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ORIGINAL ARTICLE

Prediction of atopy by skin prick tests in patients with asthma and/or persistent rhinitis

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Abstract
Background: Patient history gives important clues about the likelihood of atopy. However, the accuracy of assessment of atopy based on detailed allergy history is low. The objective of this survey was to determine the successful prediction rate of atopy by a questionnaire and the effect of various factors on the successful prediction.
Methods: A standard questionnaire including detailed allergy history was filled in by two experienced allergists for 169 patients having bronchial asthma and/or persistent rhinitis symptoms. Skin prick test (SPT) results were predicted based on the clinical data obtained by a questionnaire. Final diagnosis was made after SPT. Sensitivity and specificity analysis of SPT results prediction was investigated using two different cut-off values (3 mm and 5 mm) for positive tests, and factors associated with successful atopy prediction were analysed.
Results: SPT was predicted to be positive in 42.6% and was positive in 36.1%. Depending on SPT results with the cut-off value 3 mm, prediction sensitivity was 77%, specificity was 65.3%, positive predictive value was 65%, and negative predictive value was 86%. Successful positive atopy prediction was associated with age; true negative prediction was also associated with age and high education. With the threshold of 5 mm for a positive test, sensitivity, specificity, positive and negative predicted values were 91%, 61%, 14% and 99%, respectively.
Conclusion: It seems that the success rate of detailed history is high for negative prediction. However, detailed history alone does not seem to be efficient for atopy prediction.

Introduction

Skin prick test (SPT) is standard for diagnosis of atopy and identifying the sensitisation to specific allergens. In clinical allergy practice, diagnostic management is made by performing SPT, which is a simple and safe procedure.[1] However, in general practice, SPT is not used very commonly and allergy diagnosis is usually made by doctors' opinion. One of the reasons for not integrating SPT into general practice is its cost. Another reason is the need for training and time for performing and interpreting the results of SPT.

Although patient history gives important clues about the likelihood of atopy, the accuracy of an assessment of atopy based on detailed allergy history is low.[2] There is no

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standard validated questionnaire for identifying atopic status. Detailed allergy history, including age, gender, age at onset of disease, duration of disease, exacerbating factors, seasonality of symptoms, symptom differences at indoors and outdoors, pet ownership, family history of allergic disease, smoking status, etc. can help to predict patients' allergic status. Successful prediction is important to distinguish allergic and non-allergic disease correctly and to take the right decisions for the treatment, including allergen avoidance. The aim of this survey was to determine the successful prediction rate of atopy in patients having bronchial asthma (BA) and/or persistent rhinitis (PR) symptoms by a questionnaire based on detailed history and the effect of various factors on the successful prediction.

Materials and methods

Patients and questionnaire

We identified adult patients (16–79 years of age) admitted to our Adult Allergy Unit for the first time with symptoms of BA and/or PR. One hundred and sixty-nine patients who had still active problems regarding their disease and who had not requested a disease-related allergy consultation in the previous years were included. None of the patients were refereed from primary practice or specialist practice. Patients with a history of anaphylaxis, urticaria or angio-oedema were excluded and those who had had an SPT in the past were also excluded. The university ethical committee approved the study and informed consent was obtained from all participants. A standard intake history questionnaire was completed by direct face-to-face interactions by two experienced allergists (professor of allergy and pulmonology; 18 years of allergy practice, associate professor of allergy and pulmonology; 8 years of allergy practice). The questionnaire included age, gender, duration of symptoms, age onset of disease, education level, familial atopy, pet ownership, smoking status, and accommodation in urban/rural region. Patients not eligible to respond to the questionnaire were not included. After examination by the same two physicians, possible diagnosis was made. Physical criteria found during the exam were not used in making the prediction of atopy. Standardised questions were not used to detect allergy symptoms and allergists made their prediction of atopy and SPT results depending on patients' anamnesis and the clinical data obtained by a questionnaire. After performing SPT, final diagnoses were made. The results of the test and the predicted results by the allergists were compared.

Skin prick tests

Atopy was tested by SPT reactions to nine common aero-allergens, prepared by the firm Alyostal (France) (*Dermatophagoides pteronyssinus*, *Phleum pratense*, *Olea europea*, *Artemisia vulgaris*, *Parietaria officinalis*, *Corylus avellana*, *Betula verrucosa*, cat, and dog). Tests were carried out as described by Österballe and Weeke.[3] Histamine and saline were used as positive and negative controls, respectively. Resulting wheals were measured after 15 min. A positive reaction was defined as a wheal with geometric mean diameter of at least 3 mm. SPT was not performed in cases of pregnancy, dermographism and use of antihistamines.

Statistical analysis

Skin prick test was used as the gold standard to describe atopic status. Prediction success was described as true positive and true negative rates. Sensitivity and specificity analysis of SPT results prediction was investigated using two different cut-off values (3 mm and 5 mm) for positive test and factors associated with prediction success (accuracy, positive predictive value, and negative predictive value) were analysed according to the descriptions below.

