

Main Article

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Abstract

Background. Eosinophils are the principal effector cells involved in the pathogenesis of allergic rhinitis. Cell numbers increase in non-allergic rhinitis patients with eosinophilia, aspirin hypersensitivity and nasal polyposis, as well as in allergic rhinitis patients. Exfoliative nasal cytology can be used in the differential diagnosis of allergic rhinitis.

Objective. To evaluate nasal eosinophilia in nasal smears of patients with mild, persistent and intermittent allergic rhinitis.

Methods. The study comprised 60 patients with allergic rhinitis and 20 healthy volunteers. The patients were divided into intermittent and persistent allergic rhinitis groups. Nasal smear status, eosinophil numbers and Total Nasal Symptom Scores were compared.

Results. Nasal smear results were pathological in 40 of 60 allergic rhinitis patients, which was significantly higher than the rate in controls. The mean nasal eosinophilia score was significantly higher in the intermittent allergic rhinitis than in the persistent allergic rhinitis group ($p = 0.029$). There was a positive correlation between nasal eosinophilia score and Total Nasal Symptom Score ($r = 0.652$; $p < 0.05$) in persistent allergic rhinitis and intermittent allergic rhinitis patients.

Conclusion. The nasal smear test is inexpensive, objective and simple to perform, and should be part of the diagnostic investigation.

Introduction

Allergic rhinitis is an inflammatory disorder of the nasal mucosa triggered by immunoglobulin E.¹ Although allergic rhinitis does not exhibit a severe course, it compromises one's quality of life and imposes an economic burden on patients.² The incidence of allergic rhinitis has increased in recent years, and has been reported to vary between 1.4 per cent and 39.7 per cent.³ The prevalence of allergic rhinitis was reported to have increased by up to 24.1 per cent in China in one cross-sectional study; of these cases, 25.6 per cent had persistent allergic rhinitis.⁴

There are two forms of allergic rhinitis, intermittent and persistent allergic rhinitis, which are graded in terms of severity as 'mild' or 'moderate to severe'.⁵ Intermittent allergic rhinitis is accompanied by sneezing, watery rhinorrhoea, pruritus, nasal obstruction, vesicle formation and allergic conjunctivitis. In contrast to persistent allergic rhinitis, the symptoms of intermittent allergic rhinitis are not continuous; however, persistent allergic rhinitis is milder.^{5–8} The principal symptom is nasal obstruction.

Eosinophils are the principal effector cells in terms of allergic rhinitis pathogenesis. Cell numbers increase not only in allergic rhinitis patients, but also in those with non-allergic rhinitis with eosinophilia, aspirin hypersensitivity and nasal polyposis.^{9,10} Exfoliative nasal cytology can be used in the differential diagnosis of allergic rhinitis and non-allergic rhinitis with eosinophilia.¹¹

This study aimed to investigate nasal eosinophil levels in persistent allergic rhinitis and intermittent allergic rhinitis, and to compare these data with disease severity and symptom scale scores.

Materials and methods

Patients

The study protocol was approved by the Ethics Committee of Okmeydanı Education Hospital (Istanbul, Turkey). Eighty patients treated in the hospital's out-patient clinic between January 2014 and June 2017 were included. Allergic rhinitis was diagnosed by history-taking, physical examination and the skin prick test. Of the 80 study participants, 60 had allergic rhinitis; these participants were divided into 2 groups. Twenty patients (the control group) were non-symptomatic volunteers with no history of allergic rhinitis. We explored the participants' eosinophil levels in nasal smears.

The exclusion criteria were: pregnancy, malignant disease, chronic autoimmune disease, acute respiratory tract infection, use of local or systemic anti-inflammatory drugs

(e.g. antihistamines, corticosteroids or disodium cromoglicate) in the week prior to diagnostic testing, use of oral corticosteroids in the previous six weeks, use of antihistamines and/or leukotriene receptor antagonists in the preceding two weeks, and a history of polypectomy within the previous six months.

All patients were divided into two groups – intermittent allergic rhinitis and persistent allergic rhinitis – based on the Allergic Rhinitis and its Impact on Asthma system.⁵ Nasal smear status, eosinophil numbers and Total Nasal Symptom Scores were recorded. The eosinophil numbers and Total Nasal Symptom Scores of the persistent and intermittent allergic rhinitis groups were compared.

Nasal smear eosinophilia

After anterior rhinoscopy, Rhino-Probe™ curettes were used to obtain smears of the inferior meatus mucosae. All cyto-grams were encoded and read by a single-blinded investigator using light microscopy after haematoxylin and eosin staining. We defined four groups: less than 5 per cent eosinophils (score of 1); 5 to less than 10 per cent eosinophils (score of 2); 10 to less than 50 per cent eosinophils (score of 3), and 50 per cent or more eosinophils (score of 4) (Table 1). A score of 1 was considered to reflect normal findings.

