KBB ve BBC Dergisi 15 (3):115-119, 2007

Nasal Specific IgE for Dermatophagoides in Perennial Allergic Rhinitis and Its Correlation With Serum Specific IgE, Prick Test and Nasal Provocation Test

Perennial Allerjik Rinitte Dermatophagoides Nazal Spesifik IgE'nin Serum Spesifik IgE, Prick Test ve Nazal Provokasyon Testi ile Korelasyonu†

***Müge ÖZCAN, MD, **Betül ATAMAN GÜLBUDAK, MD, ***Işıl OLCAY, MD, ****Kemal TEKİN, *Adnan ÜNAL, MD**

*Ankara Numune Education and Research Hospital, 1-ENT Clinic,
**Ankara Numune Education and Research Hospital, Siteler Polyclinic
***Ankara Numune Education and Research Hospital, Chest Diseases Dept.
****Ankara Numune Education and Research Hospital, Metabolism Laboratory, ANKARA

ABSTRACT

Objectives: Detection of specific IgE in the nasal secretion is not commonly used due to difficulty of obtaining standardized secretions from the nose. The correlation of the nasal specific IgE with the nasal provocation test, specific IgE in the serum and the prick test is important in order to identify the value of the nasal specific IgE in the diagnosis of house dust mite allergy.
Material and Methods: In this study, specific IgE for *Dermatophagoides pteronyssinus* (Dp) was determined in the noses of 40 patients with perennial allergic rhinitis by means of the "nasal test". Nasal provocation test, prick test and serum specific IgE values for the same allergen were also obtained.
Results: Nasal IgE had a correlation rate of 90% with the nasal provocation test. Nasal IgE had correlation rates of 72.5% and 67.5% with the serum IgE and the prick tests respectively. In six patients (15%) with a positive provocation test, the prick tests and serum IgE were negative, however, the nasal IgE was positive.
Conclusion: As a result, we may suggest the nasal test as a safe and practical alternative to nasal provocation test in Dp allergy especially if there is any discrepancy between the history and routine diagnostic tests.

Keywords
Immunoglobulin E, perennial allergic rhinitis, nasal provocation tests, skin tests

ÖZET

Amaç: Nazal sekresyonda spesifik IgE tayini burundan standardize sekresyon alımındaki zorluk nedeniyle sık uygulanmamaktadır. Nazal spesifik IgE'nin nazal provokasyon testi, serum spesifik IgE ve prick testle olan korelasyonu, nazal spesifik IgE'nin ev tozu akarı allerjisi tanısındaki değerinin açısından önemlidir.
Yöntem ve Gereçler: Bu çalışmada, *Dermatophagoides pteronyssinus* (Dp) için spesifik IgE perennial allerjik rinitli 40 hastanın burunlarında "nasal test" yoluyla ölçüldü. Aynı alerjen için nazal provokasyon testi, prick test ve serum spesifik IgE değerleri belirlendi.
Bulgular: Nazal IgE ile nazal provokasyon testinin korelasyonu %90'dı. Nazal IgE Serum IgE ve prick testi ile sırasıyla %72.5 ve %67.5 oranında koreleydi. Provokasyon testi pozitif olan 6 hastada (%15) prick test ve serum IgE negatif olmasına rağmen, nazal IgE pozitifti.
Sonuç: Sonuç olarak, Dp allerjisinde özellikle hikaye ve rutin diyagnostik testler arasında çelişki olduğu durumlarda, nazal testin, nazal provokasyon testinin güvenli ve pratik bir alternatifi olduğunu düşünmekteyiz.

