

ORIGINAL ARTICLE

Skin prick test reactivity to common aeroallergens in asthmatic patients with and without rhinitis

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Objective: The aim of this study was to investigate the prevalence of skin prick test (SPT) reactivity to common aeroallergens among Malaysian asthmatic patients with and without rhinitis.

Methodology: An SPT using eight aeroallergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cat fur, cockroach, *Acacia* sp., *Bermuda grass*, *Aspergillus fumigatus* and *Aspergillus niger*) was performed on 206 asthmatic patients.

Results: One hundred and forty patients (68%) were reactive to at least one of the aeroallergens. Among the SPT-positive patients, a positive prick test reaction to the house dust mites, *D. pteronyssinus* (93.6%), and *D. farinae* (81.4%) was most common, followed by cat fur (20.0%), cockroach (7.9%), *Bermuda grass* (7.9%), *Acacia* sp. (7.9%), *A. fumigatus* (0.7%) and *A. niger* (0.7%). A history of rhinitis was elicited in 111 (53.9%) patients and 95 (85.3%) of these patients were SPT-positive compared with only 45 (47.4%) of 95 patients with asthma symptoms alone ($P < 0.001$). The presence of rhinitis and a young age of onset of asthma were independent factors for positive SPT reaction to at least one of the aeroallergens.

Conclusions: The prevalence of SPT reactivity to common aeroallergens is high among Malaysian asthmatics, particularly in those with an early age of onset and in those with coexisting rhinitis.

Key words: aeroallergens, asthma, rhinitis, skin prick test.

INTRODUCTION

It is well known that rhinitis and asthma coexist in many patients. Allergic rhinitis is a recognized risk factor for asthma, with 20–30% of these patients having asthma.¹ Conversely, 60–80% of patients who have asthma have coexisting allergic rhinitis.¹ A 23-year study in the USA found that asthma was three times more likely to occur in individuals with allergic rhinitis who had positive skin prick tests (SPT) to allergens.²

There have been several published reports on aeroallergens affecting Southeast Asian patients with

asthma^{3–7} and allergic rhinitis.^{5,8,9} This study was undertaken to determine the frequency of SPT positivity to common aeroallergens among Malaysian asthmatics with and without rhinitis, to evaluate the relationship between SPT reactivity and the age of onset of asthma and to assess the relationship between asthma severity and SPT reactivity as well as the coexistence of rhinitis.

METHODS

Patients

The University of Malaya Medical Centre is a community teaching hospital. Over a period of 5 months from July to November 2000, asthmatic patients aged 12 years and over who attended the weekly Asthma Clinic of the University of Malaya Medical Centre, Kuala Lumpur, Malaysia, were interviewed by one of the authors (KLL). Patients attending the clinic were mostly those on long-term follow up with the clinic although some were new cases referred from the

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Primary Care Department of the hospital and private general practitioners. All patients had typical symptoms of asthma consisting of episodic wheezing, cough or shortness of breath, and had a documented 15% or greater improvement (at least 200 mL) in FEV₁ (15 min after inhalation of β_2 -agonist) within the last year.

The patients' age, gender, age of onset of asthma and any history of rhinitis were recorded. The diagnosis of rhinitis was based on the presence of recurrent episodes of the symptom complex of sneezing, nasal pruritis, nasal congestion, rhinorrhea with or without associated postnasal drip, and with or without itching and watering of the eyes. Only patients who were non-smokers or who had stopped smoking or who had avoided passive smoking for at least 6 months were included in the study, since tobacco smoke can increase asthma severity.¹⁰ Patients who had a respiratory tract infection during the month preceding the study were excluded. Also excluded were patients with documented left ventricular failure, reflux oesophagitis or a known occupational hazard to the lower respiratory tract as these were regarded as confounders in assessing asthma severity.

