ORIGINAL ARTICLE

The Predictive value of Phadiatop Paediatric in the Determination of Atopy in Allergic Diseases in Children

by

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Abstract

We obtained 28 patients with asthma bronchiale in this study. The presumptive diagnosis of allergy was made on the basis of history and physical examination. The positive result of the skin test to inhalant extracts and positive history of inhalant allergy add a confirmatory evidence in the diagnosis of inhalant allergy. The diagnosis of food allergy was judged by positive result in the provocation test. This study provided 15 patients with food allergy and 13 patients with food and inhalant allergy. House dust and mites were the most prevalent positive result in the skin test. While in the provocation test, egg and milk were found as the most prevalent food causing symptoms of allergy. The skin test predicted the atopy with an efficiency of 53.5%, while Phadiatop Paediatric predicted the atopy with an efficiency of 82.1%. We concluded, as a screening procedure in allergy, the Phadiatop Paediatric is better than the skin test. Nevertheless the skin test has its superiority in the development of logical environmental controls and as a guide to immunotherapy in inhalant allergy.

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Introduction

The diagnosis of allergic diseases can be established on the basis of 4 clinical view points i.e. : the history of the disease, the physical examination, the laboratory examination and of so called "elimination and provocation test" [1] The history and physical examination are the most important elements for the evaluation of possible allergic disease. If after completing such an interview and examination the physician suspects strongly that the patient's complaint are due to allergy to environmental factors, further investigation is not always necessary. General environmental control measures with or without medication, such as antihistamines, may control the symptoms sufficiently to avoid further diagnostic tests. Often such an approach is not sufficient either because the patient is not convinced that an allergy is really the cause, or because a direct relationship is not clear. Specialized diagnostic procedures then may be valuable adjuncts to the history and physical examination. The physician must formulate a differential diagnosis that will serve as a guide for selection of appropriate test [2].

The diagnosis of atopy in clinical practice is frequently based on skin test using several combinations of allergenic extracts [3] A complete allergy work up should be based on detailed clinical history, skin test and determination of specific IgE in the serum. The measurement of circulating serum levels of specific IgE can be used as an alternative to skin testing. The use of the Radioallergosorbent test for specific IgE has been shown to correlate with the result of skin tests, and accord at least as well with patient's history of allergic disease and the result of direct allergen provocation. Its routine use in clinical practice, however is controversial. It often provides confirmatory evidence of hypersensitivity and can be valuable in the management of patients in whom skin test are not possible, for example in cases of wide spread dermatitis, dermographism or drug induced supression of the cutaneous reactivity. The major critism concerns the RAT's lack of sensitivity and high cost, two drawbacks which limit the use of the test as a screening procedure in allergy.

Phadiatop Paediatric, a new method for simultaneous measurement of specific IgE directed against some different allergens, either foods and inhalant allergens has recently been developed employing enzyme immuno assay. The multiple allergosorbent enzyme immuno assay needs the minimum requirement of technical knowledge to perform and the result can be obtained within 24 hour of analysis of a single blood sample. Since the technique is potential as a diagnostic tool to determine atopy in allergic diseases, we try to compare it with the result of skin test and "elimination and provocation test".

Materials and methods

Every patient which was refered to the Allergic clinic, Department of Child Health, Dr. Soetomo Hospital with the suspicion of various allergic diseases was selected for this study. From the history, physical examination and laboratory examination we obtained patients indicative of having an allergic disease. Eosinophils

count and skin test add a contributory evidence of atopy. Skin scratch testing to the following allergenic extracts was performed: housedust, milk, shrimp, fish, egg, dog dander, cat dander, mites *(Dermatophagoides pteronyssinus)*, feather and rice. Testing to all 10 allergens together with histamine and diluent control was performed on the right forearm [4,5]. The allergenic extracts were provided by Bencard Laboratory. Skin test results were recorded as the maximum diameter of wheal at 20 minutes and the diameter of erythema at the same time. Subjects then completed a simple systematic questionnaire to define their allergic status. In the case of positive skin test to inhalant allergen supported with a history of inhalant allergy, the diagnosis of inhalant allergy was considered to be confirmed.