Anahtar Sözcükler
Immunoglobulin E, perennial alerjik rinit, nazal provokasyon testleri, deri testleri

†Presented in 20th ERS and 23rd ISIAN Congress (Rhinostanbul) June 18-25, 2004, İstanbul

Çalışmanın Dergiye Ulaştığı Tarih: ***29.12.2006*** *Çalışmanın Basıma Kabul Edildiği Tarih:* ***01.04.2007***

≈

Correspondence

Dr. Müge ÖZCAN
Ankara Numune Eğitim ve Araştırma Hastanesi, 1.KBB Kliniği, ANKARA, TURKEY
Tel: 0 312 508 50 17 E-posta: mugeozcan@yahoo.com

INTRODUCTION

Clinical history is the most important tool for the diagnosis of allergic rhinitis. The diagnosis is usually confirmed by the detection of specific IgE in the serum or the skin of the patient. In vivo detection of the specific IgE in the target organ is possible by means of a provocation test, but this test has some well-known limitations. RAST and ELISA methods enable in vitro detection of specific IgE in the nasal secretion. These methods, however, are not commonly used due to difficulty of obtaining standardized secretions from the nose. However, detection of specific IgE in the nose may be the only way to diagnose allergy in some patients with allergic rhinitis.[1-5] In case of local allergy in the absence of systemic allergy, one can also hypothesize production of allergen specific IgE in the target organ, ie.nose in allergic rhinitis.[1,2,6]

House dust mite allergy is one of the most common causes of perennial allergic rhinitis. It was reported that the skin tests and the serum RAST showed many discrepancies for *Dermatophagoides.*[6] Therefore, a nasal provocation test may be required to diagnose house dust mite allergy in a number of patients. Use of a more practical alternative of nasal provocation test may be beneficial for these patients.

In this study, we determined the nasal specific IgE for *Dermatophagoides pteronyssinus* (Dp) in patients with perennial allergic rhinitis by means of the "nasal test". In this method, there is no need to collect the nasal secretion. We evaluated the correlation of the nasal specific IgE with the nasal provocation test, specific IgE in the serum and the prick test in order to identify the value of nasal specific IgE in the diagnosis of house dust mite allergy.

MATERIALS AND METHODS

Patient selection: The study involved 40 patients (35 females and 5 males) with perennial allergic rhinitis and 10 healthy adult volunteers.

The patients had symptoms for at least 12 months. All of them had clinical histories strongly suggestive of perennial allergic rhinitis against house dust mite, and their ages ranged between 14-63 with a mean of 34.9 years. A complete otolaryngological examination was performed. The patients with purulent nasal discharge and/or nasal polyposis were not included in the study. The patients did not use any antihistamines, β_2 mimetics or steroids for 2 weeks before the study.

Skin test: A prick test for Dp was performed using an allergen extract (ALK, Copenhagen, Denmark). A positive control was obtained using histamine, and a negative control was obtained using the negative control solution supplied by the same company. A wheal and flare reaction equal to negative control was graded as 0, a reaction 1mm bigger than negative control was graded as 1, a reaction equal to positive control (histamine) was graded as 2, a reaction bigger than positive control was graded as 3 and a reaction bigger than 20 mm and/or formation of pseudopodia was graded as 4. Skin reactions equal to or greater than 2 were regarded as positive.

Nasal provocation test: The nasal challenge kit for Dp was used for nasal provocation (ALK, Copenhagen, Denmark). The test was performed in increasing concentrations with 15 minute intervals and was considered positive if total symptom score for rhinorrhea, sneezes, itching, eye symptoms and nasal obstruction was more than 5,[7] and there was an intranasal temperature increase equal to or greater than 2^oC.[8]

Serum specific IgE: Quantitative specific IgE (against Dp) determination in serum was obtained by "coated microtiter enzyme immunoassay method" using Dr.Fooke equipment. The *allergen-coated disc* for Dp was placed into the equipment. Then the serum of the patient was introduced. The enzyme-linked anti-IgE antibodies were added. Addition of the substrate resulted in a colour change that was measured by the microplate reader (microELISA reader).

Nasal test (Nasal specific IgE): Quantitative specific nasal IgE against Dp was determined using the same method as the serum. One finger of a polyethylene glove was cut and was pierced by a fine lancet to create multiple pores. The *allergen-coated disc* was placed into this cut and pierced glove finger and the apparatus was introduced into the nose touching the medial surface of the middle turbinate. The pores allowed the nasal fluid contact with *allergen-coated disc*. The specific IgE against Dp, if present, bound the disc in situ during the incubation period. The glove finger and the disc were taken out of the nose after 5 minutes and the disc was placed into its microwell. Then the disc was placed into the equipment and a neutral buffer solution was administered instead of the serum (the discs had already bound the IgE antibodies in the nasal fluid). The enzyme-linked anti-IgE antibodies and then the substrate were added. The colour change was measured by microplate reader.

