
The determinants of bronchial hyperresponsiveness in patients with allergic rhinitis

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Background: Patients with allergic rhinitis and bronchial hyperresponsiveness (BHR) may be at higher risk of developing asthma.

Objective: To investigate whether reactivity to aeroallergens in skin prick testing (SPT) and serum eosinophil cationic protein levels can be used to predict BHR in allergic rhinitis patients.

Methods: Fifty-nine consecutive patients with allergic rhinitis underwent SPTs using grass, tree, weed, parietaria, *Alternaria*, *Aspergillus*, mites, and cat and dog dander extracts. Methacholine challenge tests were performed using spirometry.

Results: Methacholine-induced BHR was detected in 23 patients (39%). Of 59 patients, 14 had 1 positive SPT response, 35 had 2 to 4 positive responses, and 10 had more than 4 positive responses. There was a significant inverse correlation between methacholine provocation concentration that caused a decrease in forced expiratory volume in 1 second of 20% (PC₂₀) and the number of positive SPT responses ($r = -0.28$; $P = .03$). The BHR-positive patients had a mean of 4 positive SPT responses, whereas BHR-negative patients had a mean of 2.6 ($P = .04$). Nine BHR-positive patients (39%) and only 1 BHR-negative patient (3%) had more than 4 positive SPT responses ($P < .001$). There was no correlation between serum eosinophil cationic protein levels and methacholine PC₂₀ doses. There was a strong association between hyperresponsiveness to methacholine and both cat and dog dander sensitivity ($P < .001$ and $P = .001$, respectively).

Conclusions: Allergic rhinitis patients with SPT responses to a higher number of allergens are more likely to have BHR. Whether the number of positive SPT responses correlates with the risk of developing asthma in allergic rhinitis patients remains to be determined.

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INTRODUCTION

Bronchial hyperresponsiveness (BHR) is a frequent finding in patients with allergic rhinitis.¹ Although the results of studies addressing the prognostic significance of BHR in allergic rhinitis have been inconclusive, several studies^{2,3} suggested that patients with allergic rhinitis and BHR are at higher risk of developing asthma. The determinants of BHR in atopy (defined as a positive skin prick test [SPT] response or increased specific IgE levels in serum with or without allergic symptoms) and asthma have been investigated. *Dermatophagoides farinae*, cat dander, and grass pollen sensitizations seem to increase the risk of BHR.^{4,5} In addition to these aeroallergens, the number of positive SPT responses was related to methacholine reactivity in patients with asthma.⁶ However, the relation of BHR and individual sensitization patterns to aeroallergens in allergic rhinitis patients without asthmatic symptoms has not been determined. The correlation between the number of positive SPT responses and methacholine reactivity in these patients is also unknown. The first purpose of this study was to investigate whether

factors that predict BHR in patients with allergic asthma also predict BHR in patients with allergic rhinitis. If the determinants of BHR in both diseases are similar, the proportion of patients with allergic rhinitis who will eventually be diagnosed as having asthma could be predicted.

Bronchial hyperresponsiveness is associated with an inflammatory process in the lower respiratory tract in patients with asthma.⁷ Inflammation is also a common feature in allergic rhinitis.⁸ Bronchoalveolar lavage, bronchial biopsy, and sputum studies have provided evidence that patients with seasonal allergic rhinitis may demonstrate an inflammatory process in the lower airways that is commonly associated with eosinophilic accumulation. Furthermore, in these patients, the number of eosinophils in sputum seems to correlate with the degree of methacholine hyperresponsiveness.⁹ Eosinophil cationic protein (ECP) is known as an activation marker of eosinophils.^{10,11} Several groups have investigated the relationship between BHR and serum ECP (sECP) levels in patients with asthma. In some studies,^{12,13} sECP levels have been found to be stronger predictors of the severity of the asthmatic symptoms than pulmonary function tests. Other researchers^{14,15} found no correlation between sECP and BHR in asthma. Increased ECP levels in sputum together with increased BHR was reported in patients with allergic rhinitis without asthmatic symptoms.^{16,17} The relationship between levels of sECP and the degree of BHR, as measured by methacholine provocation, has not been documented clearly

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in patients with allergic rhinitis. In view of these findings, the second purpose of this study was to determine whether sECP levels correlate with methacholine doses that induce BHR and whether measurement of sECP levels could be used to identify BHR-positive patients with allergic rhinitis.

