

House-dust mite nasal provocation: A diagnostic tool in perennial rhinitis

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ABSTRACT

Background: In perennial allergic rhinitis (PAR), the skin-prick test (SPT) is a good diagnostic tool to identify the specific allergens. A nasal provocation test (NPT) is used to identify allergens and to confirm the diagnosis. The aim of this study was to determine the optimal cutoff values of symptom and peak nasal inspiratory flow (PNIF) changes after dust-mite NPT for predicting PAR. We also studied the relationship of the changes of symptoms in NPT and the wheal size of SPT.

Methods: One hundred five patients with perennial rhinitis underwent the NPT to *Dermatophagoides pteronyssinus* and the SPT. The NPT was assessed by changes in symptoms and PNIF. The optimal cutoff values of the symptoms score and PNIF changes after the NPT for predicting the SPT were determined using a receiver operating characteristic (ROC) curve. The relationship of the wheal sizes of SPT and the changes from the NPT were analyzed.

Results: Forty-eight patients had a positive SPT to *D. pteronyssinus*, of whom 33 patients had a positive NPT by increases of the symptom score. Twenty patients had a positive NPT by decreases of PNIF. The area under the ROC curve was 0.85 for symptom score changes and it was 0.612 for PNIF changes. There was a significant correlation between the wheal size of the SPT and symptom changes in the NPT.

Conclusion: Nasal provocation is a valuable test to confirm the diagnosis of *D. pteronyssinus* allergy, especially when the wheal from the SPT is small. The symptom change after the house-dust mite NPT is better than the PNIF change for predicting the PAR.

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Key words: Allergic rhinitis, diagnostic tool, house-dust mite, nasal provocation, perennial rhinitis, receiver operating characteristic curve, sensitivity, specificity

House-dust mites are major allergens in perennial allergic rhinitis (PAR). It is hard for patients to know the precipitating allergen because most are exposed to many all-year allergens such as house-dust mites and others including cockroaches, molds, or grasses. The definite diagnosis of AR depends on the clinical history supported by diagnostic tests to confirm the diagnosis and identify specific allergens. It has been accepted that the skin-prick test (SPT) is the gold standard diagnostic tool for AR in clinical practice. It has been suggested that the nasal provocation test (NPT) correlates better with nasal symptoms than the SPT but it is not practical in a clinical setting because only one allergen can be tested that day. The NPT is useful for confirming clinical relevance of a specific allergen in patients with positive reactions to multiple allergens at the SPT and for confirming nasal reactivity to specific allergens before initiating immunotherapy.¹ The technique of the NPT and the cutoff value for positive results vary.^{1–3} Although the NPT has been used for evaluating AR for a long time, there was no universal consensus and no published literature determining the optimal cutoff value of either the symptom changes or the various objective measurements. Furthermore, there are only a few studies evaluating the relationship of the SPT for house-dust mites and a house-dust mite NPT.^{4–7} The aim of this study was to determine the optimal cutoff values of symptoms score and peak nasal inspiratory flow (PNIF) after house-dust mite provocation as a predictor of AR and to study the relationship of the changes by the NPT and the wheal size of the SPT.

METHODS

One hundred five patients with clinical symptoms of perennial rhinitis (median age, 30 years; range, 15–60 years; 27 male patients) were recruited. Exclusion criteria were acute upper and lower respiratory tract infection, nasal polyps, markedly deviated nasal septum, asthma, pregnancy, severe underlying diseases, history of allergen-specific immunotherapy, and history of taking intranasal corticosteroids within 2 weeks and antihistamines within 1 week. The Ethics Committee of our institution approved the study and all patients gave written informed consent.