Total Nasal Symptom Score

The Total Nasal Symptom Score was used to evaluate nasal symptoms (four in total: nasal obstruction, nasal itching, sneezing and rhinorrhoea). All symptoms were graded between 0 and 3 (0 = absent, 1 = mild, 2 = moderate and 3 = severe).

Statistics

The software IBM SPSS Statistics version 22 (Armonk, New York, USA) was used for all statistical analyses. The Shapiro–Wilk test was employed to evaluate data distributions. Normally distributed data were analysed with the aid of the student’s *t*-test and non-normally distributed data were analysed using the Mann–Whitney U test. The Fisher’s exact chi-square test with a continuity correction (that of Yates) was used when analysing non-numerical data. Spearman’s rho correlations were employed to compare non-normally distributed data. A *p*-value of less than 0.05 was considered to reflect significance.

Results

The mean age was 40.03 ± 13.71 years (range, 18–67 years) in the allergic rhinitis patients and 37.10 ± 7.65 years (range, 22–48 years) in the control participants; thus, there was no significant difference. The nasal smear results were pathological in 40 of the 60 allergic rhinitis patients, which was significantly higher than the rate in the control group (*p* = 0.001). Disease severity did not differ between groups (*p* > 0.05) (Table 2).

There was no difference between the persistent and intermittent allergic rhinitis groups in terms of Total Nasal Symptom Scores (*p* > 0.05) (Table 3). However, the mean nasal eosinophilia score of the intermittent allergic rhinitis group was significantly higher than that of the persistent allergic rhinitis group (*p* = 0.029) (Table 3).

We found no significant difference in the nasal eosinophilia score distribution. A score of 1 was most common in the persistent allergic rhinitis group and a score of 3 in the intermittent

Table 1. Scale used to interpret nasal eosinophilia

Eosinophilia score	Eosinophils in nasal smears (%)	Description	Pathology?
1	<5	No eosinophilia	Normal findings
2	5 to <10	Slight eosinophilia	Pathology doubtful
3	10 to <50	Moderate eosinophilia	Pathological
4	≥50	Marked eosinophilia	Pathological

Table 2. Evaluation of allergic rhinitis patients based on disease severity

Disease severity	Persistent allergic rhinitis	Intermittent allergic rhinitis	<i>p</i>
Mild	22 (56.4)	8 (38.1)	0.2791
Moderate to severe	17 (43.6)	13 (61.9)	

Data represent numbers (and percentages) of patients, unless indicated otherwise. Analysed using Yates’ correction for continuity.

Table 3. Nasal eosinophilia scores and Total Nasal Symptom Scores of allergic rhinitis patients

Score	Persistent allergic rhinitis	Intermittent allergic rhinitis	<i>p</i>
Total Nasal Symptom Score	7.23 ± 2.18 (7)	8.05 ± 2.08 (8)	0.164
Nasal eosinophilia score	2.10 ± 1.14 (2)	2.76 ± 0.94 (3)	0.029*

Data represent mean ± standard deviation (median) score, unless indicated otherwise. Analysed using the Mann–Whitney U test. **p* < 0.05.

Table 4. Evaluation of nasal eosinophilia scores

Nasal eosinophilia score	Persistent allergic rhinitis	Intermittent allergic rhinitis	<i>p</i>
1	17 (43.6)	3 (14.3)	0.0643
2	7 (17.9)	3 (14.3)	
3	9 (23.1)	11 (52.4)	
4	6 (15.4)	4 (19.0)	
Total	39 (65)	21 (35)	

Data represent numbers (and percentages) of patients, unless indicated otherwise. Analysed using the chi-square test.

Table 5. Nasal eosinophilia level by disease severity

Nasal eosinophilia score	Mild disease	Moderate to severe disease	<i>p</i>
1	19 (63.3)	1 (3.3)	0.0002*
2	8 (26.7)	2 (6.7)	
3	2 (6.7)	18 (60)	
4	1 (3.3)	9 (30)	

Data represent numbers (and percentages) of patients, unless indicated otherwise. Analysed using the chi-square test. **p* < 0.05.

allergic rhinitis group (*p* > 0.05) (Table 4). A significant difference in score distribution between those with mild and moderate to severe disease was evident (*p* < 0.05) (Table 5).

Table 6. Correlations between nasal eosinophilia scores and Total Nasal Symptom Scores of allergic rhinitis patients

Variable	Total		Persistent allergic rhinitis		Intermittent allergic rhinitis	
	r	p	r	p	r	p
Total Nasal Symptom Score	0.652	0.000*	0.652	0.000*	0.593	0.005*

Analysed using the Spearman's rho test. * $p < 0.05$.