The severity of the patients' asthma was classified according to clinical features which included day and night-time symptoms, either PEF rate or FEV₁ measurement and treatment intensity in the 3-month period prior to the SPT. The severity of the patients' asthma was classified into four categories according to the Global Initiative for Asthma (GINA) guidelines:¹¹ mild intermittent, mild persistent, moderate persistent and severe persistent.

Skin prick test

An SPT was carried out with a panel of eight aeroallergens which were selected based upon local presence and perceived clinical importance according to previous studies.^{3,4,12} These aeroallergens consisted of two house dust mite species (*Dermatophagoides pteronyssinus* and *D. farinae*), cockroach (*Periplaneta* sp.), cat fur, two types of mould (*Aspergillus fumigatus* and *A. niger*) and two types of pollen (*Bermuda grass* and *Acacia* sp.). All the allergens (mixed with 50% glycerine, 6% sodium chloride and 0.5% phenol as preservative) were supplied by Bencard Ltd, Brentford, UK. The atopy index represents the total number of allergens out of the eight tested to which the subject had a positive response. Skin prick tests were performed by the same investigator (KLL) between 14:00 and 17:00 hours to avoid any circadian variation in the allergic response.¹³

A volume of 6 μ L of each extract was dropped on the skin, 3 cm apart, on the volar surface of patient's forearm, approximately 3 cm below the elbow and 5 cm above the wrist.¹³ Histamine dihydrochloride, 10 mg/mL solution (diluted in 50% glycerine) and saline diluted in 50% glycerine and 0.5% phenol served as the positive and negative control, respectively. A sterile syringe needle (Terumo^R needle 23G; Terumo Corporation, Tokyo, Japan) was used to prick

the skin through the extract and control solutions. The needle held at 45° to the surface, bevel downwards, was pressed vertically and gently through the drop of test extract so that its point penetrated the epidermis and on withdrawal raised the skin. The needle tip was thoroughly rinsed with sterile water and dried with a sterile gauze to avoid contaminating subsequent pricks. For all subjects, the order of skin prick was first the positive histamine control followed by saline and then *D. pteronyssinus* followed by *Bermuda grass*, *Acacia* sp., *Periplaneta* sp., *A. fumigatus*, *A. niger*, cat fur and *D. farinae*. When the test was completed, sterile absorbent gauze was carefully applied to remove the residual extracts. The patient was instructed not to scratch, and the test was read after 20 min. The diameter of the wheal was measured. The largest diameter (D) of the wheal was added to the diameter (d) at right angle to it and the sum was divided by 2 (i.e. (D+d)/2). Only wheals of at least 3 mm in diameter larger than that of the negative control were regarded as positive.¹³ For the purpose of the present study, subjects with negative responses to all eight aeroallergens were considered non-atopic, while those having one or more tests with wheal diameters at least 3 mm larger than that of the negative control were considered to be atopic.

Thirty age-matched healthy subjects, aged 15–70 years, who did not have a history of atopic diseases such as rhinitis, eczema, asthma or documented food or drug allergy served as control subjects and were similarly tested.

Patients and control subjects were not tested if they had taken short-acting antihistamine drugs within the preceding 5 days or long-acting antihistamine drugs within the preceding 30 days or systemic corticosteroids equivalent to more than 10 mg of prednisolone per day within the preceding 28 days before skin testing. Inhaled forms of sodium cromoglycate, corticosteroid, and β_2 -agonist, oral theophylline and low-dose long-term systemic corticosteroids equivalent to 10 mg or less of prednisolone per day were not considered to be exclusion criteria for the test.¹³

The study was approved by the ethics committee of the University of Malaya Medical Centre and signed informed consent was obtained from all the patients.