The diagnosis of food allergy was still suspected whether the skin test to food allergen is positive or negative. Elimination diet must be initiated. Depending on the result of the prior examination, one of the died regimen can be selected (1). For the diagnosis of food allergy, three provocations was needed. Phadiatop test was applied to subjects, both with inhalant allergy and suspected food allergy. The diet must be continued for three weeks. If improvements occurred, a provocation could be performed. All previously excluded foods can be reinstituted one at a time, in a sufficient amount everyday for one week. If no symptoms reappeared during the provocation, the food could be considered as non allergenic to the patient. If symptoms reappeared, the food should be suspected as causing the allergy. For the diagnosis, three provocations were required. The result of Phadiatop tests were matched with these patients and the former patients with inhalant allergy.

The Phadiatop Paediatric assay were examined in the Laboratory "PRODIA". A 10 ml sample of venous blood was obtained, and allowed to clot at room temperature. The methodology has been described elsewhere. Briefly, Phadiatop Paediatric is a direct enzyme immunoassay. A mixture of relevant food and inhalant allergens were covalently coupled to a paper disc. One day or overnight procedure could be used. Two paper discs were used, reference disc was added with 50 ul reference serum and another disc was added with 50 ul undiluted control or sample. These discs were then incubated in the test chamber at room temperature for 1 hour using the shaker or for 3 hours without shaker. Specific IgE antibodies in the patient sample react with the allergens on the disc. After a quick wash, immunosorbent purified enzyme labelled anti-IgE was added. The specimens were incubated at room temperature for 2 hours with shaker or overnight without shaker. After a second reaction unbound enzyme activity was washed away for three times. After incubation for 1.5 hour at 37°C waterbath with a developing agent using development buffer, 17 ml and stopping the reaction using stop substance, 4.2 g, the absorbance of a yellow colored product was measured. A positive test result indicated that the patient was atopic, a negative test result indicated that the patient was not atopic. Five replicates were assayed in each of 5 consecutive runs with fresh reagents from the same batch. The within assay coefficient of variation was less than 10% based on the Abas Values, for both the reference serum and the positive control.

Results

Asthma bronchiale comprised all of the cases in this study. Twenty eight out of 29 of the subjects in this study were identified as allergic in having at least one positive inhalant skin test and positive history of inhalant allergy, positive history of food allergy and positive result of provocation with certain offending food. Twenty four out of those 28 patients had an elevated serum IgE as judged by a positive Phadiatop Paediatric. One patient was identified as non allergic because of negative history of food allergy, negative history of inhalant allergy, negative skin test to both inhalant and food extracts and negative result in the provocation. Phadiatop Paediatric was also negative in this patient. Fifteen patients showed positive results for one or more allergenic extracts in the skin test, in 3 of them the Phadiatop Paediatric were negative. Eleven patients were identified as having food and inhalant allergy, 9 of them the Phadiatop Paediatric were moderately positive and 2 of them were strongly positive. The rest 17 patients were identified as having food allergy, in 4 of them the Phadiatop Paediatric was negative. The skin test predicted the atopy with an efficiency of 53.5%, while the Phadiatop Paediatric predicted the atopy with an efficiency of 82.1%. The overall results is illustrated in table 1.

In a total of 31 positive skin tests to inhalant allergens, 26 were Phadiatop Paediatric positive, the rest 5 were negative. On the other hand, we obtained 10 positive skin test to food allergens, where Phadiatop Paediatric were all positive. Phadiatop Paediatrics still showed 12 and 16 positive results in 15 and 22 negative skin tests to inhalant and food allergens respectively. The overall feature is shown in table 2.

