatric Allergy, Dr. Sami Ulus Woman's Health and Children Education and Research Hospital, Ankara, Turkey.
Conflict of interest: No potential conflict of interest was disclosed.
Correspondence: Uzm.Dr. Mahmut Doğru, Çocuk Allerjisi Bölümü, Dr. Sami Ulus Kadın Doğum, Çocuk Sağlığı ve Hastalıkları Eğitim ve Araştırma Hastanesi, Babür Cad No: 44 Altındağ, Ankara, Türkiye.
Email: mdmahmut@yahoo.com
Received 3 June 2013. Accepted for publication 4 December 2013.

after a period of approximately 4 years in children with allergic disease.

METHODS

SPT of 170 patients among 2485 children with asthma and/or allergic rhinitis and/or atopic dermatitis, who had undergone SPT between January 1, 2005 and December 31, 2007 in the Clinic of Pediatric Allergy and Immunology, were prospectively repeated after an interval of at least 3 years. The exclusion criteria were: 1. patients aged over 18 years, 2. intake of drugs that could affect the SPT result (antihistamines, corticosteroids, etc.), 3. the presence of extensive skin lesions, 4. currently taking or have taken allergen immunotherapy, 5. severe cardiovascular disease, 6. taking beta-blockers and 7. Those who patients didn't have written informed consent. The study was approved by the local ethics committee. Informed consent was obtained from all subjects and/or their parents.

PROTOCOL

A questionnaire was completed for all subjects. Details regarding patient demographics and medical history were recorded in the questionnaire. "Atopy" with SPT was defined as a positive reaction to any one of the allergens. Familial atopy was defined as being positive when having allergic disease in first degree relatives. The diagnosis of allergic rhinitis and asthma were made according to international guidelines, the diagnosis of AD was made according to the criteria of Hannifin and Rajka.[13] The diagnosis of food allergy was made according to the patient's history and SPT positivity to specific foods.

SKIN PRICK TEST

Skin prick tests to cow's milk, egg yolk, egg white, and common aeroallergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinea*), mixture of grass pollens (*Lollium perenne*, *Dactylis glomerata*, *Phleum pratense*, *Anthoxanthum odaratum*, *Poa pratensis*, *Festuca eliator*, *Agrostis vulgaris*, *Holcus lanatus*, *Cynodon dactylon*, *Avena sativa*, *Avena fatua*, *Lotus Corniculatus*), a mixture of grain pollens (oats, wheat, barley, corn), a mixture of tree pollens (*Acer pseudoplanatus*, *Aesculus hippocastanum*, *Robinia pseudoacacia*, *Tilia platyphyllos*, *Platanus vulgaris*), weed-mix pollens (*Medicago sativa*, *Trifolium pratense*, *Brassica nigra*, *Urtica dioica*, *Rumex acetosa*), *Alternaria alternaria*, cockroaches (*Blatella germanica*), cat dander and dog dander (Stallergenes SA, 92160 Antony, France) were performed using Quantitest. Skin prick tests were applied on the anterior surface of the forearm. Histamine (10 mg/ml) and physiological saline were used as positive and negative references, respectively. Skin reactions were evaluated 20 minutes after the application of the skin test, and indurations of ≥3 mm was considered indicative of a positive reaction. Skin-prick tests with the same allergens were repeated in all patients after an interval of at least three years. According to test changes to the SPT, patients were divided into 3 groups as following: stable rest (Group I), new sensitization (Group II), and loss of sensitivity (Group III). More than one sensitization is called polisensitization whereas more than three defined as multi-allergen sensitivity.

SPIROMETRY

Pulmonary function tests (PFT) were performed on children older than five able to do with spirometry (SpirolabII-MIR, Wisconsin, USA) and parameters of FVC, FEV1, PEF and MEF25-75 were measured. Values were recorded as a predicted percentage according to height and age. Patients underwent PFT during the stable period (not using β2-agonists). After PFT, 200 mcg of salbutamol inhaled by inhalation chamber, and 15 minutes after PFT was repeated. Increment over 12% when compared with baseline in FEV1, 25% in FEF 25-75% was considered positive for reversibility.