METHODS

Subjects

Between February 1, 2001, and February 1, 2002, a total of 131 patients were newly diagnosed as having allergic rhinitis in the clinics of the Ege University Hospital. Fifty-nine patients (41 women and 18 men; mean $\pm$ SD age, 28.71 ± 9.66 years; age range, 17–48 years) who fulfilled the following criteria were enrolled into the study: newly diagnosed and symptomatic allergic rhinitis, normal lung function test results, and normal findings on chest and sinus radiography. All patients gave informed consent.

A total of 72 patients were excluded from the study for active tobacco smoking (27 patients), the presence of symptoms compatible with sinusitis (21 patients), respiratory tract infections during the previous 2 months (11 patients), a history of nasal corticosteroid use within the preceding 2 months (7 patients), and a diagnosis of ulcerative colitis (1 patient). Five patients declined to participate in the study.

Twenty-eight (47%) of the 59 patients had seasonal rhinitis, 9 (15%) had perennial rhinitis, and 22 (37%) had perennial rhinitis with seasonal exacerbation.

Study Design

The study was performed on 2 consecutive days. On day 1, the patients underwent clinical and physical evaluation. Samples of venous blood for total IgE, eosinophil, and ECP measurements were collected. On day 2, patients underwent methacholine bronchial provocation testing (M-BPT). Also, SPTs were performed on day 2 after M-BPT. Patients stopped taking oral antihistamines 5 days before having SPTs and M-BPTs.

Skin Prick Tests

We tested for the most common inhaled allergens: grass, tree, weed, parietaria, *Alternaria*, *Aspergillus*, mites (*Dermatophagoides pteronyssinus* and *D farinae*), and albumin-free cat and dog extracts (Stallergenes, Paris, France). The same technician performed all the tests, and a lancet for epicutaneous testing was used, with the forearm as the skin test site. Each test was separated by approximately 3 cm. Histamine phosphate base (10 mg/mL) and glycerinated saline were used as the positive and negative controls, respectively. The results of the SPTs were read at 15 minutes. Wheal diameters at least 3 mm greater than those of the negative controls were considered positive.

Measurement of sECP and Total IgE Levels

Blood sampling for ECP measurement was performed before the BPT. Venous blood samples were drawn into serum separator tubes (Vacuette; Greiner Bio-one, Northrhine, Germany) and were allowed to clot at room temperature for 60 to 120 minutes, followed by centrifugation at 1,300g for 10

minutes at room temperature according to the manufacturer's instructions. Serum samples were then collected and stored at -20°C until ECP assay. Eosinophil cationic protein was analyzed quantitatively by using Unicap ECP FEIA Kit and Unicap 100 instrument (ImmunoCAP; Phadebas, Pharmacia, Uppsala, Sweden). Total IgE levels were also measured using CAP-FEIA (Pharmacia).

Methacholine Bronchial Provocation Test

First, baseline spirometry was performed using a spirometer (SensorMedics 2200; SensorMedics, Yorba Linda, CA), and forced expiratory volume in 1 second (FEV_1) and the FEV_1 /vital capacity index were recorded. Bronchial response challenges with methacholine were performed using a dosimetric aerosol delivery system based on a jet nebulizer (Pari-Boy; PARI GmbH, Starnberg, Germany). A 2-minute tidal breathing dosing protocol was used. Methacholine (acetyl- β -methyl choline chloride) dilutions at increasing concentrations of 0.031, 0.062, 0.125, 0.25, 0.5, 1, 2, 4, 8, and 16 mg/mL were used, and the dilutions were prepared on the day the test was performed. The test ended when a fall in FEV_1 values of 20% or greater of the baseline value was achieved or when the highest concentration of methacholine was inhaled. If a subject did not react after the highest dose had been given, he or she was assigned a censored provocation concentration that caused a decrease in FEV_1 of 20% (PC_{20}) of 32 mg/mL for the purpose of analysis. If subjects reacted to 8 mg/mL or less of a methacholine dose, they were grouped as patients with BHR. Results were expressed in terms of the M-PC_{20} (provocation concentration dose of methacholine). In all patients, the methacholine provocation tests and the measurement of sECP and total IgE levels were performed during their symptomatic period.

