

**The relationship between symptoms and the results of the skin prick test in patients with
allergic rhinitis**

Running title: Allergic Rhinitis symptoms and skin prick test

Category of Manuscript: Original Manuscript

Authors:

**Hayriye Karabulut, M.D.*, Emre Gunbey M.D, Baran Acar, M.D.*,*,Emrah Celik
M.D* Mehmet Ali Babademez, M.D.* , Riza Murat Karasen, M.D.***

* Kecioren Training and Research Hospital, Department of Otorhinolaryngology

Ankara, TURKEY

There is no conflict of interest between all authors.

Count of tables: 2

Count of figures: 2

Corresponding Author:

Hayriye KARABULUT, MD

Kecioren Training and Research Hospital, Department of Otorhinolaryngology

Pinarbası mahallesi sanatoryum caddesi Ardahan sok.no:1 Kecioren, Ankara, TURKEY

Tel: +90 312 356 90 00

Fax: +90 312 356 90 22

The relationship between symptoms and the results of the skin prick test in patients with allergic rhinitis

Abstract

Objectives: The aim of this study was to determine; the relationship between the skin prick test results and the allergic symptoms, and which symptom or symptoms are more associated with the skin prick test.

Methods: Of the 1462 patients who underwent the skin prick test, with the prediagnosis of allergic rhinitis (AR), 495 subjects who completed the symptoms inquiry form were included in the study.

Results: Out of 495 cases, the skin prick test was found to be positive in 358 and negative in 137. No significant relationship was found between sneezing, runny nose, itchy nose, nasal obstruction, headache, postnasal drip and the skin prick test positivity ($p>0.05$). **There was a significant relationship between ocular complaints (watering, itching, dripping in the eyes) and skin prick test results ($p=0.027$).** When the groups with positive and negative prick test results were compared in terms of severe symptoms, while the difference between itchy nose and ocular symptoms was found to be significant, this difference was not significant in terms of nasal obstruction, postnasal drip and sneezing.

Conclusion: While no significant relationship was found between symptoms accepted as allergic, such as sneezing and itchy nose, symptoms such as eye itching and watering were found to be related to allergy. We recommend performing the skin prick test routinely on patients presenting with the allergic rhinitis symptoms. This would also prevent unnecessary antihistaminic use.

Keywords: Allergic rhinitis, skin prick test, allergic rhinitis symptoms

Introduction:

Allergic rhinitis (AR) is a symptomatic inflammatory disease of the nose characterized with specific IgE-related hypersensitivity emerging clinically following the exposure of the nasal mucosa to the allergen [1]. Allergic rhinitis is the most common type of allergic diseases, and is encountered at a rate of 10-40% in the community [2,3]. Factors exposing to allergic diseases can vary between countries or different parts of a country, related to geographic, climatic and various social circumstances [4]. Allergic reactions comprise two phases of the early and the late phase. Early phase allergic reaction begins with binding of the allergen and allergen-specific IgE to the IgE receptor on the surface of mast cells and excretion of prostaglandins and leukotrienes, mainly histamine. However, late phase reaction is characterized by infiltration of various inflammatory cells like neutrophils, basophils, mainly eosinophils, and excretion of cytokines (IL-4, IL-5, IL-13), chemokines and adhesion molecules (VCAM-I, ICAM-1) along with mediators like histamine, and leukotriene produced by these cells. T cells and mast cells are important cytokine sources along with eosinophils and basophils [5].

The characteristic symptoms of Allergic rhinitis (AR) are sneezing, itching of the nose, eye and the pharynx, a runny nose and nasal obstruction [6]. AR has very important effects on the quality of life and school performance. High treatment costs emerge, and it causes loss of labor due to its high prevalence [2].

The skin prick test is a test that can be applied using commercially available inhalent and food allergens, latex or (more rarely) drugs. It is used in the diagnosis of allergic rhinoconjunctivitis, bronchial asthma, atopic dermatitis, contact urticaria and food and drug allergies [2-4].

The most important step in the treatment is determination of the causative allergens and removing them from the environment. Antihistamines and topical steroids are effective in the control of symptoms and inflammation. When this control proves to be insufficient, drug therapy or immunotherapy must be considered as alternatives [3].

The aim in this study was to compare the correlation of AR symptoms with the results of the skin prick test.

Patients And Methods:

Of the 1462 patients who underwent the skin prick test between January 2008 and February 2010 with the prediagnosis of AR, 495 subjects who completed the symptoms inquiry form were included in the study.