TOTAL IgE AND EOSINOPHIL COUNTS

Serum total IgE levels were analyzed with the nephelometry system (Siemens Healthcare Diagnostics, Deerfield, Germany) and values of over 100 IU/ml were considered high. Total eosinophil counts and the percentage of blood eosinophils were measured with an automated blood analyzer-ABX Pentra 80 (HORİBA Medical, Montpellier, France) and values more than 4% were considered increased.

STATISTICAL ANALYSIS

Data was analyzed by using the program "Statistical Package for Social Sciences" (SPSS for Windows 11.0, Chicago, USA). Values for continuous variables were given as either mean ± standard deviation or as median, based on the normality of distribution. Student t test and ANOVA was used in the comparison of normal and homogeneous distribution of the parametric values. Chi-square and Mann Whitney U test was used to compare nonparametric values. Pearson's and Spearman's correlation test was used for the correlation between the two continuous variables. McNemar test was used to compare nominal variables of the two dependent groups. Multinomial logistic regression analysis with backward elimination was used to examine the impact of variables on the susceptibility to develop new allergic reactions and for the disappearance reactions, respectively, between the 2 times of testing. In this analysis, SPT status (stable Vs new and loss of sensitivity at follow-up) was the dependent variable; age, sex, duration of breastfeeding, use of formula, family atopy, exposure to smoke, pets at home, monthly income, house changes, the presence of asthma, AR, disease duration, follow-up time, eosinophilia, elevation of IgE lev-

Table 1 Comparison of the allergen sensitivity in the two tests

Allergen/disease	Positivity rate in the first test *n* (%)	Positivity rate in the second test *n* (%)	*p*
Grass-mix pollens	51 (30)	63 (37.1)	0.017*
Asthma *n*: 151	36 (23.8)	49 (32.5)	
Allergic rhinitis *n*: 84	42 (50)	52 (61.9)	
Atopic dermatitis *n*: 20	6 (30)	8 (40)	
Cereal-mix pollens	44 (25.9)	52 (30.6)	0.008*
Asthma *n*: 151	30 (19.9)	38 (25.2)	
Allergic rhinitis *n*: 84	37 (44)	44 (52.4)	
Atopic dermatitis *n*: 20	6 (30)	7 (35)	
DP	36 (21.2)	30 (17.6)	0.07*
Asthma *n*: 151	33 (21.9)	26 (17.2)	
Allergic rhinitis *n*: 84	19 (22.6)	15 (17.9)	
Atopic dermatitis *n*: 20	3 (15)	3 (15)	
DF	32 (18.9)	31 (18.2)	0.99*
Asthma *n*: 151	28 (18.5)	27 (17.9)	
Allergic rhinitis *n*: 84	18 (21.4)	17 (20.2)	
Atopic dermatitis *n*: 20	4 (20)	3 (15)	
Weed-mix pollens	13 (7.6)	12 (7.1)	0.99*
Asthma *n*: 151	8 (5.3)	11 (7.3)	
Allergic rhinitis *n*: 84	10 (11.9)	11 (13.1)	
Atopic dermatitis *n*: 20	1 (59)	2 (10)	
Alternaria alternata	12 (7.1)	11 (6.5)	0.99*
Asthma *n*: 151	9 (6)	10 (6.6)	
Allergic rhinitis *n*: 84	7 (8.3)	8 (9.5)	
Atopic dermatitis *n*: 20	3 (15)	5 (25)	
Cat	11 (6.5)	14 (8.2)	0.60*
Asthma *n*: 151	9 (6)	12 (7.9)	
Allergic rhinitis *n*: 84	9 (10.7)	11 (13.1)	
Atopic dermatitis *n*: 20	1 (5)	1 (5)	
Dog	5 (2.9)	19 (11.2)	0.000*
Asthma *n*: 151	5 (3.3)	12 (7.9)	
Allergic rhinitis *n*: 84	4 (4.8)	12 (14.3)	
Atopic dermatitis *n*: 20	1 (5)	2 (10)	
Egg yolk	3 (1.8)	2 (1.2)	0.99*
Asthma *n*: 151	3 (2)	2 (1.3)	
Allergic rhinitis *n*: 84	2 (2.4)	2 (2.4)	
Atopic dermatitis *n*: 20	2 (10)	2 (10)	
Egg white	3 (1.8)	2 (1.2)	0.99*
Asthma *n*: 151	3 (2)	2 (1.3)	
Allergic rhinitis *n*: 84	2 (2.4)	2 (2.4)	
Atopic dermatitis *n*: 20	2 (10)	2 (10)	
Trees-mix pollens	2 (1.2)	4 (2.4)	0.62*
Asthma *n*: 151	1 (0.7)	3 (2)	
Allergic rhinitis *n*: 84	1 (1.2)	2 (2.4)	
Atopic dermatitis *n*: 20	0	1 (5)	
Blatella germanica	2 (1.2)	5 (2.9)	0.45*
Asthma *n*: 151	2 (1.3)	3 (2)	
Allergic rhinitis *n*: 84	1 (1.2)	2 (2.4)	
Atopic dermatitis *n*: 20	0	1 (5)	
Milk	2 (1.2)	0 (0)	**
Asthma *n*: 151	2 (1.3)		
Allergic rhinitis *n*: 84	1 (1.2)		
Atopic dermatitis *n*: 20	1 (5)		
Total	89 (52.4)	95 (55.9)	

