

The correlation between intradermal testing and serum specific IgE to house dust mite in negative skin prick test allergic rhinitis adult patients

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Summary

Background: Diagnosis of allergic rhinitis (AR) is based on history, physical examination, and skin prick test (SPT) while intradermal (ID) test can be performed to confirm the diagnosis in case of negative result of SPT. However, the ID test is not recommended for cat and timothy grass allergy because of its high false positive rate. As a result, the “quantitative” technique of serum specific IgE (sIgE) measurement might be helpful to diagnose AR with more confidence.

Objectives: To evaluate the correlation between ID tests and sIgE in the diagnosis of house dust mite (HDM)-sensitive AR patients.

Methods: Patients with chronic rhinitis (CR) were recruited and SPT was performed. If SPT was negative, ID test and sIgE to HDM [*Dermatophagoides pteronyssinus* (Dp)] measurement were performed.

Results: Eighty-two patients with chronic rhinitis (CR), whose SPTs were negative for Dp, were included. There were 39 males (47.6%) and 43 females (52.4%) aged between 18 and 76 years old (mean age = 43.3 years). The ID test was positive in 13 patients (15.9%), and was negative in 69 patients (84.1 %). sIgE to HDM was positive (≥ 0.35 kUA/l) in 2 patients (2.4%).

There was a fair to moderate correlation between the size of wheal of ID test and sIgE to HDM ($r = 0.44$, 95% confidence interval: 0.19 to 0.67, $p < 0.01$).

Conclusion: ID test has a fair to moderate correlation with sIgE *Dermatophagoides pteronyssinus* and it can be used in CR patients with negative SPT where sIgE is not feasible. (*Asian Pac J Allergy Immunol* 2015;33:308-11)

Keywords: allergic rhinitis, skin prick test, intradermal test, specific immunoglobulin E, house dust mite

Introduction

Most allergic diseases are caused by the antigen and immunoglobulin E (IgE) antibody reaction. Allergic rhinitis (AR) is the most common allergic disease. Its prevalence ranges from 10 to 30% in adults, and up to 40% in children.¹ Allergic inflammation is caused by the contact of airborne allergens with the nasal mucosa, leading to IgE-mediated type I hypersensitivity. The symptoms of AR include nasal congestion, rhinorrhea, sneezing and itching. These symptoms are similar to those caused by non-allergic nasal inflammation. To precisely diagnose AR, skin prick test (SPT) is the preferred technique because it is relatively non-traumatic and reproducible.²

But when there is a conflicting result between SPT and the clinical symptoms, nasal allergen provocation test (NAPT) can be used to reveal the existence of IgE-mediated nasal inflammation. Until now, there is no consensus on positive criteria of NAPT and this technique is time-consuming and required sophisticated instruments for airflow measurement.

Intradermal (ID) test is usually done in patients who are suspected to have venom and drug allergy.¹ ID test is also used for aeroallergen that show negative SPT, yet allergy being suspected following examination of the environmental history. For instance, all of our AR adult patients are exposed to

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HDM, but only about 60% showed positive SPT to HDM.

In some patients, SPT or ID test may not be safe, so sIgE measurement is recommended. Recently, the advance technique of sIgE measurement has been developed from the original Radioallergosorbent test (RAST), which is now obsolete, to the *quantitative* measurement of IgE antibody such as the immunoCAP system. While the immunoCAP has now improved accuracy, it also comes with higher cost. If we can identify the value of ID test, it may be the alternative choice for the immunoCAP.

Only few studies have investigated the correlation between ID test and sIgE.² Some of them studied the cat and timothy grass allergens.^{3,4} Other research investigated SPT and ID test with the semi-quantitative sIgE measurement.² Regarding ImmunoCAP sensitivity for sIgE to HDM when compared to SPT recent findings show 69 % of similarity (in process of preparing manuscript). In the continuity of this work, the objective of this study was to determine the degree of correlation between ID test and sIgE level to HDM in patients with suspected AR but *negative SPT*.

Methods

Patients

The study was done at the Allergy Clinic of the Department of Otorhinolaryngology, Faculty of Medicine Siriraj Hospital. Between July 2011 and February 2014, patients with history of allergic rhinitis who had 'negative' SPT to HDM were recruited for ID test and serum sIgE measurement. The medications which may affect the result of ID were stopped according to the standard practice parameters.^{1,5}

Skin testing

SPT was done with extracts of *Dermatophagoides pteronyssinus* – Dp (10,000 AU/ml in 50% glycerine). Positive and negative controls of SPT were histamine (1mg/ml) and normal saline solution, respectively. When the SPT was negative, ID test was performed using 25 AU/ml of Dp. The results were read after 15 minutes and wheal reaction was measured in millimeters according to the standard guideline.⁵

Specific IgE

Serum of all patients were tested in a blind fashion for specific IgE antibodies using the immunoCAP system (Pharmacia Upjohn, Sweden) and the result was expressed according to the

Table 1. Results of intradermal test (ID test) and specific IgE (sIgE) in 82 subjects whose skin prick test were negative.

	sIgE +	sIgE -	Total
ID test +	1	12	13
ID test -	1	68	69
Total	2	80	82

manufacturer's criteria (KUA/ml) and classified.^{5, 6} The Class ≥ 2 (≥ 0.35 KUA/ml) were considered positive.