Age, gender, presence of nasal, ocular, pulmonary and dermatological symptoms were questioned. Patients with the prediagnosis of AR were asked to complete the symptoms inquiry form which included sneezing, runny nose, itchy nose, nasal obstruction, headache, postnasal drip, and ocular complaints for 5 days. The patients were asked to choose one of the options that matched their complaints best (absent, mild, moderate and severe) in this form. These options were scored as 0, 1, 2, 3 respectively in the assessment process. The symptoms assessment forms were required to be completed by the patients in the morning every day.

Diagnosis of AR was made on the basis of history, physical examination findings, nasal endoscopic examination findings and the skin prick test results. Presence of sneezing, watery runny nose, nasal obstruction and itchy nose, and serous secretion in the nasal cavity, pale nasal mucosa, edematous, and pale or purple conchae were interpreted in favour of AR.

The patients were examined in terms of skin findings and the presence of a rash, itching, urticaria and erythema was recorded. Coughing, dyspnea and wheezing were

evaluated as respiratory symptoms. The skin prick test was not performed on patients who had been treated with the diagnosis of asthma, on those who had a suspicion of asthma, or on those who had been using beta-blockers. The skin prick test was performed on patients who were considered as having isolated AR. Patients who were detected to have dermographism were excluded from the study.

Alyostal ST-IR (Stallegenes S.A.France) standard allergen extracts were used for the skin prick test. **For the skin prick test**, antihistamines had to have been withdrawn 10 days previously, H₂ receptor blockers had to have been withdrawn 24 hours previously, and antidepressant drugs withdrawn 20 days previously. Allergen extracts that were taken in standard doses in Quick test applicators with 8 distinct edges were applied onto the skin after having cleaned the ventral part of the forearm with alcohol. The results were evaluated 15 minutes later. Histamine hydrochloride was used as positive control and isotonic NaCl was used as negative control. The validity criterion for the test was accepted as >3mm for positive control and <3 mm for negative control. Skin reaction against the allergen with an endurance of >3mm in diameter was accepted as a positive reaction [7].

The most common 30 allergen extracts and positive and negative controls were applied using a total of 4 applicators onto the skin of forearm for the skin prick test. Two house dust mites, 3 fungal spores, 1 insect, 3 animal epithelia, 15 pollens and 6 food allergens were used.

Statistical analysis:

Statistical analysis was performed using the SPSS 15.0 program. Consistency of the data with a normal distribution was assessed using the Kolmogorov-Smirnov test. Parametric measurements were made using the intergroup Independent Sample T test, and the non-

parametric measurements were made using the Wilcoxon and the Mann Whitney U test. A p value of <0.05 was considered statistically significant.

Results:

Totally 495 subjects included in the study. According to skin prick test results, patients divided into two groups as positive and negative. The skin prick test was found to be positive in 358 and negative in 137 subjects. The mean age of the patients with was 31.7 ± 12.4 (15-66 years) in the negative group and 33.6 ± 12.1 (15-73 years) in the positive group, and there was no difference between the groups. Distribution of the patients according to gender has been presented in Table 1.

When the between groups were compared in terms of symptoms (sneezing, runny nose, itchy nose, nasal obstruction, headache, and postnasal drip) no significant relationship was found ($p > 0.05$). A significant difference was found in terms of ocular complaints (watering, itching, dripping in the eyes) ($p = 0.027$). The symptom graph between the groups was demonstrated in Figure 1, and the mean daily scores of ocular complaints were presented in Figure 2. When the groups with positive and negative prick test results were compared in symptom severities. The difference between itchy nose and ocular symptoms was found to be significant. This difference was not found to be significant in terms of nasal obstruction, postnasal drip and sneezing (Table 2).

Discussion:

Allergic rhinitis is an inflammatory disease of the nasal mucosa presenting with IgE-dependent hypersensitivity reaction, characterized with paroxysmal sneezing and a runny nose, nasal obstruction and itching [8]. Its prevalence is higher among women [7]. The distribution of gender in our study supports that of the literature. Although it appears in the nose, considering the disease as a systemic disorder is still a subject of debate [9]. Patients

usually have concomitant symptoms of allergic rhinitis and conjunctivitis and sometimes all the respiratory system is effected. Conjunctival symptoms are usually mild and almost always associated with the condition. Allergens can be divided into two groups as intrinsic and extrinsic allergens. While house dust mites, feathery domestic animals, cockroaches and fungal spores are accepted as intrinsic allergens, pollens of trees, grasses, grains are considered extrinsic allergens [10].