Statistical analysis

The data were analysed using Statistics Package Social Sciences (SPSS, Chicago, IL, USA) version 10.0 for Windows. The χ^2 test was used to compare different percentages. For continuous variables that were normally distributed, the Student's *t*-test was used for the means. Otherwise, the non-parametric Mann-Whitney *U*-test or Kruskal-Wallis test was used to compare the data as groups. Correlation analysis was performed using the Spearman rank test. Multiple logistic regression was used to assess the strength of influence of the patient's current age, age of onset of asthma and the coexistence of rhinitis on the reactivity of the SPT. A *P*-value of less than 0.05 for a two-tailed test was considered statistically significant.

RESULTS

Two hundred and six asthmatic patients with a mean ($\pm$ SD) age of 48.0 ($\pm$ 15.5) years (range, 12–76 years) who fulfilled the inclusion criteria for the present study were interviewed and underwent the skin prick test. There were 150 (72.8%) female patients.

Skin test reaction

Of the 206 patients, 140 (68.0%) tested positive to at least one allergen while only four (13.3%) of the 30 normal controls reacted to at least one allergen ($\chi^2=32.85$, $P<0.001$). The proportion of female patients who were SPT-positive (103 (68.7%) of 150) was not significantly different from that of male patients (37 (66.1%) of 56; $\chi^2=0.126$, $P=0.722$). Similarly, the atopy indices of female and male patients were not significantly different.

No control subject and only five asthmatic patients showed reaction (e.g. wheals of <3 mm in diameter) to saline. Of the 140 SPT-positive asthmatic patients, 131 (93.6%) patients reacted to *D. pteronyssinus* and 114 (81.4%) to *D. farinae*. Taken together, 137 (97.9%) of 140 SPT-positive patients reacted to either or both of the dust mites. Cat fur was the next most common allergen and sensitization to the outdoor aeroallergens, pollens of *Acacia* sp. and *Bermuda* grass was less frequent (Table 1). The number of positive aeroaller-

gen skin tests amounted to only one in 11.7% of all the patients tested, two in 38.8%, three in 13.3%, four in 1.9%, five in 1.9%, and six in 0.5%.

The mean ($\pm$ SD) age of SPT-positive patients at 44.9 ($\pm$ 15.2) years was significantly lower than that of SPT-negative patients at 54.2 ($\pm$ 14.3) years ($P<0.001$). There was a significant negative correlation between the patient's age and the atopic index ($r=-0.281$, $P<0.001$).

Age of onset of asthma

The majority (117 of 140 (83.6%)) of SPT-positive patients were younger than 40 years at the time of onset of their asthma (Table 2). There was a significant difference in the distribution according to age of asthma onset between SPT-positive and skin SPT-negative patients; patients were less likely to be SPT-positive if the age of asthma onset was above 40 years (23 of 54 (42.6%) vs 117 of 152 (77%); $\chi^2=26.542$, $P<0.001$).

The atopic indices were significantly higher in patients whose asthma first occurred before the age of 40 years. There was a significant negative correlation between the age of asthma onset and the atopic index ($r=-0.318$, $P<0.001$). The mean age of onset of asthma for the atopic patients was 24.0 ($\pm$ 15.9) years compared with 36.5 ($\pm$ 18.6) years for the non-atopic patients ($P<0.001$).

Table 1 Frequency of skin test positivity to specific allergens ($n=140$)

Allergen	With rhinitis ($n=111$) No. patients showing a positive reaction (%)	Without rhinitis ($n=95$) No. patients showing a positive reaction (%)	Total no. patients showing positive reaction ($n=140$)
<i>Dermatophagoides pteronyssinus</i>	88 (79.3%)	43 (45.3%)	131 (93.6%)
<i>Dermatophagoides farinae</i>	79 (71.2%)	35 (36.8%)	114 (81.4%)
Cat fur	24 (21.6%)	4 (4.2%)	28 (20.0%)
Cockroach (<i>Periplanata</i> sp.)	8 (7.2%)	2 (2.1%)	11 (7.9%)
<i>Bermuda</i> grass	10 (9.0%)	1 (1.1%)	11 (7.9%)
<i>Acacia</i> sp.	11 (9.9%)	0	11 (7.9%)
<i>Aspergillus fumigatus</i>	1 (0.9%)	0	1 (0.7%)
<i>Aspergillus niger</i>	1 (0.9%)	0	1 (0.7%)