Statistical Analysis

Statistical analysis of the data were performed using a statistical software program (SPSS for Windows 10.0; SPSS Inc, Chicago, IL). Descriptive statistics were used to summarize clinical and demographic characteristics of the patients. Results are expressed as mean $\pm$ SD. Nonparametric Mann-Whitney *U* tests were used to evaluate differences between groups. Correlations between variables were analyzed using the Spearman rank correlation coefficient. $P < .05$ was considered statistically significant.

RESULTS

Fifty-nine patients were enrolled in the study. Based on the temporal relationship of the allergic symptoms and the seasons, patients were categorized as those with seasonal symptoms, those with perennial symptoms, and those with perennial symptoms and seasonal exacerbation. There were no significant differences among these groups in age, sex, disease duration, presence of BHR, and total IgE, PC_{20} , and sECP levels. However, peripheral blood eosinophil counts were significantly higher in patients with perennial symptoms and seasonal exacerbation than in those with seasonal symptoms ($P = .007$; Table 1).

Table 1. Demographic Characteristics and Sensitization Data of Patients with Allergic Rhinitis*

Variable	Patients with seasonal symptoms (n = 28)	Patients with perennial symptoms and seasonal exacerbations (n = 22)	Patients with perennial symptoms (n = 9)
Women, No. (%)	18 (64)	16 (73)	7 (78)
Age (range), y	28.8 ± 9.1 (21–36)	29 ± 10.5 (17–48)	27.4 ± 10.1
Disease duration, y	5.4 ± 3.3	7.3 ± 7.2	5.8 ± 2.8
Blood eosinophils, cells/mm ³	238.9 ± 217.6	375.8 ± 285.9†	291.6 ± 164.4
Total IgE, kU/L	190.3 ± 179	309.8 ± 287.2	210.1 ± 184.6
PC ₂₀ , mg/mL	20.7 ± 14.4	20.9 ± 14.9	18.3 ± 16.2
Presence of BHR, No. (%)	11 (39)	8 (36)	4 (44)
Serum ECP, µg/L	14.23 ± 11.59	17.05 ± 13.05	20.65 ± 23.55

Abbreviations: BHR, bronchial hyperresponsiveness; ECP, eosinophil cationic protein; PC₂₀, provocation concentration that caused a decrease in forced expiratory volume in 1 second of 20%.

* Data are given as mean ± SD, except where noted otherwise. Comparisons among groups were made using the Mann-Whitney *U* test.

† *P* = .007 vs patients with seasonal symptoms.

Mean M-PC₂₀ doses were determined for patients grouped according to number of positive SPT responses to aeroallergens (Fig 1). There was a significant inverse correlation between mean M-PC₂₀ dose levels and the number of positive SPT responses ($r = -0.28$; $P = .03$). Patients who had only 1 positive SPT response ($n = 14$) had a PC₂₀ value of 23.4 ± 14.0 mg/mL, whereas those with 2 ($n = 8$), 3 ($n = 15$), 4 ($n = 12$), 5 ($n = 3$), 6 ($n = 3$), and 8 ($n = 4$) positive SPT responses had values of 21.5 ± 14.6 , 21.7 ± 14.9 , 27.4 ± 10.8 , 11.6 ± 17.6 , 4 ± 3.4 , and 0.88 ± 0.84 mg/mL, respectively. The M-PC₂₀ dose was 5.05 ± 9.72 mg/mL in patients with more than 4 positive SPTs responses, $23.6 \pm$

13.4 mg/mL in patients with 2 to 4 positive responses, and 23.4 ± 14.0 mg/mL in patients with 1 positive response ($P = .001$ for >4 vs 2 to 4, $P = .002$ for >4 vs 1).