Runny nose, nasal obstruction, sneezing and itchy nose are 4 cardinal symptoms for allergic rhinitis. Persistence of 2 or more symptoms for over an hour in a day for many days is important for the diagnosis. The complaints of the patients are usually seen in the morning [11,12]. Ocular symptoms and irritative symptoms (itchy nose and sneezing) are more common in seasonal allergic rhinitis compared to perennial allergic rhinitis [10]. Frequency, prevalence and severity of symptoms are assessed and monitored using several quality of life questionnaires in AR patients [13-15]. These studies that are carried out using questionnaire forms include general symptom scores and allergen types.

Brown et al. [16] stated that the severity of seasonal allergic rhinitis symptoms is closely associated with grass pollen and used the conjunctival provocation test and the quantitative skin prick test for a single pollen in the assessment of seasonal allergic rhinitis. Mediators released from mast cells are effective in creating the early phase responses in allergy, and histamine is responsible in the early phase reaction in the conjunctival provocation test. The conjunctival provocation test and the skin prick test are markers of early phase reaction. Late phase reaction can be considered as the most appropriate factor for clinical disease. As a result, the skin prick test can be insufficient for indicating the clinical condition and symptom questionnaires are insufficient for prediction of the skin prick test results. Symptoms not correlating with the skin prick test or conjunctival provocation test can be related to different specific tissue factors [17].

Radcliffe et al. [18] found no correlation between the standard skin test, quantitative skin test and the conjunctival provocation tests, and the symptom scores. They compared conjunctival and pre-seasonal skin test results with the seasonal symptoms and quality of life scores of 91 patients with seasonal allergic rhinitis. The other non-nasal symptoms except for the ocular symptoms are thirst, lack of concentration, and headache, which are effective in the deterioration of the quality of life. Rhinitis-related quality of life can be assessed for example with the mini rhinitis quality of life questionnaire, along with measurement of rhinitis symptoms using conventional methods (eg. symptom scores, rhinomanometer, nasal cytology) [19]. A weak correlation was found between rhinitis-specific quality of life and symptom scores. This weak correlation was explained by using the skin prick test as a target organ. In placebo trials, investigating the relationship between allergy tests and clinical responses, there was no decreases in the symptoms with placebo. Bousquet et al. stated that the skin prick test showed stability in their study carried out using placebo. Nevertheless, they found a correlation between the quantitative skin prick test and seasonal allergic rhinitis [20]. Studies performed in the literature investigating the correlations between symptom questionnaires and the skin prick tests have usually focused on the relationship between allergen types and/or skin prick test positivity and general symptom scoring.

Chaiyasate et al. [21] could not find a significant difference between persistent and total symptom scores in their study investigating the predictive symptoms for positive skin prick test carried out on 434 patients. In the same study, severe itchy nose was found to be more prevalent in the group with positive skin prick tests; however, no significant differences were found between the symptoms in terms of predictive value when symptom characteristics were compared. In our study, ocular symptoms were also found to be significantly more prevalent along with itchy nose when severe symptom scores were compared (Table 2).

Although sneezing, runny nose and itchy nose are common symptoms of AR, no statistically significant relationship was found between skin prick test positivity in patients who had presented to our clinic with these complaints. Thus, the presence of these symptoms only seems to be insufficient for the diagnosis of allergic rhinitis in patients with allergic complaints. Diagnosis must be confirmed with the skin prick test. Besides, beginning antihistamine treatment for nasal symptoms only increases the treatment costs and causes unnecessary drug use.

In our study, the correlation value between the ocular symptoms in particular, among allergic rhinitis complaints, and the skin prick test result was found to be higher than for nasal symptoms.

Conclusion:

No significant relationship was found between skin prick test results and allergic symptoms, such as sneezing and itchy nose. Eye symptoms such as eye itching and watery eye were found to be related to skin prick test positivity.