DP, *Dermatophagoides pteronyssinus*; DF, *Dermatophagoides farinae.*

*McNemar testi. ** Since the predicted value was not able to be calculated statistics could not be performed.

Table 2 Comparison of socio-demographic and time-related characteristics of the groups

	Group I *n*: 104	Group II *n*: 37	Group III *n*: 18	*p*
Gender (M/F)	68/36	26/11	16/2	0.135*
Age (years) †	10.4 ± 3.0	11.2 ± 3.0	11.1 ± 2.8	0.302**
Time of birth				
Term/preterm	98/6	35/2	17/1	0.996*
Birth weight				
Small/Appropriate/Large	6/90/8	2/30/3	2/14/2	0.264*
Duration of breastfeeding (months) †	14.0 ± 10.3	11.5 ± 8.3	10.7 ± 9.7	0.989***
Additional food time (months) †	6.2 ± 2.0	5.1 ± 1.6	5.7 ± 1.8	0.093***
Formula				
Usage %	42	55	28	0.171*
Duration (months) †	4.5 ± 6.7	7.8 ± 9.1	3.0 ± 6.8	0.067***
Hospitalization *n* (%)	37 (36)	18 (49)	2 (11)	0.024*
To have any operation *n* (%)	15 (14.4)	4 (10.8)	3 (16.7)	0.805*
Consanguineous marriages *n* (%)	26 (25)	7 (19)	7 (39)	0.277*
Family atopy *n* (%)	32 (31)	21 (57)	8 (44)	0.017*
Exposure to smoke *n* (%)	52 (50)	19 (51)	10 (56)	0.908*
Pets at home *n* (%)	13 (13)	4 (11)	3 (17)	0.827*
Monthly income *n* (%)				0.447*
Below the poverty line *n* (%)	41 (39)	19 (51)	8 (44)	
Above the poverty line *n* (%)	63 (61)	18 (49)	10 (56)	
The presence of the home change *n* (%)	11 (11)	3 (8)	1 (6)	0.759*
Onset of the symptoms (months) †	21.2 ± 24.3	32.2 ± 31.1	22.3 ± 15.3	0.179***
Time of diagnosis of asthma (months) †	45.3 ± 29.4	57.1 ± 32.6	51.2 ± 22.8	0.070***
Follow-up duration (months) †	63.8 ± 15.7	65.3 ± 21.9	58.2 ± 10.8	0.302***
Duration of the disease (years) †	7.6 ± 2.8	7.9 ± 2.9	7.8 ± 2.9	0.827**
The time between the skin tests (months) †	51.5 ± 12.0	50.3 ± 11.7	48.2 ± 11.1	0.755***

† Mean ± SD. * chi-square test. ** ANOVA testi. ***Kruskal Wallis test.

Table 3 Changes in skin tests according to diseases

	Allergic rhinitis *n*: 84	Asthma *n*: 151
Stable (%)	43 (51.2)	100 (66.2)
Development of new sensitization (%)	29 (34.5)	35 (23.2)
Loss of sensitization (%)	12 (14.3)	16 (10.6)

els, the time between skin tests, and multiple allergen sensitivity. Results are expressed as odds ratios. $p < 0.05$ was considered the significant value.