Of the 59 patients, 23 (39%) were reactive to methacholine doses of 8 mg/mL or less. No significant differences were found in the frequency of BHR among patient groups composed of individuals with seasonal symptoms, those with perennial symptoms, and those with perennial symptoms and seasonal exacerbation ($P > .99$ for allergic rhinitis patients with seasonal symptoms vs perennial symptoms, $P = .7$ for allergic rhinitis patients with seasonal symptoms vs perennial symptoms and seasonal exacerbation, and $P > .99$ for allergic rhinitis patients with perennial symptoms vs perennial symptoms and seasonal exacerbation). When BHR-positive and BHR-negative patients were compared with regard to sex, disease duration, eosinophil count, and total IgE levels, no significant differences were found between the 2 groups. Patients with BHR were younger than those without BHR (25.47 ± 7.34 vs 30.77 ± 10.47 years; $P = .05$). Patients with BHR had significantly higher numbers of positive SPT responses. Methacholine-responsive patients had a mean of 4.04 positive responses, whereas methacholine-unresponsive patients had a mean of 2.63 positive responses ($P = .04$; Table 2).

Patients were divided into 3 subgroups according to the number of allergens they tested positive for in SPTs. Group I comprised patients who had only 1 positive SPT response; group II comprised those with 2 to 4 positive responses, and group III comprised those with 5 or more positive responses. In group III patients, the mean methacholine dose that induced BHR was significantly less than that in groups I and II ($P = .002$ and $P = .001$, respectively; Table 3). However, there was no significant difference between groups I and II in mean BHR-inducing methacholine doses. The BHR-positive patients were reactive to higher numbers of allergens in SPT compared with BHR-negative patients. The percentage of patients with positive SPTs to 5 or more allergens was 13 times higher in patients with BHR compared with those without BHR ($P = .008$).

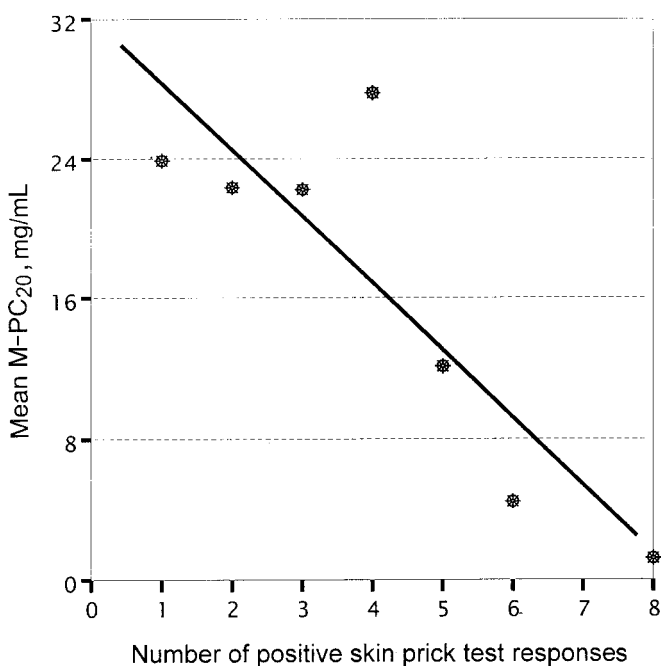


Figure 1. Correlation between mean methacholine provocation concentration that caused a decrease in forced expiratory volume in 1 second of 20% (M-PC₂₀) levels and the number of positive skin prick test responses in all allergic rhinitis patients ($r = -0.28$; $P = .03$, Spearman correlation test).

Table 2. Characteristics of BHR-Positive and BHR-Negative Patients*

n	BHR-positive patients (n = 23)	BHR-negative patients (n = 36)	P value
Women, No. (%)	16 (70)	25 (69)	.9
Age, y	25.47 ± 7.34	30.77 ± 10.47	.05
Disease duration, y	6.13 ± 3.52	6.27 ± 6.00	.39
Blood eosinophils, cells/mm ³	338.43 ± 326.29	272.18 ± 172.36	.8
Total IgE, U/L	301.78 ± 291.15	197.13 ± 264.74	.1
Serum ECP, µg/L	14.20 ± 12.02	19.49 ± 17.18	.2
Skin prick test positive responses, No.	4.04 ± 2.43	2.63 ± 1.24	.04

Abbreviations: BHR, bronchial hyperresponsiveness; ECP, eosinophil cationic protein.