Evaluation of the results: The equipment double measured the standard solutions (0, 2, 5, 20,100, 500,

1000 IU) and a mean value for each was calculated. A standard curve was obtained using these means. The samples of the patients (both serum and the nose) were evaluated according to this standard curve.

The results for both the serum and the nose were expressed as IU/ml. Concentrations ≥0.35 IU/ml were considered as positive for both serum and the nose.[9]

Statistical analysis: Pearson's correlation test and Wilcoxon signed rank tests were applied for the statistical analysis.

RESULTS

The nasal provocation test was positive in 36 patients (90%). The prick test was positive in 24 patients (60%). The serum specific IgE was positive in 28 patients (70%) whereas the nasal specific IgE was positive in 38 patients (95%) (Table 1).

Serum and nasal IgE concentrations for Dp were in correlation (Pearson's r=0.690, p=0.01). The concentration of nasal IgE was higher than the serum concentration in 37 patients whereas the serum IgE concentration was higher than the nasal IgE in only 3 patients and this result was statistically significant (Wilcoxon signed rank test; Z=-4.664; p<0.001).

The prick test was positive in 24 patients (60%). The nasal specific IgE was positive in all of those patients whereas specific IgE in the serum was positive in 18 of them.

Both the prick test and the serum specific IgE were negative in 6 patients (15%). The provocation test was positive in 5 of them. In all of these patients, the nasal IgE was positive and was ≥0.70 IU/ml.

Nasal provocation test was negative in all of the controls. Prick test and serum specific IgE were positive in 1 control (10%). Nasal test was positive in 2 controls (20%).

The correlations of the nasal IgE, serum IgE and prick tests with the nasal provocation test are shown in Figure 1. Nasal IgE had a correlation rate of 90% with the nasal provocation test. The serum IgE and the prick tests had correlation rates of 72.5% and 67.5% with the provocation test.

All patients tolerated the nasal test well. No complications were observed related to the test.

DISCUSSION

The results of this study suggest that the measurement of nasal specific IgE against Dp by means of the "nasal test" is a highly sensitive method and is very well correlated to the nasal provocation test. The correlation of nasal specific IgE for Dp to nasal provocation test is better than either serum IgE or the prick test. The nasal test is tolerated well by the patients and may be suggested as an alternative to the nasal provocation test in house dust mite allergy.

The significance of local allergic response in the mucosal tissue of the shock organ, rather than the systemic immune response has been stressed for years.[1,10] The nasal provocation test and the clinical symptoms of allergic rhinitis correlated much better with the local level of specific IgE than with the serum concentrations or the prick test.[6,10] Although useful for identification of the responsible allergen in vivo,[11] the nasal provocation test has some important limitations. First, nasal provocation test is a time consuming test (50-60 minutes per allergen). In case of a positive reaction, one can test only one allergen per day with a free interval of two days. In addition, this test is associated with a high risk of developing an anaphylactic shock syndrome, particularly in polyvalent-sensitised patients.[9]

It was reported that the skin tests and the RAST in serum showed many discrepancies for *Dermatophagoides*.[6] Miadonna et al.[6] studied Dp allergy in 8 patients in all of whom the skin tests and the serum RAST were not in agreement with the clinical history. The authors reported that there was a complete agree-

Table 1. The relation of nasal IgE, serum IgE and prick test with the provocation test.