RESULTS

The mean age of the patients was 10.7 ± 3.1 (5-18) years and 119 (70%) were male. Sensitivity was detected in89 (52.4%) patients in the first SPT. The second skin tests were performed on patients after an average period of 50.86 ± 12.3 (36-72) months. The percentage of sensitivity in the second SPT was 55.9 (95 patients). The sensitivity to grass pollen mixture sensitivity was the most frequent in both SPT. There was statistically significant increase in sensitivity to grass-mix, cereal-mix and dog dander when comparing the sensitivity in both SPTs (respectively $p = 0.017$ and $p = 0.008$, $p = 0.000$). The comparison of allergen sensitivity in the two tests is shown in Table 1.

According to the first SPT, a change in sensitivity was noted in 52 patients (58%) who were atopic, while 14(%17) patients (who were nonatopic) were found to have change who were nonatopic. A total of 66 (39%) patients had changes in SPT. The distribution of change, a loss of sensitivity was detected in 18 (11%) patients. The onset of sensitivity was as following noted in 37 (22%) patients. Both an onset and loss of sensitivity was detected in 11 (6%) patients. Grass-mix and dog dander allergens were the most frequently detected allergens in those patients developing a new sensitivity. DP and *Alternaria alternata* allergens were the most frequent among those losing sensitivity. The development of a new sensitivity to dog dander was significantly lower in those with exposure to pets ($p = 0.037$). The numbers of subjects having dog at home in the first and second tests were 5 and 10, respectively.

Table 4 Comparison of the laboratory findings of the groups

	Group I *n*: 104	Group II *n*: 37	Group III *n*: 18	*p*
Eosinophilia%	33	67	50	0.002*
The percentage of eosinophils†	3.7 ± 4.0	6.0 ± 4.6	3.8 ± 2.4	0.001**
Elevation of IgE %	45	82	56	0.001*
Log IgE†	1.8 ± 0.6	2.2 ± 0.5	2.0 ± 0.7	0.018***
FVC (predicted %)†	86.3 ± 14.3	89.1 ± 7.5	89 ± 11.6	0.740**
FEV1 (predicted %)†	89.2 ± 14.1	94.5 ± 6.7	92.5 ± 13.4	0.179**
FEV1/FVC (predicted %)†	99.2 ± 8.5	101.2 ± 8.1	99.6 ± 7.9	0.251**
PEF (predicted %)†	89.5 ± 16.7	92.8 ± 14.9	92.2 ± 20.7	0.607***
FEF25-75 (predicted %)†	93.4 ± 18.7	100.7 ± 14.9	93.8 ± 30.8	0.201***
Reversibility, yes/no	40/20	13/4	3/5	0.257*

† Mean ± SD. * chi-square test. ** Kruskal Wallis test. ***ANOVA test.

Table 5 Factors affecting change in sensitivity

	Odds ratio	%95 confidence interval	*P*
The development of new sensitivity			
Family atopy	5.88	1.7-20.6	0.005
The presence of allergic rhinitis	20.91	3.4-130.4	0.001
Elevation of immunoglobulin E	7.97	1.6-39.9	0.012
Loss of sensitivity			
Multiple allergens sensitivity	7.97	1.6-54.6	0.035

According to changes in the SPT, the patients were divided into 3 groups as "stable rest" (Group I), "new sensitization" (Group II), and "loss of sensitivity" (Group III). Eleven patients who developed both new sensitivity and loss of sensitivity were excluded from the study. There was no significant difference between the three groups for socio-demographic and time-related characteristics except for hospitalization and family atopy (Table 2).

Seventy five (47.2%) patients had asthma, 8 (5%) had allergic rhinitis, 56 (35.2%) had asthma an allergic rhinitis, and 20 (12.6%) had asthma-allergic rhinitis-atopic dermatitis. In evaluation of changes in the patients with allergic rhinitis, whereas the new sensitization was significantly ($p = 0.001$), there was no statistically significant difference in terms of loss of sensitivity ($p = 0.600$). There was no significant difference in terms of changes in skin tests for patients with asthma ($p = 0.05$). Changes in skin tests in all patients with allergic rhinitis/asthma are shown in Table 3.