* Data are given as mean ± SD, except where noted otherwise. Comparisons were made using the Mann-Whitney *U* test.

Table 3. Degree of Reactivity by BHR Group and Methacholine PC₂₀ Level

Degree of reactivity	Methacholine PC ₂₀ level, mean ± SD, mg/mL	BHR-positive patients, No. (%)	BHR-negative patients, No. (%)
Group I (1 positive)	23.4 ± 14.0	4 (17)	10 (27)
Group II (2–4 positive)	23.6 ± 13.4	10 (43)	25 (69)
Group III (≥5 positive)	5.0 ± 9.7*	9 (39)†	1 (3)

Abbreviations: BHR, bronchial hyperresponsiveness; PC₂₀, provocation concentration that caused a decrease in forced expiratory volume in 1 second of 20%.

* *P* = .002 vs group I and *P* = .001 vs group II.

† *P* = .008 vs BHR-negative patients.

In this study, cat and dog dander sensitivities were found to be strongly associated with hyperresponsiveness to methacholine (*P* < .001 for cat and *P* = .001 for dog). Of 23 patients with BHR, 9 (39%) had cat dander sensitization and 8 (35%) had dog dander sensitization, whereas only 1 (3%) of 36 patients without BHR had cat and dog sensitivities each. We could not find an association between sensitivity to house dust mite, *Alternaria*, *Aspergillus*, and grass pollen and BHR in our patients (*P* = .57, .42, .06, and .47, respectively; Fig 2).

Serum ECP levels ranged from 2.4 to 78.8 µg/L in the 59 patients included in the study; 33 patients (60%) had sECP levels of 10 µg/L or greater. Of these 33 patients, 15 (45%) had levels of 20 µg/L or greater. Serum ECP levels did not

correlate with the degree of methacholine reactivity (*P* = .23). When patients were grouped according to sECP levels of less than 10 µg/L (*n* = 26), 10 to 20 µg/L (*n* = 18), and greater than 20 µg/L (*n* = 15), no significant differences were found among the groups in age, sex, disease duration, number of positive SPT responses, presence of BHR, and PC₂₀ levels (Table 4). There was no correlation between sECP and total IgE levels (Fig 3), but a positive correlation was found between peripheral eosinophil counts and sECP levels (Fig 4; *P* = .01).

DISCUSSION

In this study, we addressed the relationship among SPT reactivity, individual sensitization, sECP levels, and BHR in patients with allergic rhinitis. We found that 39% of the patients with active allergic rhinitis had BHR. In other studies,^{18–20} BHR was found in 24% to 40% of patients with active rhinitis. We found a similar frequency of BHR to methacholine in the 3 groups of patients with seasonal rhinitis, perennial rhinitis, and perennial rhinitis with seasonal exacerbations. In a study by Verdiani et al,²¹ patients with perennial rhinitis were shown to have a higher risk of BHR than those with seasonal rhinitis. Di Lorenzo et al¹⁸ reported that the number of patients with BHR increased at least 2-fold during the pollen season in patients with seasonal rhinitis. In our study, methacholine provocation testing was performed during the symptomatic period in all patients. Therefore, we cannot rule out the possibility that differences in the frequency of BHR exist among the 3 groups of patients with seasonal rhinitis, perennial rhinitis, and perennial rhinitis with seasonal exacerbations.