		Nasal IgE		Serum IgE		Prick test	
		Positive	Negative	Positive	Negative	Positive	Negative
Provocation	Positive	36	2	27	10	22	11
	Negative	2	0	1	2	2	5
Total		38	2	28	12	24	16

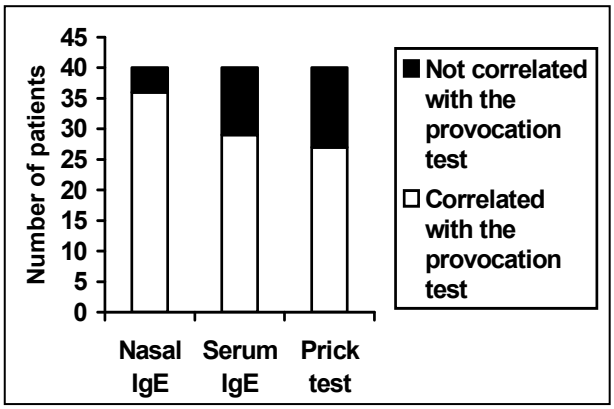

Figure 1. The correlation of nasal specific IgE, serum specific IgE and prick tests to nasal provocation test for Dp.

ment between the nasal IgE for Dp and the provocation test. Neither the prick test nor the serum RAST were correlated to the nasal provocation test. They claimed that the RAST on the nasal secretion seemed useful for detection of allergy against *Dermatophagoides*, and could be widely used in diagnosis even as an alternative to the provocation test. Huggins and Brostoff [1] found specific antibodies against Dp in nasal secretions of 14 patients who had negative results for both serum RAST and prick tests. All of the patients had positive nasal provocation tests against Dp. The authors stated that the diagnosis could have been missed in these patients if undue emphasis were placed upon the absence of a skin response. Rondon et al.[2] reported that 54% of the patients with non-allergic perennial rhinitis showed a positive nasal provocation test with Dp and 22% of them had nasal specific IgE to Dp. Botey et al.[8] compared the measurement of specific IgE against Dp in the nasal secretions of 17 patients affected by rhinitis with serum RAST, skin test and challenge test. They found a significant correlation between the serum RAST and the nasal RAST. The nasal RAST and the challenge test produced an 82% match whereas the match between the serum RAST and challenge test was 88.2%. The authors concluded that the in those cases where there were mismatches between the routine diagnostic tests, the determination of nasal RAST might be useful in producing a better diagnostic profile.

Determination of nasal specific IgE is still not widely used in the diagnosis of allergic rhinitis despite the promising results of the aforementioned studies. The main reason for that may be the difficulty of obtaining standardized nasal secretions. Some authors attempted to obtain nasal secretions after stimulation of the nose by hypertonic solutions,[6,8,10,12] however this technique may result in dilution and false negative results. Simple suctioning of the nasal fluid[13] is not practical in every patient and may result in insufficient collection of the nasal secretion.

An easier and perhaps a more reliable method for the identification of IgE in the nasal fluid may be the placement of the allergen impregnated solid phase (e.g. *allergen coated disc*) into the nose and let it soak with the nasal fluid in situ instead of removing the nasal secretion and use it as a substrate for the same solid phase in vitro. Marcucci and Sensi[14] have used this method to overcome the problems of nasal secretion sampling. They used an applicator to put the allergen impregnated paper solid phase into the nose, incubated it in situ for 5 minutes, and removed. The bound IgE was assayed with RAST. They suggested that this method for determination of nasal IgE was reliable, reproducible, and was well correlated to the serum RAST and the skin prick test. No comparison was made with the nasal provocation test. Similarly, Hauswald et al.[9] used ELISA technique, and put the allergen impregnated solid phase into the nose for identification of nasal specific IgE. They found a concordance of 86.6% between the nasal test and serum specific IgE whereas the concordance between the nasal test and the prick test was reported as 86.9%. These authors did not perform a nasal provocation test, either. Comparing the results of the nasal test with the nasal provocation test may give more information on the sensitivity and reliability of this method.

We placed the *allergen-coated disc* (the allergen impregnated solid phase) into the nose in our study and this technique eliminated the difficulty of obtaining nasal secretions. We chose Dp for the study because an alternative to nasal provocation test is needed to overcome the discrepancies of the laboratory tests against this allergen.[6]

The test was well tolerated without any complications. No problems were encountered related to the technique of the nasal test. The *allergen-coated disc* coupled with the specific IgE in the nasal secretion in situ was directly introduced into the equipment. We did not experience any problems related to the procedure of measurement of nasal specific IgE.