		Test result (atopic status)	
		Negative (N)	Positive (P)
Prediction	Negative	True (T) N	False (F) N
	Positive	FP	TP
		Specificity %: $(TN/N) \times 100$	Sensitivity %: $(TP/P) \times 100$

True positive: Test result and the prediction are positive.
True negative: Test result and the prediction are negative.
False positive: Although test result is negative prediction is positive.
False negative: Although test result is positive prediction is negative.

Sensitivity: Determining true positivity among atopic patients (test positive and atopic): TP/P
Specificity: Determining true negativity among non-atopic patients (test negative and non-atopic): TN/N
True positive prediction rate: TP/(TP + FP)
True negative prediction rate: TN/(TN + FN)
Accuracy (correct prediction rate): (TP + TN)/(TP + FP + TN + FN)

Chi-square test was used in comparisons of categorical variables. Fisher's exact test was used when predicted frequency was less than five in at least 25% of the cells. Student's *t*-test and Mann–Whitney *U*-test were used in comparisons of continuous variables with and without normal distribution, respectively. $P < 0.05$ was considered significant in statistical comparisons.

Results

The mean age of the patients was 34 ± 12.5 and 71% were females. The mean symptom duration was 93.3 ± 105.5 months. The rates of familial atopy, smoking status, having pets, high education and living in urban area were 52.1%, 23.1%, 10.1%, 50.3% and 95.9%, respectively. SPT results were predicted to be positive in 42.6% and they were determined positive in 36.1% after the test. Depending on SPT results with the cut-off value of 3 mm, sensitivity, specificity, true positive prediction and true negative prediction rates were 77% (47/61), 77% (83/108), 65.3% (47/72) and 85.6% (83/97), respectively. When the sensitivity and specificity analysis was repeated with the threshold of 5 mm for positive

test, the prevalence of atopy was found to be 6.5%. Comparison of sensitivity and specificity analysis for different cut-off values are given in Table 1.

Although successful positive prediction was associated with age (35.5 ± 12.4 and 29.1 ± 11.9; *P*: 0.004, in successful and unsuccessful prediction groups, respectively); it was not associated with duration of disease and age onset of disease ($P > 0.05$). Gender and familial atopy were not associated with true positive prediction. Successful prediction rate was similar in bronchial asthma patients compared to perennial allergic rhinitis and seasonal allergic rhinitis groups. Sensitisation of patients to pollen or mite did not affect the true atopy prediction rate. False positive prediction was high in familial atopic patients (72% and 27% in familial

Table 1 Sensitivity, specificity and the accuracy values of SPT result prediction.

	3 mm	5 mm
	Percentage (95% CI)	
Sensitivity	77.0 (66.4–87.5)	90.9 (73.1–1.00)
Specificity	76.9 (68.9–85.0)	60.8 (53.1–68.4)
Accuracy	76.9 (70.5–83.4)	62.7 (55.4–70.0)
PPV	65.3 (53.8–76.1)	13.9 (5.8–21.9)
NPV	85.6 (78.9–93.0)	99.0 (96.9–1.00)

PPV: positive predictive value; NPV: negative predictive value.

Table 2 Association between successful SPT result prediction and patient related factors.

Factor	*N*	Accuracy %	PPV %	NPV %
Gender		*P: 0.78*	*P: 0.86*	*P: 0.75*
Female	*120*	77.5	64.6	86.1
Male	*49*	75.5	66.7	84.0
Age (years) mean (SD)		***P: 0.004***	*P: 0.65*	***P: 0.003***
	34.0 (12.5)	**35.5 (12.4)****	28.7 (8.2)	**39.3 (12.7)****
Duration of symptoms (years) median (IQR)		*P: 0.22*	*P: 0.34*	*P: 0.75*
	4 (2–10)	4 (1.9–10.0)	5 (3–10)	10 (3–20)
Smoking status		*P: 0.38*	*P: 0.96*	*P: 0.09*
Never	*130*	74.6	65.6	81.3
Ex-smoker	*17*	88.2	60.0	100.0
Current-smoker	*22*	81.8	66.7	100.0
Pet animals		*P: 0.20*	*P: 0.26*	*P: 1.00*
Yes	*17*	64.7	44.4	87.5
No	*152*	78.3	68.3	85.4
Familial atopy		*P: 0.53*	*P: 0.16*	*P: 0.19*
Yes	*88*	75.0	70.8	80.0
No	*81*	79.0	54.2	89.5
High education		*P: 0.55*	*P: 0.58*	***P: 0.01***
Yes	*85*	78.8	62.8	**95.2***
No	*84*	75.0	69.0	78.2
Living in the city		*P: 0.72*	*P: 0.60*	*P: 1.00*
Yes	*162*	77.2	66.2	85.1
No	*9*	71.4	50.0	100
Asthma		*P: 0.36*	*P: 0.95*	*P: 0.26*
Yes	*80*	80.0	65.6	89.6
No	*89*	74.2	65.0	81.6
Mite positive		*P: 0.11*	*P: 0.11*	
Yes	*58*	60.3	60.3	NA
No	*14*	85.7	85.7	
Pollen positive		*P: 0.11*	*P: 0.11*	
Yes	*26*	76.9	76.9	NA
No	*46*	58.7	58.7	