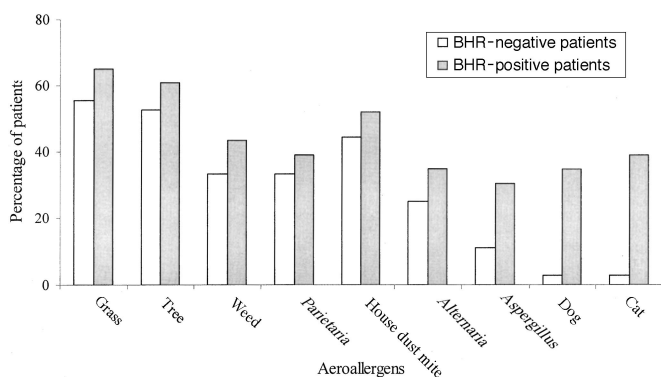


Figure 2. Frequency of individual sensitization to aeroallergens in bronchial hyperresponsiveness (BHR)-positive and BHR-negative patients. Dog and cat hypersensitivities were more frequent in BHR-positive patients (*P* < .001 for cat and *P* = .001 for dog, Mann-Whitney *U* test).

Table 4. Characteristics of Patients Stratified by Serum ECP Levels*

	Serum ECP, $\mu\text{g/L}$		
	<10 (n = 26)	10–20 (n = 18)	>20 (n = 15)
Women, No. (%)	19 (73)	12 (67)	9 (60)
Age (range), y	30.1 $\pm$ 10.7 (18–49)	26.8 $\pm$ 9 (17–42)	28.5 $\pm$ 8.5 (18–47)
Disease duration, y	6.6 $\pm$ 5.8	5.7 $\pm$ 0.5	6 $\pm$ 4.8
Blood eosinophils, cells/mm ³	245.9 $\pm$ 188.8	220.1 $\pm$ 126	481.6 $\pm$ 337.6†
Total IgE, kU/L	225.6 $\pm$ 324.7	181.8 $\pm$ 156.5	326.6 $\pm$ 297.5
PC ₂₀ , mg/mL	21.8 $\pm$ 14.3	22.3 $\pm$ 14.1	15.7 $\pm$ 15.7
Presence of BHR, No. (%)	6 (34.6)	(36.4)	4 (44.4)
Skin prick test reactivity, No.	3.6 $\pm$ 2.1	2.8 $\pm$ 1.5	2.8 $\pm$ 1.8

Abbreviations: BHR, bronchial hyperresponsiveness; ECP, eosinophil cationic protein; PC₂₀, provocation concentration that caused a decrease in forced expiratory volume in 1 second of 20%.

* Data are given as mean $\pm$ SD, except where noted otherwise.

† $P = .001$ vs group I and group II.

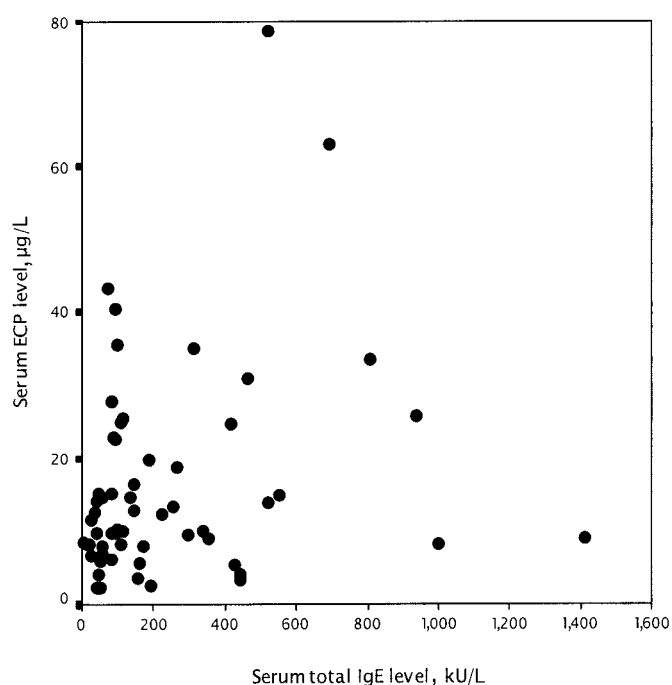


Figure 3. There was no correlation between serum eosinophil cationic protein (ECP) and total IgE levels in all allergic rhinitis patients ($r = 0.23$; $P = .07$, Spearman correlation test).