Nasal provocation response to *Dermatophagoides pteronyssinus* was assessed by changes in symptoms from baseline recording and recording of nasal and eye symptoms and objective measurement of PNIF. Rhinorrhea, sneezing, nasal blockage, itchy nose, and itchy eyes were recorded on a 6-point visual analog score (VAS): 0, no symptoms; 1, very mild symptoms; 2, mild symptoms; 3, moderate symptoms; 4, severe symptoms; and 5, very severe symptoms. Total symptoms scores were calculated by the sum of all symptoms (0–25). PNIF (in-check inspiratory flow meter with facemask; Clement Clarke, Harlow, U.K.) was used to measure PNIF using three repeated measurements after training. The highest value of nasal airflow from three measurements was used for calculation. The baseline of VAS and PNIF were recorded. After the patients were adapted to room temperature for at least 30 minutes, a challenge to diluents (buffered saline) was performed. Bilateral nasal provocation was performed using a nasal spray (metered-dose bottle) delivering a fixed volume of 0.125 mL/puff. If the patients had no increase of symptom score to >2 or decreases of inspiratory nasal flow of >20% after 5 minutes, the nasal provocation with *D. pteronyssinus* was performed. Bilateral nasal provocation used a nasal spray (metered-dose bottle) delivering a fixed volume of 0.125 mL/puff, 1 puff in each nostril of 1000 AU/mL of *D. pteronyssinus* (ALK Abello, Port Washington, NY). If there was no increase of symptoms within 5 minutes, then another provocation of 1 puff of 5000 AU/mL of *D. pteronyssinus* in each nostril was performed. The VAS and PNIF were recorded at 5, 15, and 30 minutes after the last dose of *D. pteronyssinus* challenge.

After NPT, all underwent SPT at the forearm to 10 inhalant allergens including Bermuda grass, Johnson grass, mold mix, feather mix,

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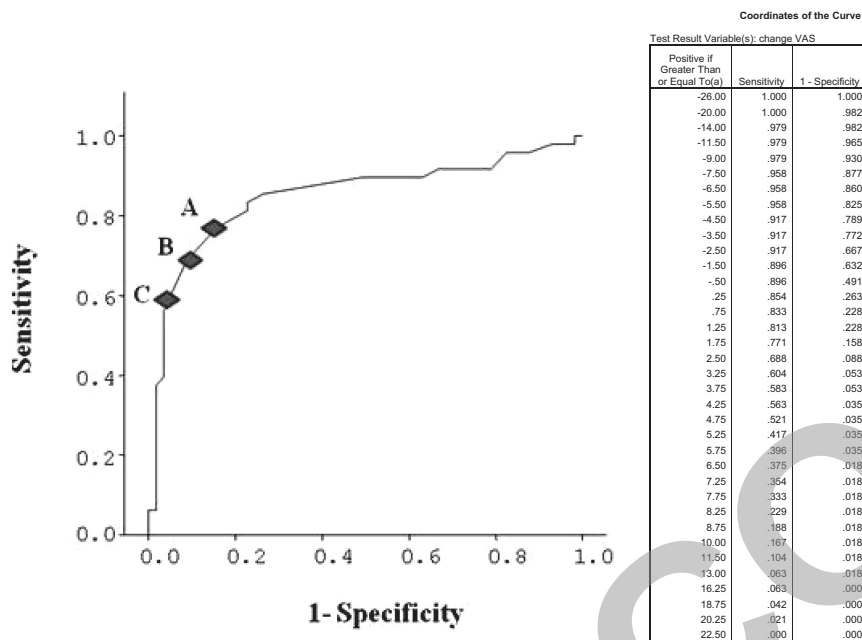
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The test result variable(s): change VAS has at least one tie between the positive actual state group and the negative actual state group.
 a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Point	VAS changes	Sensitivity	Specificity	PPV	NPV
A	2	77.08	84.21	80.43	81.35
B	3	68.75	91.22	86.84	77.61
C	4	58.83	94.73	90.32	72.97

Figure 1. The receiver operating characteristic curve of the increase of symptom scores after the house-dust mite nasal provocation test (NPT) for predicting house-dust mite allergic rhinitis. Three cutoff points of visual analog score changes after the NPT was shown including sensitivity, specificity positive predictive value, and negative predictive value of each point.

cockroach mix, dog, cat, house dust, *D. pteronyssinus* and *Dermatophagoides farinae* (ALK Abello). Histamine and glycerinated saline served as a positive and negative control. A skin-test response was considered positive if the wheal size was at least 3 mm. The wheal size of skin reactivity to *D. pteronyssinus* was recorded in all cases. AR was diagnosed if the patients had a clinical history of chronic rhinitis combined with a positive SPT.