The median number of allergen sensitivity was two (min 1-max 7). There were weak-to-moderate correlations between the number of allergen sensitivity and age, eosinophils and IgE levels (r = 0.347; $p = 0.000$, r = 0.350; $p = 0.000$, r = 0.309; $p = 0.000$). In 79 atopic patients (88.8%) had more than one allergen sensitivity (polisensitization). The most common association is grass-mix and cereal mix sensitivity detected in 53.2% of atopic patients. The frequencies of polysensitization in the groups are 34%, 54% and 78%, respectively. There was a significant difference between the groups in terms of polysensitization ($p = 0.001$). The frequencies of sensitivity to multiple allergens (>3 allergens) in the groups are 3%, 5% and 22%, respectively. There was a significant difference between the groups in terms of sensitivity to multiple allergens ($p = 0.005$).

There were statistically significant differences between the groups in terms of the presence of eosinophilia, mean percentage of eosinophils, serum total IgE levels and log IgE levels (respectively $p = 0.002$, $p = 0.001$, $p = 0.001$, $p = 0.018$). The difference was not significant for pulmonary function test parameters (FVC, FEV1, FEV1/FVC, PEF, and FEF25-75) (Table 4).

In logistic regression analysis, a family history of atopy, the presence of AR, and IgE levels were found to be determinants of the formation of a new sensitivity (respectively, odds ratio = 5.88, 95% confidence interval = 1.7 to 20.6, $p = 0.005$, odds ratio = 20, 91, 95% confidence interval = 3.4 to 130.4, $p = 0.001$, odds ratio = 7.97, 95% confidence interval = 1.6 to 39.9, $p = 0.012$). The logistic regression analysis using the same parameters, sensitivity to multiple allergens was found as a marker of susceptibility to loss of sensitivity (odds ratio = 7.97, 95% confidence interval = 1.6 to 54.6, $p = 0.035$) (Table 5).

DISCUSSION

The determination of sensitivity by SPT is one of the basic steps in the treatment of allergic diseases. In addition to the economic costs of allergic diseases they can cause social losses such as school and work loss, impaired quality of life, and reduction in productivity. Once the allergen sensitization has been determined by SPT, the patients are kept away from the offensive allergen. Thus, the social losses could be reduced. Therefore, it is important to determine sensitivity and a change of sensitivity in people with aller-

Table 6 Features in published studies with repeated skin-prick testing

Author (reference)	Number of population/ Age-years (mean)	Sensitivity at first SPT (%)	Sensitivity at last SPT (%)	Number of allergens	Duration (years)	Cut off limit (mm)	Factors affecting change (OR)
Aslund *et al.*[3]	344/30	61.2	62.7	10	3	>3	Female sex (1.9)
Barbee *et al.*[4]	1333/8.1	39.1	50.7	5	8.1	??	Unvalued
Johnson *et al.*[6]	114/9	52	56	3	2	≥2	Unvalued
Kaleyias *et al.*[7]	127/14.4	43	52	9	5.2	>3	Unvalued
Karakaya *et al.*[8]	222/36.4	58.6	47.7	10	3.6	>3	Time
Kuehr *et al.*[9]	587/11	23.9		Grasses	2	≥2	Unvalued
Kuehr *et al.*[9]	587/11	12.9		Cat	2	≥2	
Peat *et al.*[10]	380/8-10	24	39	13	2	≥4	Unvalued
Rönmark *et al.*[11]	1700/17-18	21	30	10	10	>3	Male sex (1.3), Family history of atopy (1.7), Siblings having more than 2 (0.96)*, Ever cat at home (0.7)*, Rural living (0.81)*, Ever living on a farm (0.88)*, Heavy traffic road 200 m (1.28)
Ulrik *et al.*[12]	408/12	26	44	5	6	?	Maternal smoking (2), increased serum IgE (1.9), and new symptoms of asthma (1.6) or rhinitis (2.1)

*Negatively associated OR: odds ratio

gic diseases.