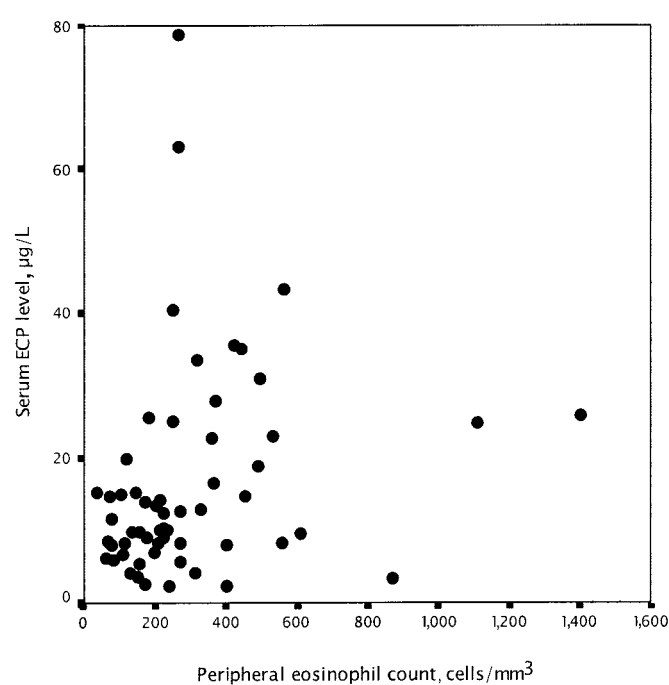


Figure 4. A positive correlation was found between serum eosinophil cationic protein (ECP) levels and peripheral eosinophil counts in all allergic rhinitis patients ($r = 0.32$; $P = .01$, Spearman correlation test).

It is well known that atopy is a risk factor for BHR. Some population-based studies^{22,23} revealed that patients who had serum specific IgE to aeroallergens and patients who had a positive SPT response with at least 1 aeroallergen had a higher risk of BHR than nonatopic subjects. Recently, Fowler and Lipworth⁶ showed that not only the presence but also the degree of IgE-mediated allergy (as defined by a positive SPT response) were related to the increased frequency of BHR to methacholine in patients with asthma. They reported that the doses of methacholine required to lower FEV₁ measurements by 20% or more correlated with the number of positive SPT

responses to aeroallergens in patients with asthma. In keeping with these results, we show that the number of positive SPT responses is an important factor for BHR in patients with allergic rhinitis. Patients with allergic rhinitis who have a higher number of positive SPT responses are more likely to have BHR to methacholine challenge in our study. Especially, patients with 5 or more positive SPT responses seem to have the highest probability of BHR. There were no differences between patients with 1 positive SPT response and 2 to 4 positive SPT responses in the frequency of BHR and mean M-PC₂₀ levels. Similar results were obtained in asthmatic

patients. In the study by Fowler and Lipworth,⁶ asthmatic patients with only 1 positive SPT response and those with 2 to 4 positive SPT responses did not differ in the mean M-PC₂₀ dose that induced BHR. However, asthmatic patients with 5 or more positive SPT responses had a higher frequency of BHR and a lower M-PC₂₀ dose than the other groups. Therefore, it can be concluded that if BHR precedes asthmatic symptoms in patients with allergic rhinitis, having 5 or more positive SPT responses to aeroallergens may be a risk factor for asthma. In the literature, to our knowledge, there is no study of the relationship between the degree of SPT response and the M-PC₂₀ dose in patients with allergic rhinitis. We believe our data are novel in this aspect.

