
Skin prick reaction and nasal provocation response in diagnosis of nasal allergy to the house dust mite

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Background: The allergen skin test is commonly used to ensure the diagnosis of allergic rhinitis even though positive results do not necessarily indicate that rhinitis is of allergic origin.

Objective: To determine the association between skin prick reactions and nasal provocation responses to *Dermatophagoides pteronyssinus* (Der p) allergen extract.

Methods: Twenty-six patients with perennial rhinitis and 25 controls underwent skin prick and nasal provocation tests to standardized Der p allergen extract. With the use of allergen extract titration delivered by a metered dose pump, nasal stuffiness, itching, and sneezing were noted, the amount of secretions measured, and nasal airway resistance was recorded by active anterior rhinomanometry.

Results: The majority of the patients with rhinitis (20/26), but none of the controls, exhibited strong skin test positivity (4⁺) to Der p allergen extract. In addition, the majority of the patients with 4⁺ skin reactions (16/20) had moderate to severe rhinitis. Significantly increased nasal reactivity to the allergen was also observed among those with 4⁺ skin test positivity. The controls exhibited nasal provocation responses only with significantly higher end-point doses of the allergen extract regardless of the skin test results.

Conclusion: Only 4⁺ skin test positivity was closely associated with increased nasal reactivity to Der p allergen among the patients with perennial rhinitis. The nasal provocation technique would be a useful adjunct testing to ensure the diagnosis of nasal allergy to the Der p mite, particularly among those patients with rhinitis with only mild to moderate skin test positivity.

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INTRODUCTION

House dust mites are one of the most common sources of allergen worldwide.^{1–6} The perennial presence of house dust mite allergens in the environment makes it difficult to ensure the diagnosis of nasal allergy to the house dust mites, which is based primarily on the clinical history. Commonly, the al-

lergen skin test has been used to ensure the diagnosis because of its sensitivity, low cost, and reproducibility even though positive skin test results do not necessarily indicate that rhinitis is allergic in nature as some nonallergic individuals may have specific IgE antibody without any allergic symptoms. Nasal provocation to the suspected allergen, on the other hand, may provide more meaningful results. Correlation of skin and nasal provocation testing to some common allergens has been reported previously.^{7–10}

Nonetheless, differences in methods and assessments of nasal provocation made comparisons of the results obtained from different laboratories difficult. Further, there has been no consensus about the recommendation for a

standardized method of nasal provocation.

This study presented a methodologic approach as an attempt to establish which method of evaluating dose-response curves of allergen extracts discriminated best between patients with perennial rhinitis and the controls. An association between the results of skin and nasal provocation testings to *Dermatophagoides pteronyssinus* (Der p) was also determined.

METHODS

Subject Selection

Subjects were recruited from the local community including patients from the University Hospital Allergy Clinic, students, and hospital staffs. They were classified at the time of recruitment as having symptomatic perennial rhinitis or no rhinitis, based on clinical features. Subjects without rhinitis had no rhinologic complaints whereas patients with rhinitis had typical perennial complaints of nasal stuffiness, sneezing and aqueous rhinorrhea, which occurred on at least 50% of the days in every month of the year. All classification was performed by a single investigator. Of the 26 patients with perennial rhinitis (median age 22 years, range 8 to 38 years), 17 were male and 9 were female. For the control group (median age 22 years, range 8 to 41 years), 13 were male and 12 were female. None of the subjects had evidence of nasal polyposis or septal deformity by anterior rhinoscopy.

Short-acting antihistamines were withheld at least two days and topical corticosteroids and long-lasting antihistamines were withheld 4 weeks before the test. Patients who had had

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airways infections during the month preceding the test were excluded. None of the subjects had previously received immunotherapy.

Patients with rhinitis were interviewed, at which time they rated their symptoms of nasal congestion, rhinorrhea, and itching/sneezing for the previous 2 weeks prior to their visit. Signs of rhinitis were evaluated by direct nasal inspection observing for mucosal/turbinate swelling and secretion. Scoring of both symptoms and signs was done on a scale of 0 to 3 (0, absent; 1, mild; 2, moderate; and 3, severe). A composite score was obtained by adding all of the various individual symptoms and signs scores with a possible maximal total score of 15. Rhinitis patients were then classified accordingly for their baseline composite score as mild, moderate, or severe (determined as composite scores of <5, 5 to 10, and >10, respectively). The study was approved by the Research Ethical Committee of the Chiang Mai University Faculty of Medicine and all subjects provided written informed consent.