Statistical Analysis

We used receiver operating characteristic (ROC) curves to determine the optimal cutoff values of VAS and PNIF changes after the NPT for predicting AR. The points along the ROC curve represent the sensitivity and the specificity at those cutoff points and the AUC indicates the discriminatory ability of the test. The relationship of the wheal size in SPT and changes of symptoms of the NPT and of nasal flow by measurement of PNIF after the NPT were analyzed by using Spearman's rank correlation coefficient, and a two-tailed value of $p < 0.05$ was considered statistically significant. The statistical analysis was performed using SPSS Statistical Package (Version 15; SPSS, Inc., Chicago, IL).

RESULTS

Forty-eight patients had positive SPTs to *D. pteronyssinus*, of whom 33 patients had positive NPTs by an increase of the symptom score. Twenty patients had positive NPTs by a decrease of PNIF. The most prominent symptoms after house-dust mite nasal provocation were nasal blockage (29/33) and rhinorrhea (29/33). Thirteen patients (13/33) had itchy eyes and 21 patients (21/33) had an itchy nose after

nasal provocation. One patient reported itchy palate after nasal provocation. Forty-nine patients had negative skin tests to inhalant allergens. The NPT was positive by using a VAS in seven patients in this group. Eight patients with non-AR had positive NPTs using PNIF changes' criteria. Eight patients among 105 had positive skin tests to other allergens but not to *D. pteronyssinus*. In this group, the NPT was negative in all patients using PNIF measurements; but it was positive in two patients using symptom score criteria.

The area under the ROC curve was 0.85 for VAS changes and it was 0.612 for PNIF changes (Figs. 1 and 2). The optimal three cutoff points from ROC curve of the symptom score changes for calculating the diagnostic values. The sensitivity, specificity, positive predictive value and negative predictive value of each cutoff point in the increased symptom score were are shown in Fig. 1. There was a strong significant correlation between wheal size in the skin test and symptom changes of nasal provocation to *D. pteronyssinus* ($r = 0.549$; $p < 0.0001$). There was a statistically significant mild correlation for the relationship of wheal size in the skin test and the PNIF changes ($r = 0.258$; $p = 0.008$).

DISCUSSION

To assess the positivity of the NPT, there is no consensus for the criteria for subjective assessment using symptom score and objective measurements.^{3,8,9} Because of differences of the NPT techniques and interpretation, studies using the NPT as the gold standard to assess the sensitivity and specificity of skin-prick testing give various results.^{5,10} For determining the optimal cutoff value of the NPT, our study used two outcomes including PNIF and VAS.