From table 3, we can see that the relationship between Phadiatop Paediatric and several selected clinical features is quite clear. From the positive provocation of food, which we considered the most important point in diagnosis of allergy, mainly food allergy, the Phadiatop Paediatric detected 19 out of 24. From the other less important points i.e. positive history of inhalant allergy, positive history of food allergy, history of previous atopy and history of atopy in the relative, the Phadiatop Paediatric comprised a vast majority of positive results : a total of 23 positive and 6 negatives.

Table 1 : *The characteristics of subjects*

No.	Name	Skin Test Positive	Provocation Positive	Allergy Status	Phadiatop Paediatric
1.	DP	Housedust, shrimp, feather	Milk, egg, fish	Food & inhalant Allergy	0,227 (+)
2.	Y		Egg, banana	Food Allergy	0.156 (+)
3.	KN		Egg, chicken, orange	Food Allergy	0,183 (+)
4.	SY		Egg	Food Allergy	0,224 (+)
5.	AS		Egg	Food Allergy	0,189 (+)
6.	BI	Housedust, mite, shrimp, cat	Chicken, banana, milk	Food & inhalant Allergy	0,238 (+)
7.	RH		Banana, "papaya"	Food Allergy	0,096 (−)
8.	EPR		Fish	Food Allergy	0,123 (+)
9.	NNH		Milk	Food Allergy	0,149 (+)
10.	IK	Housedust, dog	Chicken, Chocolate	Food Allergy Allergy	0,100 (−)
11.	A	Housedust, mite	Milk, orange	Food & inhalant Allergy	0,108 (−)
12.	NFR		Milk	Food Allergy	0,096 (−)
13.	FA		Milk, egg, banana	Food Allergy	0,210 (+)
14.	EP	Housedust, cat, dog, milk	Chicken	Food & inhalant Allergy	0,273 (+)
15.	F		"Rambutan"	Food Allergy	0,112 (+)
16.	DK	Housedust, mite	Milk, Fish	Food & inhalant Allergy	2,092 (+)
17.	Y	Dog, cat	Fish, mungbean	Food & inhalant Allergy	0,075 (−)
18.	KO	Housedust, mite, dog	Milk	Food & inhalant Allergy	0,326 (+)
19.	FZ	Housedust, cat, dog, feather	Egg, shrimp, fish, peanut	Food & inhalant Allergy	0,141 (+)
20.	NS		Egg, mungbean	Foof Allergy	0,199 (+)
21.	LT	Fish	Banana	Food Allergy	0,137 (+)
22.	Y	Housedust, mite	Shrimp	Food & inhalant Allergy	0,380 (+)
23.	ENA			No Allergy	0,104 (−)
24.	IA	Housedust, egg	Milk	Food Allergy	0,148 (+)
25.	RA		Egg, orange, mungbean	Food Allergy	0,158 (+)
26.	Y	Housedust, mite, dog, shrimp	"Rambutan"	Food & inhalant Allergy	2,288 (+)
27.	BDP	Housedust	Egg, fish	Food & inhalant Allergy	0,198 (+)
28.	Z		Milk	Food Allergy	0,233 (+)
29.	F	Mite, milk, shrimp, fish	Egg	Food & inhalant Allergy	0,292 (+)

Table 2 : *Relationship between Skin Scratch Testing and the Phadiatop Paediatric*

	Phadiatop Paediatric (+)	Phadiatop Paediatric (−)
Inhalant extracts positive :		
- house dust	10	2
- mite	6	1
- cat	3	1
- dog	4	1
- feather	2	-
Food extracts positive :		
- shrimp	4	-
- fish	3	-
- milk	2	-
- egg	1	-
Inhalant extracts negative	12	3
Food extracts negative	16	6

Table 3 : *The relationship between Phadiatop Paediatric and clinical features*

	Phadiatop Paediatric (+)	Phadiatop Paediatric (−)
Positive history of inhalant allergy	1	1
Positive history of food allergy	17	4
Positive provocation of food	19	5
Wheezing	3	1
Hyperaeraetion as shown by thorax photo	1	-
History of previous atopy	2	-
History of atopy in the relatives	3	1