Skin Prick Test

The prick test was performed with *Dermatophagoides pteronyssinus* (Der p) allergen extract (10,000 AU/mL, 50% vol/vol glycerin and 0.4% phenol as a preservative, Greer Laboratories, Inc., Lenoir, NC, USA). A disposable hypodermic needle (no. 25 Gillett) was almost horizontally introduced into the superficial epidermis with a gentle lifting motion through a drop of allergen extract on the forearm skin. Histamine solution (1 mg/mL) was used as positive control. After 15 minutes, interpretation was done as: 0 or negative, erythema only or no reaction; 1⁺, wheal <3 mm; 2⁺, wheal 3 to 5 mm with flare; 3⁺, wheal >5 to 7 mm with flare; and 4⁺, wheal >7 mm usually with pseudopods and flare. The prick test as well as the interpretation were performed by a single investigator.

Nasal Provocation Test

Subjects waited 30 minutes before the test to allow nasal mucosa to become acclimatized. After rhinoscopy, control

solution (phosphate-buffered saline with 0.4% phenol) was sprayed into each nostril with a metered dose pump delivering a fixed volume of 0.1 mL aqueous solution per puff. After provocation with control solution, 0.1 mL of increasing concentrations of Der p allergen extract (5, 50, 250, 500, and 1,000 AU/mL) were applied in both nostrils at 15-minutes intervals. After each provocation, each subject was asked to bend forward and nasal secretion was collected on a handkerchief paper during the 15-minute interval. Secretion amount was measured by weighing the handkerchief paper before and after nasal secretion collection. Subjective nasal symptoms including itching and stuffiness were evaluated and scored, numbers of sneezes were counted, and immediately before the next provocation, nasal airway resistance was measured three times in each nostril separately using a technique of active anterior rhinomanometry (Rhinomanometer PC 200, ATMOS, Germany). The median value of three consecutive measurements was taken as the nasal airway resistance. The more reactive side was used for analysis.

Statistical Analysis

End-point nasal provocation doses were compared among groups using analysis of variance on the logarithmically transformed values. Fisher's exact test was used to determine an association between the degree of skin prick reactivity and nasal provocation response as well as severity of rhinitis. A *P* value of <.05 was considered statistically significant.

RESULTS

Skin Prick Test

Der p allergen extract elicited the following reaction: strongly positive (4⁺) in the majority (20/26), moderately positive (2⁺ to 3⁺) in 5/26, and negative to weakly positive (0 to 1⁺) in 1/26 of the patients with perennial rhinitis while negative or weakly positive in majority (17/26) of the control subjects with no rhinologic complaints (*P* < .0001, Table 1). When the pa-

Table 1. Correlation Between Skin Prick Reaction to Der p Allergen Extract and Diagnosis of Perennial Rhinitis

Prick Test	Clinical Diagnosis*	
	Rhinitis (n = 26)	Controls (n = 25)
0-1 ⁺	1	17
2-3 ⁺	5	8
4 ⁺	20	0

* *P* < .0001, two-tailed Fisher's exact test.

† Same as text.

tients with rhinitis were classified according to their baseline composite symptoms and signs scores, the majority of those with moderate and severe rhinitis (16/19) exhibited 4⁺ positive skin test reactions to the allergen extract, whereas none was observed with negative or weakly positive skin test results. Nonetheless, four of seven patients with only mild rhinitis also exhibited 4⁺ skin test reactions to the extract. The association between the degree of skin test reactivity and severity of rhinitis when classified according to the baseline composite symptoms and signs scores was not statistically significant (*P* = .28).

Correlation Between Skin Test Reaction and Nasal Provocation Response

There was no significant difference in the end-point dose of Der p allergen extract observed among the controls regardless of the skin test reaction. The rhinitis patients with 4⁺ skin test reactions, on the other hand, had significantly increased nasal reactivity to the allergen extract, regardless of the threshold criteria determined (Table 2). For those patients with rhinitis with moderate (2 to 3⁺) skin test positivity, significantly increased nasal reactivity to the allergen extract was also noted, but only when nasal stuffiness and/or itching was the determining end-point criterion. Individual data are shown in Figure 1. When the patients with 4⁺ skin test reactivity were classified according to their baseline composite symptoms and signs scores, only those with moderate or severe rhinitis had significantly increased nasal reactivity

Table 2. Correlation Between the Skin Prick Reaction and Nasal Response to Der p Allergen Extract. Data represent geometric mean (range) unless indicated otherwise.

End-point Der p Allergen Extract Concentration (AU/mL)				
Threshold Criteria	Rhinitis			Controls (n = 25)
	SP: 0-1† (n = 1)	2-3† (n = 5)	4† (n = 20)	
Nasal airway resistance†	1000‡	144.5 (10-1000)	8.8§ (0.5-1000)	325.0 (25-1000)
Secretion weight¶	500	500 (5-1000)	30.9§ (0.5-1000)	467.7 (5-1000)
Nasal stuffiness*	1000	22.9§ (5-1000)	27.5§ (0.5-500)	199.5 (5-1000)
Itching*	1000	5.9§ (5-1000)	7.8§ (5-1000)	316.2 (5-1000)
Sneezing††	1000	218.8 (5-1000)	22.9§ (0.5-500)	660.7 (5-1000)

SP = results of skin prick testing.