The low correlation rates of serum specific IgE and the prick tests with the nasal provocation test (72.5% and 67.5%) in our study strengthened the comment for the need of a more reliable test for diagnosing house dust mite allergy. The low rate of positivity of the prick test for Dp in our study may be related to our evaluation method of the prick test positivity since we regarded the test positive if

the test result was equal to or greater than the reaction with histamine. The high correlation rate of nasal IgE with the nasal provocation test (90%) may allow us to suggest the nasal test to be a safe and practical alternative to nasal provocation test in house dust mite allergy.

Our result also suggests the presence of "local allergy" in the absence of the systemic allergy. Six patients of our study group had positive nasal provocation tests against Dp but their serum specific IgE and prick tests were negative. This group of patients represent 15% of our study group. The nasal specific IgE was positive in all of them.

CONCLUSION

The nasal test may be suggested as an alternative to provocation test in house dust mite allergy owing to its high correlation rate to provocation test and its high sensitivity. It does not have the risks of the provocation test and performed easily. There is no need to collect the nasal secretion for the nasal test, so the disadvantages related to the collection of the nasal fluid are not encountered. In case of any discrepancy between the history and routine diagnostic tests, a nasal test may be performed to obtain a better diagnostic profile.

REFERENCES

1. Huggins KG, Brostoff J. Local production of specific IgE antibodies in allergic rhinitis patients with negative skin tests. Lancet 1975;26:148-50.
2. Rondon C, Romero JJ, Lopez S, Antunez C, et al. Local IgE production and positive nasal provocation test in patients with persistent nonallergic rhinitis. J Allergy Clin Immunol 2007;119: 899-905.
3. Powe DG, Jagger C, Kleinjan A, Carney AS, Jenkins D, Jones NS. 'Entopy': localized mucosal allergic disease in the absence of systemic responses for atopy. Clin Exp Allergy 2003;33:1374-9.
4. Powe DG, Jones NS. Local mucosal immunoglobulin E production: does allergy exist in non-allergic rhinitis? Clin Exp Allergy 2006;36:1367-72.
5. KleinJan A, Vinke JG, Severijnen LWFM, Fokkens WJ. Local production and detection of (specific) IgE in nasal B-cells and plasma cells of allergic rhinitis patients. Eur Respir J 2000;15: 491-97.
6. Miadonna A, Leggieri E, Tedeschi A, Zanussi C. Clinical significance of specific IgE determination on nasal secretion Clin Allergy 1983;13:155-64.
7. Linder A. Symptom scores as measures of severity of allergic rhinitis. Clin Allergy 1988;18:29-37.
8. Botey J, Gutierrez V, Pena JM, Eseverri JL, Marin A, Aulesa C. Specific IgE antibodies in nasal secretions: correlation with serum values and clinical tests. Ann Allergy 1993;70:26-9.
9. Hauswald B, Langbein A, Neumeister V, Hüttenbrink KB. Der nasale applikator test (NAPT)- ein neues verfahren zur allergiediagnostik. Allergo Journal 1998;3:143-47.
10. Merrett TG, Houri M, Mayer ALR, Merrett J. Measurement of specific IgE antibodies in nasal secretion- evidence for local production. Clin Allergy 1976;6:69-73.
11. Özcan M. Nazal Provokasyon Testi. Turkiye Klinikleri J Int Med Sci 2006; 2:16-9.
12. Ortolani C, Miadonna A, Adami R, Restuccia M, Zanussi C. Correlation of the specific IgE in serum and nasal secretions. Clin Allergy 1981;11:249-56.
13. Okuda M. IgE and IgE antibody to mite in nasal fluid. ORL J Otorhinolaryngol Relat Spec 1975;37:344-55.
14. Marcucci F, Sensi L. A new method for IgE detection in nasal mucosa. Clin Exp Allergy 1989;19:157-62.