The study was approved by the ethical committee of the Siriraj Hospital by DOA number "403/2554 (EC3)".

Statistical analysis

The SPSS version 21 for Windows (IBM company, New York, USA) was used for the analysis. Correlation coefficients between ID wheal diameter and sIgE level were determined by Pearson's correlation. *P*-value of < 0.05 was considered statistically significant.

Results

There were 82 patients recruited in this study. Thirty-nine were males (47.6%), 43 were females (52.4%). Mean age were 44.4 years old in male and 42.4 years old in female. ID test was positive in 13 patients (15.9%). Mean diameter of ID was 0.74 mm. sIgE was positive in 2 patients (2.4%). Mean serum level of sIgE was 0.41 KUA/ml (range 0.01-0.45 KUA/ml).

The two tests were in agreement (eg. both positive or both negative) in 84 % of subjects (69/82). From 80 cases whose sIgE were negative, ID tests were negative in 68 cases (85%). From only two cases whose sIgE were positive, ID test was positive in 1 case (50%) (Table 1). The discordance of ID test and sIgE was 15.9 % [13 of 82 patients], (95% confidence interval = 8.7-25.6), as shown in Table 2. The correlation coefficient (*r*), between the diameter of ID wheal and sIgE serum level was 0.44. ($p < 0.001$, 95% confidence interval : 0.19 to 0.67)

Discussion

Diagnosis of AR requires history and the presence of sIgE to relevant allergen. sIgE can be either identified indirectly by skin test (SPT or ID test) or directly by serum level of sIgE. SPT is the

Table 2. Comparison of results obtained by intradermal test (ID test) and sIgE from the immunoCAP system.

Concordant result		Discordant result	
ID+/sIgE+	ID-/sIgE-	ID+/sIgE-	ID-/sIgE+
1	68	12	1

diagnostic technique of choice for AR because of its accuracy and reproducibility. It not only confirms the diagnosis of AR but also identifies the allergens which cause the symptoms of AR.^{5,7} In some circumstances however, SPT may be negative despite the subjects having a strong history of allergic symptoms.

ID has been recommended for venom, drug, and occupational allergy, while Nelson et al.⁴ and Woods et al.⁸ showed its reduced accuracy for diagnosing “cat allergy”. The quantitative methods of sIgE measurement have evolved from the radioallergosorbant (RAST) to the immunoCAP system. The immunoCAP system has been used in this study for “quantitatively” measuring sIgE. This method is different from the multiple allergen simultaneous test (MAST), which is simply a screening method.⁹ The practice parameter also states the accuracy of the CAP method, especially when coupled with allergy history when exposed to the suspected allergens.^{5,7}

The method of defining the sensitivity/specificity/positive predictive value (PPV)/negative predictive value (NPV) required the gold standard test as a reference. In the case of chronic rhinitis (CR), the nasal provocation test (NPT) or nasal challenge test (NCT) is considered as the gold standard. But there are some gaps in the consensus criteria of NPT especially the dose chosen for the challenge, the route of allergen administration and the criteria for defining positive response.^{10,11}

In this study we recruited *SPT-negative patients* having strong history of ‘allergy-liked’ symptoms. The underlying assumption was that despite SPT being the gold standard to diagnose allergy, sIgE (ImmunoCAP system) could be useful to clarify contradictory diagnostics. Indeed we showed that the sensitivity of sIgE (immunoCAP system) reach 70-75% suggesting that this complementary method could improve the resolution of allergy diagnostics.¹² The present study was specifically designed according to the following two predictions: 1) there is a strong agreement between SPT and quantitative measurements of sIgE by immunoCAP, 2) there is a

disagreement criteria of NPT. We thus have used the immunoCAP system as a reference for determining the sensitivity/specificity/accuracy of sIgE measurements and to assess the degree of concordance between ID test and sIgE measurements. This study showed that the ID test had 85% of specificity and 98.5% of negative predictive value when the reference was sIgE measurement made by immunoCAP system and using house dust mite as a challenge.

We also investigated the relationship between ID wheal diameter and sIgE levels. Instead of reporting the ID result as grades (1-4) or the sIgE level along a range of different classes (0-6), we preferred quantitative measurements for both variables which allowed us to implement quantitative statistical methods. For instance, we used the Pearson’s correlation coefficient to assess the relationship between ID wheal diameter and sIgE, demonstrating a fair to moderate correlation ($r = 0.44$) as reported in Chinoy et al.²

Noteworthy, we found a relatively high percentage of negative STP results otherwise diagnosed positive with ID or sIgE tests. A possible mechanism underlying these discrepancies may be that IgE are often locally distributed and particularly present in the mucosa from which samples are subsequently used in sIgE tests, exemplifying the phenomenon of Entropy applied to antibodies and antigens.¹³ The reported entropy in our study is over 40%.¹⁴ To detect the local sIgE in the target organ (nose), further studies using NPT criteria are needed.

Conclusion

In patients who are suspected to have HDM allergy, ID test has a fair to moderate correlation with sIgE. In cases of CR with negative SPT where sIgE measurements are not feasible, ID test can be used and interpretations made with a moderate degree of confidence and caution required.

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