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Comparison of *In Vitro* Assay for Specific IgE and Skin Prick Test with Intradermal Test in Patients with Allergic Rhinitis

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SUMMARY **Among many diagnostic tests for allergic rhinitis, the intradermal (ID) test is practical and reliable. However, there are several factors affecting compliance, practicability and interpretation, and also problems on hypersensitivity of the ID. For these reasons, we evaluated other tests which have been thought to have high reliability as diagnostic and/or screening assays, namely, skin prick test and specific IgE detection in seventy-four perennial rhinitis patients (51 males and 23 females whose ages were between 15-60 years). In this study, *Dermatophagoides pteronyssinus* and *D. farinae* extracts, known to be the most common aeroallergens in Thailand, were used as the allergens/antigens. Compared to the standard ID test, sensitivities to *D. pteronyssinus* and *D. farinae* of the studied patients tested by skin prick test were 90.4% and 86.4%, and specificities were 99.5% and 93.1%, respectively. Sensitivities to *D. pteronyssinus* and *D. farinae* using specific IgE assay were 96.3% and 88.9%, and specificities were 96.2% and 88.9%, respectively. It was concluded that the skin prick test can be used as a screening method for patients with allergic rhinitis, while the specific IgE detection can be used as an alternative for diagnosis of patients who are susceptible to the ID test or for those who are severely susceptible to allergic rhinitis such that medication can not be withdrawn for the ID test.**

Allergic rhinitis (AR), especially the perennial type, is a health problem of a major concern among the Thai population.[1] Beside a history taking and a physical examination, the intradermal (ID) test is used as a reliable supplementary measure to the clinical diagnosis. However, there are many factors which limit the ID validation including compliance and practicability of the method, subjective interpretation of the test results and also hypersensitivity of the patients to the allergens used. Because of these factors, its alternatives have been sought and many methods became available. These include specific IgE level determination, radioallergosorbent test (RAST), modified radioallergosorbent test (MAST), fluorescent allergosorbent test (FAST) and, recently, Pharmacia CAP system for IgE detection; all of which have given high sensitivity and specificity.[2] In this communication, the ID test, the skin prick test and specific IgE detection by Pharmacia CAP system were evaluated in patients with perennial rhinitis using *Dermatophagoides pteronyssinus* and *D. farinae*, which have been known as the most common allergens in Thailand, as allergens/antigens.[3-5] The objectives were: 1) to evaluate the sensitivity, specificity and efficiency of the skin prick test in comparison with the ID test in order to determine whether the former can be used as an alternative in vivo screening test; 2) to evaluate the sensitivity, specificity and efficiency of the Pharmacia CAP system with the ID test to determine whether the Pharmacia CAP system can be an alternative *in vitro* test of choice for the patient who cannot undergo a usual procedure of the skin test.

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MATERIALS AND METHODS

Subjects

Seventy-four perennial allergic rhinitis patients (51 males and 23 females) whose ages ranged from 15-60 years, were recruited from the Outpatient Department of the Department of Otolaryngology, Pramonkutklao Hospital, Bangkok. Their symptoms included lacrimation, itching and sneezing with nasal discharge and obstruction. All patients had clear correlation between allergen exposures and the clinical features. Exclusion criteria were: 1) eczema or skin disease at the area to be used in skin testing; 2) history of immunologic disorders; and 3) anatomic abnormalities.

Procedure

All subjects were withdrawn from the following: oral prednisolone and/or long-acting antihistamine for 1 week, or short-acting antihistamine for 3 days. Individual patients were subjected to skin prick test and IgE level measurement by the Pharmacia CAP system, using ID test as a standard method. The skin prick test using allergenic extracts *D. pteronyssinus* and *D. farinae* (approximately 0.05 ml of 5,000 AU/ml) was done on the volar surface of the forearm and it was considered positive when there was erythema with wheal (3 mm or with pseudopod. Allergenic extracts (0.01 ml) of *D. pteronyssinus* and *D. farinae* (100 AU/ml) were individually injected intradermally into the deltoid area for the ID test. A positive result was read when there was erythema with wheal (8 mm or pseudopod occurred.[6] At the same time when skin tests were done, a blood sample was collected for specific IgE measurement against extracts of *D. pteronyssinus* and *D. farinae* by the Pharmacia CAP system[7-11] and a positive result was considered when the level was > 0.35 kU/l.

RESULTS

Among the 74 subjects enrolled to this study, the skin prick test for *D. pteronyssinus* was positive in 48 and negative in 26 patients while the ID test was positive in 52 and negative in 22 patients (Table 1). The *D. farinae* skin prick test yielded 41 positive and 33 negative cases while the ID test was positive in 45 and negative in 29 patients (Table 2). Specific IgE test by the Pharmacia CAP System using *D. pteronyssinus* showed perfect agreement with the ID test, i.e. 52 patients were positive and 22 were negative (Table 3). However, the specific IgE and the ID test using *D. farinae* extract revealed that the former was positive in 43 patients while the latter was positive in 45 patients (Table 4). Sensitivity and specificity of the skin prick test and the IgE test were calculated using the ID test as a standard method. The sensitivities of the skin prick test using *D. pteronyssinus* and *D. farinae* as antigens were 90.4% and 86.4%, respectively, while the specificities were 99.5% and 93.1%, respectively. The specific IgE test using *D. pteronyssinus* and *D. farinae* extracts as the antigens had 96.3% and 88.9% sensitivity and 96.2% and 88.9% specificity, respectively (Table 5).