The rate of skin sensitivity tests in this study was consistent with studies in literature.[3-12] The study of Karakaya *et al*.[8] showed a decrease in sensitivity in adult patients while in the Aslund *et al*. study[3] there was a slight increase in sensitivity. The reason for this may be due to the relationship between the age of the and their response to allergens. In the study of Barbee *et al*.,[5] the skin test sensitivity at 3-4 years was found to be 22%. The peak prevalence of reactivity (more than 40%) occurred during the third decade. Response to allergens slightly decreased after the age of 30s and falling rapidly after age 50.[5] In the study of Karakaya *et al*.[8] the mean age 36.4 + 11.4 years is estimated as a reduction in allergen-response stage. In the Aslund *et al*.[3] study, the median age was 30 years. Therefore, in study of Karakaya *et al*.,[8] unlike other studies, reduction in sensitivity could be determined.

Changes in allergen sensitivity vary depending on the study design, age and environmental conditions. In our study, grass-mix, cereal-mix, and dog dander were significantly difference between the two test sensitivities. DP and *Alternaria alternata* are more commonly observed in loss of sensitivity, while grass-mix and dog dander are the most frequent among those who developed a new sensitivity. These findings are similar with the studies of Kjellman *et al*.[14] and Kaleyias *et al*..[7] It is worth noting that there was an increase in dog dander sensitivity from 5.6% (in 5 patients) to 20% (in 19 patients). The relationship between the development of sensitivity and allergen exposure is uncertain. Several studies have shown a negative correlation between the development of asthma-allergic sensitization and the presence of domestic animals.[15,16] In contrast, in one study a positive correlation between the number of cats in the house and allergic sensitization was shown asthma in the community.[17] There was a negative correlation in our study. Dog allergens have been shown to lead to false positive results in those people sensitive to house dust when they are contaminated with house dust.[18] For this reason, the sensitivity to dog dander allergen might have increased in our investigation.

In our study, the comparison between the sociodemographic and time related characteristics of our groups only showed a significant difference in the hospitalization and family history of atopy. Acute attacks of asthma in childhood often lead to requiring hospitalization. Exposure and sensitivity to inhalant allergens is a risk factor for hospital admission.[19] Bacharier *et al*.[19] found the increase in the number of sensitivities in SPT, elevation of IgE levels, presence of eosinophilia as risk factors for previous hospitalization due to asthma. In our study, hospitalization was significantly higher in the group which developed new sensitivity. Family history of atopy is a risk factor for allergic diseases. Likewise to our study, Rönmark *et al*.[11] reported a family history of atopy as a risk factor for the development of a new sensitivity.

The measurement of serum total IgE in predicting the risk of allergic disease or in screening allergic disease has less value. However in epidemiological studies, a high degree of correlation was found between the risk of asthma and the levels of total IgE. Immunoglobulin E at normal level doesn't exclude

the diagnosis of allergic disease. The number of eosinophils in the blood correlates with allergic diseases.[2] In our study, the elevation of IgE levels and eosinphilia in the new sensitivity group were higher than in the other groups.

The studies related to the change in skin test sensitivity were found to have various risk factors. These may include time, gender, exposure to tobacco smoke in childhood, high IgE levels, the presence of new allergic symptoms, a family history of atopy, having a siblings, any cat at home, rural living, having lived on a farm, and heavy traffic road within 200 m[3-12] (Table 6). In our study we determined the presence of family atopy, the presence of allergic rhinitis and IgE elevation were main risk factors for the development of new sensitization whereas the sensitization of multiple allergens were the risk factors for loss of sensitization. Differences in the results of this study may be due to differences in protocol, patient selection, the time interval between the tests, environmental conditions, and cut off limit at SPT.

As a conclusion, we found that there was an alteration of sensitization in 4/10 children at the end of the average 4-year period. A change in sensitivity was found to be more than a new form of sensitization. In particular, it there was a pronounced increase in susceptibility to dog epithelium. The incidence of atopy of patients had an increase. A reduction in household dust and mold sensitivity was prominent. The presence of family atopy, the presence of allergic rhinitis and serum total IgE elevation were the main risk factors for the development of new sensitization whereas the sensitization of multiple allergens were the risk factors for the loss of sensitization. This result may be useful in determining the course of taking into consideration sensitivity in the evaluation of children with allergic disease. However, a larger series of studies is needed to examine the relationship between the natural course of allergic diseases and changes in skin test sensitivity.