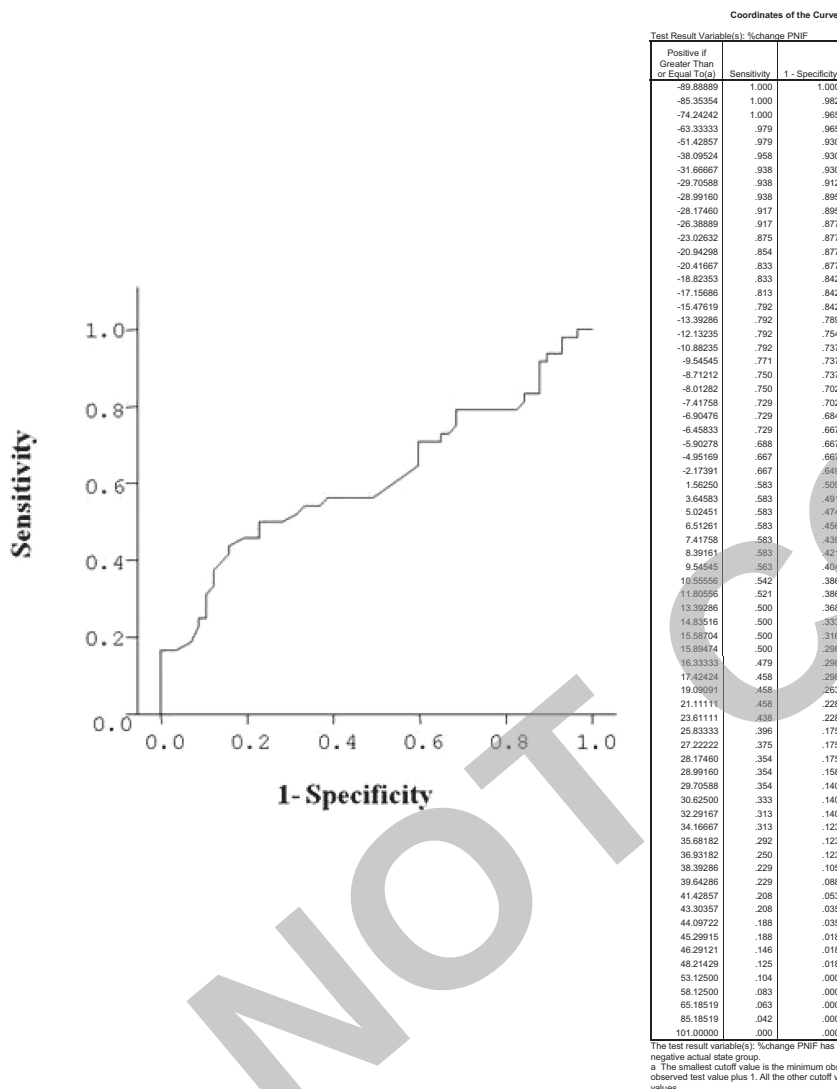


Figure 2. The receiver operating characteristic curve of the decrease of peak nasal inspiratory flow after the house-dust mite nasal provocation test for predicting house-dust mite allergic rhinitis.

PNIF was used as an objective measurement because it is easier to perform when compared with rhinomanometry and acoustic rhinometry. For ROC curve analysis, skin-prick testing was used as a reference because it was accepted as a good diagnostic tool. Comparing the ROC curves produced from VAS changes and PNIF changes, the area under the curve for VAS changes was markedly higher than PNIF changes. This suggested that the symptom score changes after the house-dust mite NPT are better than PNIF changes for predicting house-dust mite AR. We did not select the optimal cutoff value for the PNIF changes because the area under the curve was lower than 0.75, which means it is not a good diagnostic tool as a predictor of AR. The choice of the optimal cutoff point depends on the objectivity of the test. If the NPT is used as a confirmatory test, the cutoff point that gives high specificity should be used. We suggest that using an increase in the VAS of at least three from the baseline after the house-dust mite NPT is the optimal cutoff value for confirming the diagnosis of house-dust mite AR. We found a strong correlation between the symptom score after the NPT and the wheal size produced by *D. pteronyssinus*. We also found that if the wheal of *D. pteronyssinus* was between 3 and 7 mm, the NPT was positive in 24/37 (64.9%). If the wheal of *D. pteronyssinus* was >7 mm, the NPT was positive

in 9/10 (90%). We agreed with previous studies that before immunotherapy is started in house-dust mite-sensitive patients, the NPT should be performed,^{1,7} especially for patients when the diameter of the wheal from the house-dust mite SPT is <8 mm. When allergen avoidance rather than immunotherapy is planned for a patient, then only the SPT should be performed. Seven of 49 patients with negative SPT had positive NPT. This may be explained by local production of IgE antibodies as found in a previous study.¹¹ Additional investigation is needed to confirm this hypothesis.

CONCLUSIONS

Nasal provocation is a valuable test to confirm the diagnosis of house-dust mite allergy, especially when the wheal from the SPT is small. The symptom score changes after house-dust mite nasal provocation is better than from PNIF changes for predicting house-dust mite AR.

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