Atopy is defined as having specific IgE to aeroallergen(s) or at least 1 positive SPT response. In a population-based study⁵ performed in more than 30 centers, house dust mite, timothy grass, and cat dander sensitization were documented as risk factors for BHR in atopic subjects. In this study, however, a heterogeneity was noted between different centers in the sensitization patterns to aeroallergens and in the relation of BHR and individual sensitization. For example, in Spain, the frequency of BHR was significantly increased in patients sensitized to olive or timothy grass, but in England this frequency was related to sensitizations to cat, timothy grass, and *Cladosporium*. In our study, although house dust mite and grass pollen sensitizations were the most prevalent, we could not find any association between these aeroallergens and BHR. On the other hand, we found that cat and dog dander hypersensitivities significantly correlated with methacholine hyperreactivity in our patients. However, there are some important discrepancies between our study and the study by Chinn et al.⁵ The inclusion criteria in the latter study⁵ included the presence of serum specific IgE; however, the presence of allergic symptoms was not a requirement. The patient population in the study by Chinn et al⁵ was heterogeneous, including those with allergic rhinitis and allergic asthma. Patients with allergic rhinitis and allergic asthma were not separately analyzed. However, it was demonstrated that almost half of the atopic subjects were asymptomatic.²² Therefore, the observation that different aeroallergens were associated with BHR in the study by Chinn et al⁵ and in our study can be explained by the difference in the sensitization patterns between symptomatic allergic rhinitis patients and atopic individuals. There are many studies of the effects of individual aeroallergen sensitizations on asthmatic symptoms. Sensitization to house dust mite has been accepted as an independent risk factor for asthma.^{24–26} However, the relationship between sensitization to mites and BHR is less clear. In 1 study,⁴ house dust mite and cat sensitizations were found to be significantly associated with BHR. In contrast, Carter et al²⁷ revealed that a positive SPT response to house dust mite was associated with physician-diagnosed asthma but not with BHR. To our knowledge, the relationship between individual sensitization to aeroallergens and BHR in patients in allergic rhinitis has not been previously investigated. In view of our findings, we conclude that the types of aeroallergens that predict BHR in patients with allergic rhinitis are different from those in asthmatic patients.

In this study, cat and dog dander hypersensitivities were found to correlate significantly with methacholine hyperreactivity. Among our patients with newly diagnosed allergic rhinitis and BHR, 39% had cat dander sensitization and 35% had dog dander sensitization. In a previous study,²⁸ we found that 44.7% and 27.2% of the adult allergy patients attending the outpatient clinics at Ege University Hospital had cat and dog sensitizations, respectively. In that study,²⁸ cat allergens were detectable in 92.3% of the homes with no apparent relation to the presence of an indoor cat. Although indoor cats and dogs are not common in Turkey, cats and dogs living in the streets are common, and this may explain the high prevalence of cat and dog hypersensitivities observed in the present study.²⁸

It is well known that sECP levels are significantly elevated in allergic rhinitis patients compared with controls.²⁹ There are far fewer published data on BHR to methacholine and sECP levels in allergic rhinitis patients with seasonal symptoms and perennial symptoms. Tomassini et al³⁰ reported that sECP levels were higher in subjects sensitized to perennial allergens than in those sensitized to seasonal allergens. However, we did not find any difference in sECP levels between patients with seasonal allergic rhinitis and perennial allergic rhinitis even when patients with perennial symptoms with seasonal variations were excluded. We could not demonstrate any relationship between sECP levels and PC₂₀ doses in the Spearman rank correlation analysis. When patients were grouped as having low, intermediate, and high sECP levels, no significant differences were demonstrated among the groups in PC₂₀ dose levels and BHR. Therefore, we concluded that sECP levels were not predictive of the end point dose of methacholine in BPT and of the responsiveness to aeroallergens in patients with allergic rhinitis. This issue has been addressed in 1 other study. Alvarez et al¹⁷ did not find a correlation between eosinophilic inflammation and M-PC₂₀ doses in BPT. However, we found that sECP levels significantly correlated with peripheral blood eosinophil counts, as in other studies.^{15,30,31}

Our results show that allergic rhinitis patients with a higher number of positive SPT responses to aeroallergens are more likely to have BHR. Whether the number of positive SPT responses can be considered a risk factor for the development of asthma in patients with allergic rhinitis remains to be determined.

In conclusion, patients with allergic rhinitis sensitized to 5 or more aeroallergens have a higher frequency of BHR in methacholine BPT. Having sensitization to cat and dog dander in SPT strongly accompanies BHR in allergic rhinitis patients.

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