A positive correlation was evident between the nasal eosinophilia score and Total Nasal Symptom Score ($r = 0.652$; $p < 0.05$) in allergic rhinitis patients (Table 6).

Discussion

The primary aim of our study was to compare eosinophilia and symptoms in persistent allergic rhinitis and intermittent allergic rhinitis patients. We found that both persistent and intermittent allergic rhinitis patients exhibited increased eosinophilia levels, and that persistent allergic rhinitis caused a greater increase. Eosinophils act as effector cells during the pathogenesis of allergic inflammation, and their numbers are increased in the blood and nasal secretions of atopic subjects.¹² Eosinophils and mast cells play key roles in immunoglobulin E mediated allergic reactions, including allergic rhinitis.^{13,14} Although eosinophil levels may double, smear findings can be normal during asymptomatic periods.¹ One problem is that no consensus method of smear evaluation has yet emerged. Thus, the published results vary widely.^{11,15–18} Lans *et al.*¹⁶ and Jankowski *et al.*¹⁸ used 20 per cent as a cut-off value, whereas Burrows *et al.*¹⁷ employed 25 per cent and Sood¹⁵ adopted 5 per cent, as did Crobach *et al.*¹¹

Although the nasal smear has been proposed as a useful tool for the diagnosis of allergic rhinitis, no consensus exists.^{19,20} The nasal smear test is inexpensive, rapid, non-invasive and simple, yielding information on both acute and chronic rhinosinusitis.^{16,19,21,22} Bousquet *et al.*⁵ concluded that raised eosinophilia alone was not adequate for the diagnosis of allergic rhinitis. On the contrary, Bryan and Bryan²² found that the mucosae of allergic rhinitis patients exhibited increased eosinophilia while normal mucosae did not. Malmberg *et al.*²³ found a correlation between eosinophilia and allergic rhinitis. Sood¹⁵ reported nasal eosinophilia in 80 per cent of allergic rhinitis patients and in only 5 per cent of controls, but emphasised that eosinophilia in the control group was very mild. Vaheri²⁴ found an 80 per cent and Bhandari and Baldwa²⁵ an 81.6 per cent rate of eosinophilia in allergic rhinitis patients. We found a slightly lower rate.

In general, eosinophil numbers tend to be lower in those with constant, compared with seasonal, disease, suggesting that the extent of eosinophilia depends on the extent of seasonal allergen exposure. Eosinophilia and mast cell numbers were higher in intermittent and persistent allergic rhinitis groups compared with controls, and persistent allergic rhinitis patients had higher cell numbers than intermittent allergic rhinitis patients in a Chinese population.⁴ In contrast, we found a lower rate of eosinophilia in persistent allergic rhinitis patients. Of all smears, 56.4 per cent were positive in the persistent allergic rhinitis group and 85.7 per cent were positive in the intermittent allergic rhinitis group. Control patients had normal smear results, but, during exacerbation periods, the intermittent allergic rhinitis eosinophilia scores were 3 and 4 in 52.4 per cent and 19 per cent of patients, respectively.

- Allergic rhinitis incidence has increased, varying between 1.4 and 39.7 per cent
- Allergic rhinitis is intermittent or persistent, and graded as 'mild' or 'moderate to severe'
- The nasal smear results were pathological in 40 of 60 allergic rhinitis patients, significantly higher than the rate in controls
- Nasal eosinophilia score and Total Nasal Symptom Score were positively correlated ($r = 0.652$; $p < 0.05$) in persistent and intermittent allergic rhinitis patients
- The nasal smear test is inexpensive, objective and simple, and should be a part of the diagnostic investigation
- Skin prick test positivity is related to allergic rhinitis; results can be used diagnostically and for treatment planning

Okano *et al.*²⁶ stated that nasal eosinophilia could be a predictor of symptoms, and that both eosinophilia per se and symptoms could be used to guide treatment. Sood¹⁵ considered that nasal eosinophilia was a highly sensitive and specific marker of allergic rhinitis. Lans *et al.*¹⁶ found nasal eosinophilia in 43 per cent of allergy patients but not in any skin prick test negative subjects. They considered that smear positivity lacked sensitivity but was specific for allergic rhinitis. Perić *et al.*²⁷ reported that eosinophil count was higher in cases of nasal polyposis than in non-atopic patients. We found positive correlations between Total Nasal Symptom Scores and both persistent and intermittent allergic rhinitis positive patients (both $p < 0.05$).

Conclusion

Nasal eosinophil levels were elevated in both intermittent and persistent allergic rhinitis patients. The extent of eosinophilia and the Total Nasal Symptom Score correlated well. The nasal smear is an inexpensive, objective and simple test, and should be part of the diagnostic investigation.

Competing interests

None declared.

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