Table 2 Distribution of asthmatic patients according to skin test reactivity and age of asthma onset

Age at asthma onset (year)	Positive to at least one allergen	Negative to all allergens tested	Median atopic index (25th–27th percentiles)*
1–10	40 (80%)	10 (20%)	2.0 (1.0–2.25)
11–20	24 (93.2%)	2 (6.8%)	2.0 (2.0–3.0)
21–30	28 (66.7%)	14 (33.3%)	2.0 (0.0–2.0)
31–40	25 (73.5%)	9 (26.5%)	2.0 (0.0–2.0)
41–50	15 (48.4%)	16 (51.6%)	0.0 (0.0–2.0)
>50	8 (33.3%)	15 (66.7%)	0.0 (0.0–2.0)

* The atopic indices of patients with onset of their asthma at or below 40 years of age were significantly higher than those of patients with a later age of asthma onset (Kruskal–Wallis test, $P=0.029$).

Table 3 Asthmatic patients with and without rhinitis symptoms

	With rhinitis (n = 111)	Without rhinitis (n = 95)	P-value
Mean ($\pm$ SD) age of onset of asthma (years)	22.4 ($\pm$ 15.9)	34.6 ($\pm$ 17.7)	<0.001
Skin prick test (No. patients (%))			
Positive to at least one allergen	95 (85.6%)	45 (47.4%)	<0.001
Negative	16 (14.4%)	50 (52.6%)	

Table 4 Skin prick test reactivity, rhinitis and severity of asthma

	Mild intermittent (n = 10)	Mild persistent (n = 16)	Moderate persistent (n = 47)	Severe persistent (n = 133)	P-value
Skin prick test					
Positive to at least one allergen	7 (70%)	10 (62.5%)	37 (78.7%)	86 (64.7%)	0.334
Negative	3 (30%)	6 (37.5%)	10 (21.3%)	47 (35.3%)	
Rhinitis					
Present	5 (50%)	10 (62.5%)	29 (61.7%)	67 (50.4%)	0.503
Absent	5 (50%)	6 (37.5%)	18 (38.3%)	66 (49.6%)	

Association with rhinitis

One hundred and eleven (53.9%) of the 206 patients had a history of rhinitis and the mean age of asthma onset in patients with both asthma and rhinitis was significantly younger than that in patients with asthma alone (Table 3). Ninety-five (85.6%) of these 111 patients with both asthma and rhinitis had a positive SPT reaction to at least one allergen compared with 45 (47.4%) of the 95 patients with asthma alone ($\chi^2 = 34.34$, $P < 0.001$).

Clinical severity of asthma

There was no difference in clinical asthma severity between the SPT-positive and SPT-negative patients (Table 4). The proportions of patients with rhinitis were not significantly different in the four different categories of asthma severity.

Effect of the patient's current age, age of onset of asthma and coexistence of rhinitis on skin prick test reactivity

Multiple logistic regression analysis showed the presence of coexisting rhinitis ($P < 0.001$; Odds ratio (OR), 4.83; 95% confidence interval (CI), 2.33–10.0) and a young age of onset of asthma ($P = 0.013$; OR, 1.03; 95% CI, 1.01–1.05) but not the patient's current age ($P = 0.802$; OR, 1.00; 95% CI, 0.98–1.03) to be significant independent factors for positive SPT to at least one of the aeroallergens.

DISCUSSION

The results of SPT in this population of asthmatics aged 12 years and over showed that 68% were atopic.