Table 1 Comparison of skin prick test and intradermal test using *D. pteronyssinus* as antigen

Skin prick test	Intradermal test		Total
	Positive	Negative	
Positive	47	1	48
Negative	5	21	26
Total	52	22	74

Sensitivity = 90.4%
Specificity = 95.5%

Table 2 Comparison of skin prick test and intradermal test using *D. farinae* as antigen

Skin prick test	Intradermal test		Total
	Positive	Negative	
Positive	39	2	41
Negative	6	27	33
Total	45	29	74

Sensitivity = 86.7%
Specificity = 93.1%

Table 3 Comparison of specific IgE determination by Pharmacia CAP System and intradermal test using *D. pteronyssinus* as antigen

CAP	Intradermal test		Total
	Positive	Negative	
Positive	50	2	52
Negative	2	20	22
Total	52	22	74

Sensitivity = 96.2%
Specificity = 90.9%

Table 4 Comparison of specific IgE determination by Pharmacia CAP System and intradermal test using *D. farinae* as antigen

CAP	Intradermal test		Total
	Positive	Negative	
Positive	40	3	43
Negative	5	26	31
Total	45	29	74

Sensitivity = 88.9%
Specificity = 89.7%

Table 5 Performance characteristics of skin prick test and *in vitro* assay of IgE by Pharmacia CAP System compared to the standard ID test

	Percentage of skin prick test positive cases against		Percentage of specific IgE positive cases against	
	D. p.	*D. f.*	*D. p.*	*D. f.*
Sensitivity	90.4	86.7	96.2	88.9
Specificity	95.5	93.1	90.9	89.7
Efficiency	91.9	89.2	94.6	89.2
Positive predictive value	97.9	95.1	96.2	93.02
Negative predictive value	80.8	81.8	90.9	83.9
False positive	4.5	6.9	9.1	10.3
False negative	9.6	13.3	3.8	11.1

DISCUSSION

AR is common among population in Thailand. The usual diagnostic criteria for AR include a correlation between clinical outcomes and the exposure to allergen, physical examination and a positive diagnostic test.[8,12-14] Diagnostic tests for AR are classified into 2 groups: 1) *in vivo* tests (i.e. skin test and nasal challenging test) and 2) *in vitro* tests (i.e. tests for total serum IgE, specific serum IgE and/or cellular leukocyte histamine release). In the past, the diagnostic methods commonly used to diagnose AR were various skin tests. However, because of the frequent false negative results of the scratch test and the prick skin test, and the false positive results of the ID test, the ID test was modified using titration technique which could specify the degree of sensitivity to the allergens and can be used as a baseline in immunotherapy.[15]

Atopic sensitivity was previously recognized using a Prausnitz-Kustner reaction and the allergic reaction could be passively transferred from patient to the normal individual by serum.[6] This led to further study and the pathogenic role of IgE was revealed. However, there have been contradicting opinions regarding AR as to the role of IgE in disease; several studies reported no correlation between total serum IgE level with AR as there have been many other conditions that cause increase of total serum IgE, i.e. parasitic infections, some primary immunodeficiency, viral infections and Hodgkin's disease.[16] Several studies, however, reported correlation between specific serum IgE and AR.

A reliable *in vivo* test for AR diagnosis is an ID test. How-

ever, ID encounters several drawback and limitations, i.e. skin reactivity, dermographism, skin disease, chronic illness, subjects are too young or too old, drugs that suppress skin reaction (such as antihistamine, steroid, cough suppressant, tranquillizer, tricyclic antidepressants and sleeping pills), false positive results due to histamine release by other factors such as cephalosporin, sulfathiazine, morphine and meperidine.[17] As such, an *in vitro* test, i.e. specific serum IgE measurement, was introduced and it has played an important role in AR diagnosis. There are many methods used for determination of specific serum IgE level. These methods include radioallergosorbent assay and enzyme-linked immunoassay, both of which are *in vitro* assays. The common method available in many countries including Thailand is the Pharmacia CAP System, which uses β-galactosidase labelled polyclonal and monoclonal IgE as IgE detection reagents and the quantitation is done by using a fluorocount system. Our study is carried out in AR patients using the Pharmacia CAP System to trace for specific IgE in the patients compared with the diagnosis by the ID test. The study demonstrated that the sensitivities of the test using *D. pteronyssinus* and *D. farinae* as antigens were 96.2% and 88.9%, respectively. The specificity was 90.9% when test by *D. pteronyssinus* extract and 89.7% when *D. farinae* was used. In general, methods that are considered to be good in screening, despite high sensitivity and specificity, should give low false positive values. However, these values also depend on the prevalence of disease; increased prevalence results in lower false positive values. According to a World Health Organization (WHO) allergy survey in Thailand, the prevalence of allergic rhinitis is 20%[18] and these methods give a high efficiency value ~ 90% (Table 5); thus, the method should have good validity. This can imply that both the skin prick test and the Pharmacia CAP System could be used as screening methods for perennial allergic rhinitis that stem from *D. pteronyssinus* and *D. farinae*. Because of the high sensitivity and specificity of both methods, all were nearly 90 percent and above (Table 5). Both methods could be used as diagnostic tests as well. Both methods were proved to be efficient with a high efficiency value of 89.2-94.6% (Table 5), and because the procedure of the skin prick test was simple to perform, it was appropriate for use as a screening test. For those who were contraindicated for a skin test, the Pharmacia CAP System could be used as a diagnostic test. Because of the high sensitivity and specificity values, confirmation by ID test was not necessary. The conclusion was that the skin prick test can be used as a screening test for allergic rhinitis and specific IgE; it can be used as a standard test for diagnosing of patients susceptible to an ID test or those who are severely susceptible to AR symptoms who cannot cease medication.

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