REFERENCES

1. Demoly P, Bousquet J, Romano A. In vivo methods for study of allergy. In: Adkinson NF Jr, Bochner BS, Busse WW, Holgate ST, Lemanske RF Jr, Simons FER (eds). *Middleton's Allergy: Principles and Practice,* 7th edn. St. Louis: Mosby Year Book, 2008;1267-79.
2. Bernstein IL, Li JT, Bernstein DI *et al*. Allergy diagnostic testing: an updated practice parameter. *Ann Allergy Asthma Immunol* 2008;**100** (Suppl 3):1-148.
3. Aslund N, Thomsen SF, Mølgaard E, Nolte H, Backer V. Changes in skin test reactivity among adults with atopic disease: a 3-year prospective study. *Ann Allergy Asthma Immunol* 2008;**101**:524-8.
4. Barbee RA, Kaltenborn W, Lebowitz MD, Burrows B. Longitudinal changes in allergen skin test reactivity in a community population sample. *J Allergy Clin Immunol* 1987;**79**:16-24.
5. Barbee RA, Lebowitz MD, Thompson HC, Burrows B. Immediate skin test reactivity in a general population sample. *Ann Intern med* 1976;**84**:129-33.
6. Johnston SL, Clough JB, Pattemore PK, Smith S, Holgate ST. Longitudinal changes in skin-prick test reactivity over 2 years in a population of school children with respiratory symptoms. *Clin Exp Allergy* 1992;**22**:948-57.
7. Kaleyias J, Papaioannou D, Manoussakis M, Syrigou E, Tapratzi P, Saxoni-Papageorgiou P. Skin-prick test findings in atopic asthmatic children: A follow-up study from childhood to puberty. *Pediatr Allergy Immunol* 2002;**13**: 368-74.
8. Karakaya G, Kalyoncu AF. The natural course of atopy determined by skin prick tests in patients with bronchial asthma and/or rhinitis. *Allergol Immunopathol (Madr)* 2006;**34**:257-62.
9. Kuehr J, Karmaus W, Frischer T *et al*. Longitudinal variability of skin prick test results. *Clin Exp Allergy* 1992;**22**: 839-44.
10. Peat JK, Salome CM, Woolcock AJ. Longitudinal changes in atopy during a 4-year period: relation to bronchial hyperresponsiveness and respiratory symptoms in a population sample of Australian schoolchildren. *J Allergy Clin Immunol* 1990;**85**:65-74.
11. Rönmark E, Bjerg A, Perzanowski M, Platts-Mills T, Lundbäck B. Major increase in allergic sensitization in schoolchildren from 1996 to 2006 in northern Sweden. *J Allergy Clin Immunol* 2009;**124**:357-63.
12. Ulrik CS, Backer V. Atopy in Danish children and adolescents: results from a longitudinal population study. *Ann Allergy Asthma Immunol* 2000;**85**:293-7.
13. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)* 1980;**92**:44-7.
14. Kjellman H, Hesselmar B. Prognosis of asthma in children: A cohort study into adulthood. *Acta Paediatr* 1994; **83**:854-6.
15. Celedon JC, Litonjua AA, Ryan L, Platts-Mills T, Weiss ST, Gold DR. Exposure to cat allergen, maternal history of asthma, and wheezing in first 5 years of life. *Lancet* 2002;**360**:781-2.
16. Perzanowski MS, Ronmark E, Platts-Mills TA, Lundbäck B. Effect of cat and dog ownership on sensitization and development of asthma among preteenage children. *Am J Respir Crit Care Med* 2002;**166**:696-702.
17. Svanes C, Heinrich J, Jarvis D *et al*. Pet-keeping in childhood and adult asthma and hay fever: European community respiratory health survey. *J Allergy Clin Immunol* 2003;**112**:289-300.
18. van der Veen MJ, Mulder M, Witteman AM *et al*. False-positive skin prick test responses to commercially available dog dander extracts caused by contamination with house dust mite (Dermatophagoides pteronyssinus) allergens. *J Allergy Clin Immunol* 1996;**98**:1028-34.
19. Bacharier LB, Dawson C, Bloomberg GR *et al*, and Childhood Asthma Management Program Research Group. Hospitalization for asthma: atopic, pulmonary function, and psychological correlates among participants in the Childhood Asthma Management Program. *Pediatrics* 2003;**112**:85-92.