Mean and SD of age in the accurate, true positive, and true negative cases are depicted.
Median and IQR (interquartile range) of the duration of symptoms (years) are depicted.
NA: not available; PPV: positive predictive value; NPV: negative predictive value.
Significant findings are marked in bold type.
* $P < 0.05$.
** $P < 0.01$.

atopy positive and negative patients, respectively), females (68% and 32% in female and male patients, respectively), patients not having pets (20% and 80% in patients having pets and no pets, respectively) and non-smokers (76% and 24% in non-smokers and smokers, respectively). True negative atopy prediction was associated with age (39.4 ± 12.7 and 27.9 ± 14.6, *P*: 0.003; in the true and false negative groups, respectively) and high education (48.2% and 14.3%, *P*: 0.03; in true and false negative groups, respectively). Only older age was influential in making true positive and negative prediction of atopy. The summary of the results is shown in Table 2.

Discussion

This current study demonstrates the accuracy of the prediction of atopy and influential factors in making successful prediction. A previous study disclosed that the false positive rate of structured history was high and accuracy of it was low which was not enough for the correct diagnosis of allergy.[2] Our study also explains that assessment of atopy based on detailed allergy history is not efficient for true atopy prediction. The predictive value of detailed allergy history varies in individuals with different histories, and may vary in specialist and general practice populations. Generally primary care physicians treat mild allergies, allergy consultation is requested for more severe allergies and the successful prediction may depend on the severity of the allergic condition in question. Probability of true prediction of cat allergy may be difficult in a child who had no cat in his/her home or the reaction to the same allergen could be different at a different time period of life. Probability of true prediction may be reduced when a patient had a previous history of allergy that has since resolved. In this study, active symptomatic adult patients were assessed by experienced allergists according to patients' allergy histories. None of the patients were refereed from primary practice or specialist practice; they all had allergy symptoms with a long duration and were assessed by an allergist for the first time. We could not evaluate specificity analysis in a different patient setting. It was surprising that only 36% of patients were atopic and also 42% were predicted positive. This would mean that 58% of patients had unspecified symptoms and they thought that they were allergic. The true prediction rate was low. When the individual contribution of various factors including age, gender, smoking history, pet ownership, familial atopy, duration of disease, age onset of disease, education level, and accommodation in urban/rural region to successful atopy prediction rate was examined, it appeared that their influence on true prediction expect for age is not sufficient. Severity of symptoms was not used in making prediction of atopy which is a limitation. Also medical treatment was not assessed. This could be a strong predictor of atopy and the influence of age on true atopy prediction may be due to the degree of the disease in different age groups. High education was also strongly correlated with successful negative prediction; this might be due to better self description of educated patients. Urbanisation, pet ownership and smoking did not affect the prediction rate. There were very small number of patients in each category and it was difficult to establish the role of these factors. Although allergic sensitisation status of both parents and first offspring were observed to be related to the risk of allergic sensitisation and familial atopy seems to be significantly associated with successful prediction,[4] our results did not support this. False positive prediction was high in familial atopic patients.

The sensitivity and specificity of SPT result prediction was 77% with the threshold of 3 mm for a positive test. Sensitivity increased to 91% when we repeated the analysis with the 5 mm cut-off value. Negative prediction rate was almost 100% at that cut-off point. Larger skin reactions predict higher likelihood of positive response and also studies have indicated that larger wheal size would correlate better with clinical allergen reactivity.[5,6] In our study accuracy and positive predictive value of SPT result prediction was low at that high cut-off value. However it ruled out allergy more significantly compared with the 3 mm cut-off point.

In conclusion, detailed history, including the above factors except for age and education level does not seem to be efficient for atopy prediction. Comprehensive assessment of the patient is needed to identify the patient's allergic status and one the most important parts of this assessment is SPT. It seems that the success rate is high for negative prediction. Interpretation of structured history correctly in general practice may help to rule out allergy. Atopy likelihood ratio may be more useful, which is the reflexion of the patients' history to the probability that the patient has the allergy. Patients who have high likelihood ratio of atopy should be assessed in detail, including SPT in general practice. A study has been carried out in our clinic to develop a questionnaire based on a scoring system for SPT prediction.

Conflict of interest

The authors have no conflict of interest to declare.

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