Discussion

The clinical manifestation of allergic diseases is caused by exposure to certain allergens to which the patients is sensitive. The allergens, when it can be identified are generally found to be materials or foods to which the patients is exposed more frequently, sometimes continuously. Usually the allergens exist in the patient's environment. Phadiatop contains several allergens which are considered to be common allergens in the manufacturer's country, but are not always common allergens in ours. May be this fact was responsible for the negative results in this study. If it is compared with the results of the skin test with the predictive efficiency of 53,5%, the predictive efficiency of Phadiatop of 82.1% is quite satisfactory. Such a comparison have also been made in order to evaluate the relationship between the result of skin prick test, the multiple allergosorbent test and symptoms of allergic diseases. In a representative study, Finnerty et al. (1989) [3] found that MAST-CLA testing for specific IgE to cat dander predicted a history of cat allergy with an efficiency of 74.5%, while a positive MAST-CLA test for cooksfoot grass predicted a history of grass pollen allergy with an efficiency of 85.1%. They concluded that MAST-CLA gave results comparable to those obtained by SKIN prick testing and correlated equally well with the history of allergic symptoms. Their findings were consistent with ours. Phadiatop assay were positive in 26 out of 31 patients with inhalant allergy (84%), on the other hand Phadiatop assay were all positive in 10 patients with positive skin test to food allergen extracts. However we found something different with the results of their study; in our study the positive rate of skin test to food allergen extracts was low (25%), and did not predict the result of provocation test. For example skin test positive to egg did not predict positive to egg in provocation test. It is easy to understand as the real antigen reaching the target organ is not the food ingested, but the split product of enzymatic process in the intestine. So the skin test result does not correlate well with clinical symptoms. A positive skin is not a proof that an allergic illness exist or that the allergen is clinically relevant. Conversely, a negative test does not rule out the existence of an allergic problem or eliminate the clinical importance of a substance that may induce symptoms or irritant rather than an allergen [4]. Several discrepancies still exist concerning this statement as shown by previous studies, that the reactions to ingested allergens occurred in early infancy but were transient. There was a good correlation between skin sensitivity to the food concerned. Further more they found no relationship between acquisition of skin reactivity to *D. pteronyssinus* (mites)and development of the respiratory symptoms of atopic disease during the period of their study. It is possible that inhaled allergens reactivity may be related to respiratory symptoms at later ages (6).

We really agree that skin test alone cannot replace a thorough history and physical examination. We believe that a positive skin test to inhalant allergens extract has a special value. If it is supported by a positive history of inhalant allergy it should be used as an aid in the development of logical environmental controls and as a guide to immunotherapy for those major allergens that can not be avoided [1,4]. On the other hand the skin test remains unexcelled as a sensitive and cost efficient test

for specific IgE. The high degree of skin test sensitivity is very important when a patient must be evaluated for potentially life threathening allergies such as to penicillin or stinging insect [7]. The allergy skin testing for the presence of IgE antibody has withstood the test of time and the challenge of new in vitro assays to remain the laboratory aid for the allergist [5]. In vitro tests such as RAST are acceptable substitutes for skin test in some circumstances, but the use of the test as a screening procedure in allergy is limited due to the high cost and the lack of sentivity. Nevertheless some modification of the assay using Multidisc RAST as a screening method of specific IgE antibodies in serum has proven that a cost benefit analysis calculated on local data confirmed economic advantages [8].

Conclusion

We concluded, as a screening procedure in allergy, the Phadiatop Paediatric is better than the skin test, but some superiority of the skin test, the low cost, sensitivity and the ability to determine the exact allergen, mainly inhalant allergens, make it still very important in the development of logical environmental control and as a guide to immunotherapy.

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