References:

1. Schäper C, Gustavus B, Koch B, Ewert R, Hanf G, Kunkel G, et al. Effects of fexofenadine on inflammatory mediators in nasal lavage fluid in intermittent allergic rhinitis. *J Investig Allergol Clin Immunol* 2009; 19(6): 459-464
2. Bauchau V, Durham SR. Epidemiological characterization of the intermittent and persistent types of allergic rhinitis. *Allergy* 2005;60:350-3.
3. Bousquet J, Van Cauwenberge P, Khaltaev N; Aria Workshop Group; World Health Organization. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;108 (Suppl):147-334.
4. Nicolaou N, Siddique N, Custovic A. Allergic disease in urban and rural populations: increasing prevalence with increasing urbanization. *Allergy*. 2005;60:1357-60.
5. Pawankar R, Yamagishi S, Yagi T. Revisiting the Roles of Mast Cells in Allergic Rhinitis and its Relation to Local IgE Synthesis. *Am J Rhinol* 2000;14:309-317
6. Polosa R, Al-Delaimy WK, Russo C, Piccillo G, Sarv  M. Greater risk of incident asthma cases in adults with allergic rhinitis and effect of allergen immunotherapy: a retrospective cohort study. *Respirres*. 2005;28;6:153
7. Baser S, Ozkurt S, Topuz B, Kiter G, Karabulut H, Akdag B, et al. Peak expiratory flow monitoring to screen for asthma in patients with allergic rhinitis. *J Investig Allergol Clin Immunol*. 2007;17(4):211-5. *J Med Assoc Thai*. 2009;92(3):377-81.
8. **King HC, Mabry RL**. A Practical Guide to the management of nasal and sinus disorders
1.st. Ed Newyork Thieme 1993:25-58

9. Van Rijwijk JB, Blom HM, Fokkens WJ. Idiopathic rhinitis the ongoing quest. *Allergy* 2005; 60:147-81
10. Ciprandi G, Cirillo I, Vizzaccaro A, Tosca M, Passalacqua G, Pallesstrini E et al. Seasonal and perennial allergic rhinitis: is this classification adherent to real life? *Allergy* 2005;60: 882-887.
11. Howarth PH. Allergic and non-allergic rhinitis. In Middleton Adkinson NF, Yunginger JW, Busse WW et al. (edits): *Allergy principles and practice Vol II*. 6. ed., Mosby Company; 2003: 1253-1289.
12. Bousquet J, Cauwenberge PB, Khaltaev N. Allergic rhinitis and its impact on asthma: ARIA Workshop report. *J Allergy Clin Immunol* 2001; 108:147.
13. **Malling HJ**. Proposed guidelines for quantitative SPT procedures to determine the biological activity of allergenic extracts using parallel line assay. *Allergy* 1987;42:391-4.
14. Moller C, Bjorksten B, Nilsson G, Dreborg S. The precision of the conjunctival provocation test. *Allergy* 1984; 39:37-41.
15. Gergen PJ, Turkeltaub PC. The association of allergen skin test reactivity and respiratory disease among whites in the US population. Data from the Second National Health and Nutrition Examination Survey, 1976 to 1980. *Arch Intern Med*. 1991; 151:487-92.
16. Brown HM, Thantrey N, Jackson F. Species specific grass pollen sensitivity: diagnosis and treatment with single grass species allpyral vaccines. *Clin Allergy* 1979; 9: 465-72.
17. Bousquet J, Guerin B, Dotte A, Dhivert H, Djoukhadar F, Hewitt B, et al. Comparison of rush immunotherapy with a standardized grass-pollen extract and classical immunotherapy with a pyridine extracted alum adjuved extract. *Clin Allergy* 1985; 15:179-94.

18. Radcliffe MJ, Lewith GT, Prescott P, Church MK, Holgate ST. Do skin prick and conjunctival provocation tests predict symptom severity in seasonal allergic rhinoconjunctivitis? *Clinical and Experimental Allergy*, 2006;36(12): 1488-1493
19. Juniper EF, Thompson AK, Ferrie PJ, Roberts JN. Development and validation of the mini Rhinoconjunctivitis quality of life questionnaire. *Clin Exp Allergy* 2000; 30:132-40.
20. Bousquet J, Maasch H, Martinot B, Hejjaoui A, Wahl R, Michel FB. Double-blind, placebo controlled immunotherapy with mixed grass-pollen allergoids. *J Allergy Clin Immunol* 1988; 82:439-46.
21. Chaiyasate S, Roongrotwattanasiri K, Fooanant S, Sumitsawan Y. Key nasal symptoms predicting a positive skin test in allergic rhinitis and patient characteristics according to ARIA classification. *J Med Assoc Thai*. 2009; 92(3):377-81.

Table Legends:

Table 1. Distribution of gender between the groups

Table 2. Relationship between severe symptom scores and the skin prick test

Figure Legends:

Figure 1. Symptom graph between the groups

Figure 2. Mean daily scores of ocular symptoms