The prevalence of atopy among asthmatic patients has been reported to be 60–80% in other series using SPT responses to environmental inhaled allergens.^{14–16} The most frequent aeroallergen causing a positive reaction to the SPT in this group of asthmatics was house dust mites (*D. pteronyssinus* and *D. farinae*). However, testing with aeroallergens perceived to be important in the community may be a self-fulfilling prophecy. Such a practice is based on the background information provided by previous investigations conducted in the region but not all relevant aeroallergens might have been included.

As both allergen SPT reactivity and serum immunoglobulin E level tend to decrease with advancing age,^{16–18} it is not surprising that the mean age of the SPT-positive patients was younger than that of those who were SPT-negative.

In the present study, 53.9% of the asthmatic patients had a history of rhinitis. This finding is in accordance with the prevalence of 44–81% reported in other series.^{16,19} Previous studies^{20,21} showed that allergic rhinitis is the most common type of rhinitis, particularly among those patients with coexisting bronchial asthma.¹⁶ The common occurrence of allergic rhinitis and asthma together suggests that they probably have similar underlying aetiology and pathology.

A comparison of the SPT-positive patients with the SPT-negative patients in the present study revealed a number of significant differences. First, sensitivity to common aeroallergens was significantly more frequent among asthmatic patients whose age of onset of disease was before 40 years. A higher proportion of the atopic asthmatics had rhinitis compared to the non-atopic asthmatics. In fact, the present study showed that the presence of coexisting rhinitis was a significant independent factor for a positive SPT to at least one of the aeroallergens. The study by Kalliel *et al.*¹⁶ and a study from a neigh-

bouring country⁵ also show that sensitization to aeroallergens is more frequent among patients with both asthma and rhinitis than it is in those with either condition alone. Our patients who also had rhinitis were more likely than those with asthma alone to show a positive SPT reaction to three or more allergens.

Asthma severity has been difficult to quantify. Asthma severity is most often defined by its 'physiological' severity (i.e. the number of attacks or certain types of symptoms per unit time and the chronic *vs* intermittent usage of certain types of medications). This criterion was applied in the classification of asthma severity in the present study. The high proportion of patients with moderate to severe asthma in this study population is characteristic of asthmatic populations treated at a tertiary referral hospital and an asthma specialist clinic. In the present study, there was no difference in clinical asthma severity between atopic and non-atopic subjects. This finding is in agreement with those of Kalliel *et al.*¹⁶ and Inouye *et al.*²² The frequency of rhinitis did not differ in patients in different categories of asthma severity. This is in keeping with the finding of another study in which the frequency of rhinosinusitis was similar in patients with mild-to-moderate asthma and in patients with severe asthma.²³

There are several limitations of the present study. The study was conducted in a convenience sample and smokers were excluded which is not representative of Malaysian asthmatic patients in general. There may be differences in terms of urban *vs* rural populations, the effects of pollution and the effects of Westernization on the prevalence of atopic diseases. There could have been some bias in the results since the study was conducted over a limited 5-month period and asthmatic subjects with certain allergen sensitivities might present at other times of the year. The low prevalence of SPT positivity to pollens and mould may be related to an insufficient number of allergens being tested. The recall bias of the age of onset of asthma is a potential source of error. The assessment of asthma severity based on symptoms and treatment intensity in the 3-month period prior to the SPT might underestimate severity in patients with important seasonal variations in the activity of their disease.

A potential limitation is the risk of carry over of allergen by the technique of SPT. However, given the low carry over of histamine to saline results this is unlikely to be relevant.

In conclusion, there is a high prevalence of sensitization to common aeroallergens among asthmatic patients, particularly those with coexisting rhinitis. Indoor allergens, especially house dust mites, are the commonest aeroallergen affecting atopic asthmatics. Sensitization to outdoor allergens appears to be less common among this group of Malaysian asthmatics. However, the relevant aeroallergens to be included in skin prick testing panels for the country may need to be re-evaluated. Measures should be taken by asthmatics to avoid or reduce their exposure to aeroallergens to which they have been sensitized.

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