† 3-fold increase from baseline values.

¶ 5-fold increase from baseline values.

* 1-point increase in symptom score.

†† presence of sneezing.

‡ Individual data only.

§ $P < .05$ versus controls.

|| $P < .05$ versus (2-3⁺) skin test reactivity.

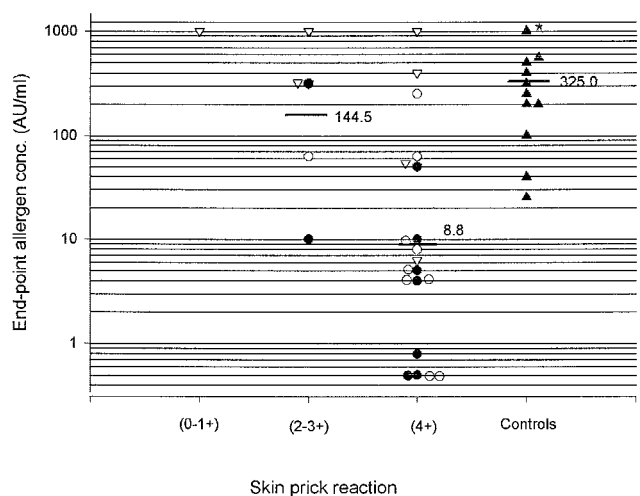


Figure 1. Correlation between skin prick test reaction and end-point nasal provocation concentrations of Der p allergen extract in patients with mild (▽), moderate (○), or severe (●) perennial rhinitis, compared with the controls (▲). Response in nasal airway resistance was the determined end-point threshold criteria. ▲* represents 15 data points.

to the Der p allergen extract. The geometric mean endpoint concentrations of the allergen extract determined by the nasal airway resistance threshold criterion, were 104.7 (range 6.3 to 1000), 6.8 (range 0.5 to 250), and 3.0 (range 0.5 to 50) AU/mL for those with mild (n = 4), moderate (n = 9),

and severe (n = 7) rhinitis, respectively ($P = .029$).

DISCUSSION

This study was primarily concerned with Der p allergen since a recent survey of house dust mite fauna in Thailand revealed that house dust mites

were identified in most dust samples collected with the highest density of mites found in dusts collected from this region and with Der p as the most abundant species found.³ Our results indeed revealed that sensitization to Der p allergen was commonly observed among perennial rhinitis patients, thus suggesting that Der p allergen might be a common cause associated with perennial rhinitis in this region.

Even though there has been no consensus about the recommendations for a standardized method of nasal provocation, the diagnostic value of measurement of changes in nasal airway resistance in nasal provocation tests has been reported.^{11,12} In this study, we compared different nasal provocation threshold criteria in an attempt to determine which methods of evaluating dose-response curves of allergen extracts discriminated best between the rhinitic patients and the controls. With the use of this method, all of the determining threshold criteria could discriminate nasal reactivity responses of severe rhinitis from the controls. The nasal stuffiness and itching response criteria could also discriminate moderate rhinitis from the controls but not from those with severe rhinitis (Table 2). This technique might be useful for objective evaluation and quantitation of nasal reactivity to the suspected antigen, which could have some clinical use in diagnosis and treatment follow-up of perennial allergic rhinitis.

Our attempt to quantitatively determine the association between the degree of skin test reactivity and nasal reactivity to the Der p allergen extract was not quite successful since the number of the patients with rhinitis who exhibited mild to moderate (1 to 3⁺) skin test reactivity in this study was rather small, and none had negative skin test reactivity to the Der p allergen extract. Our observations of the close association between 4⁺ skin test positivity and increased nasal reactivity to the Der p allergen among the majority of the patients with symptomatic perennial rhinitis, were similar to the results reported from previous

studies despite some differences in the nasal provocation technique and evaluations of the nasal response.^{7,10} Nonetheless, we observed one rhinitis patient with 4⁺ skin test positivity as well as markedly increased nasal reactivity to the Der p allergen, who presented with only mild rhinitis. Environment was possibly one of the contributing factors to explain the current mild symptoms observed in this patient. During the past few months prior to the study, after the environmental control of dust mites was introduced into his dwelling, this patient reported a remarkable improvement of his nasal symptoms.

In conclusion, the patients with perennial rhinitis with 4⁺ skin test positivity to the Der p allergen extract were very likely to have nasal allergy to the house dust mite since significantly increased nasal reactivity to the extract was observed in these patients. On the other hand, the smaller skin test reactions observed among the patients with perennial rhinitis did not necessarily indicate increased nasal reactivity. Thus, this nasal provocation technique would be a useful adjunct to ensure the diagnosis of Der p mite nasal allergy,

especially for those with only borderline skin test reactions.

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