Original Research Article

Skin prick test in diagnosis of allergy to citrus fruits among children with bronchial asthma

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Abstract

Objective: To evaluate allergy to citrus fruits in children with bronchial asthma using skin prick test and to compare with phadiotype test results. **Methods:** patients (85) with bronchial asthma were screened using standard questionnaire, skin prick test (SPT) and phadiotype blood test with citrus fruits allergens. **Results:** we had a total of 85 patients all of them with asthma, of which 57(67.1%) had positive blood test for allergy to various citrus fruits (phadiotype test). Out of the 85 patients who were tested for skin prick test all 84 (100%) were positive except 1. **Conclusion**: In our study we had a total of 85 patients of which 57 (67.1%) were positive for allergy in blood test. In skin prick test all 84 (100%) were positive for allergy except 1 patient. In our study skin prick test was found to be sensitive but not very specific compared to the blood test phadiotype test.

Key words: skin prick test, phadiotype test.

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INTRODUCTION

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.[1] Estimates suggest that Ig E mediated food allergy affects 6-8% children imparting great clinical and social burdens. [1] Food allergy commonly manifests as adverse reactions of the gastrointestinal tract and the skin, including atopic dermatitis, acute urticarial and sometimes life-threatening anaphylaxis. However, the role of foods as triggers of asthma is less clear. Food-induced symptoms occur in approximately 2% to 29% of children and about less than 1% of adults with asthma.[2] Food sensitisation in early infancy could lead to the development of respiratory allergy and is a significant risk factor for asthma in 10% to 53% of cases.[3-5] The epidemiology of food allergy is influenced by genetic, cultural and geographical dietary influences. Severe and fatal reactions can occur at any age but those at greatest risk are adolescents and young adults with asthma and a known food allergy to peanut, tree nut, fruits, milk, wine, vegetables and/or seafood.[6] The foods most commonly causing breathlessness are hazelnut in Norway, Sweden, and Germany, fruits in Iceland, Belgium, Ireland, and Italy, and peanut in the USA.[6] India represents one-seventh of the world population with diverse culture and dietary habits but little is known about the prevalence of food allergy. Recent studies12-15 in India suggest a considerable increase in the prevalence of bronchial asthma (3.9%-11.6%) than reported earlier. Allergy to foods might further aggravate the symptoms, however, the knowledge is limited to a few studies. Food such as egg, milk, cereals and legumes, commonly induce IgE-mediated reactions in children and adult population.[7,9] the present study was undertaken to test allergy (skin prick test) to citrus fruits in children with bronchial asthma and compare it phadiotype results (blood test).

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MATERIALS AND METHODS

Study population: All children in the age group of 5-18 yrs. old with clinically diagnosed asthma with pulmonary function test (spirometry) demonstrating obstruction and reversibility are included. Children with hypersensitivity, chronic lung disease were excluded. It was a cross sectional study conducted in Ramaiah medical college hospital, Bangalore over a period of 6 months.

Skin prick testing (SPT) is a reliable method to diagnose IgE-mediated allergic disease in patients with rhino conjunctivitis, asthma, urticaria, anaphylaxis, atopic eczema and suspected food and drug allergy. It provides evidence for sensitization and can help to confirm the diagnosis of a suspected type I allergy. It is minimally invasive, inexpensive, results are immediately available and when carried out by trained health professionals, reproducible. Since the first publication about SPT by Helmtraud Ebruster in 1959[10], who extensively researched this diagnostic test, it has been used as a primary diagnostic tool to detect type I hypersensitivity reactions. Although the principle of SPT still largely resembles the original methods described, a wide array of interpretations and modifications has led to diminished comparability when SPT results are reported.

SPT procedure: Patients should be appropriately screened for asthma, and, where possible, discontinued on medications that interfere with test results, accentuate systemic allergic reactions or render patients less responsive to treatment with epinephrine. In patients with a history of severe systemic allergic reactions to food or drugs, an intravenous line for immediate circulatory access can be recommended. A peak flow of less than 70% in patients with asthma is a relative contraindication. Asthma should be controlled or testing deferred until control is achieved. When testing patients with a history of a severe systemic allergic reactions, skin test titration, first utilizing diluted extracts, is recommended. The location of each allergen can be marked with a pen or by using a test grid on the forearm to properly identify test results. Tests should be applied to the volar aspect of the forearm, at least 2 – 3 cm from the wrist and the antecubital fossae [11]. The back can also be used for SPT, especially in infants. The skin on the back is more sensitive than the forearm which may result in larger wheals and thus possibly a greater number of positive test results [12]. The distance between two skin prick tests (≥ 2 cm) is critical to avoid false-positive reactions due to direct contamination of a nearby test or secondary to an axon reflex [12]. A drop of each test solution should be placed on the skin in identical order for each subject tested and immediately pricked.

A single-head metal lancet exhibits excellent reproducibility with few false-negative results and is thus the preferred testing instrument for SPT [13-15]. It is pressed through the drop of allergen extract and held against the skin for at least 1 second, with equal pressure applied for each test. The epithelial layer of the skin should be penetrated without inducing bleeding, which can lead to false-positive results. A new lancet should be utilized for each allergen since wiping a previously used one between tests could result in cross contamination from the previous allergen tested.

Assessing the SPT: Positive and negative controls should be measured first. The negative control excludes the presence of dermographism which, when present, makes the tests difficult to interpret. The histamine control should be positive to make sure that the test materials are applied correctly and to exclude negative SPT results due to potentially interfering medications taken by the test subject. The largest diameter of the wheal of each particular test is measured, a positive being a wheal of ≥ 3 mm [16].

Statistics: Sample size was calculated based on raj *et al.*[1] study in which it was found that 29.3% of the patients with asthma and allergic rhinitis showed positive skin prick test SPT to one /more foods. In the present study considering margin of error (precision of 10%) and confidence level of 95 % the required sample size was estimated to be 79.

Laboratory studies: Diagnosis of food allergy was made by skin prick test (SPT), PHADIOTYPE TEST.

As per the sample size estimated 85 patients were enrolled in the study. All the 85 patients under went SPT and phadiotype testing.

Skin prick test and sera collection: The SPTs were performed with citrus fruits allergens (orange, lemon, grapes). Histamine diphosphate (5mg/ml) and phosphate buffer saline were used as positive and negative controls, respectively. A drop of the extract was placed on the volar aspect of the forearm and the skin was pricked by a 26 1/2" G sterile needle. Skin tests were graded after 20 minutes. The SPT reactions with wheal diameter that was 3mm or greater than the reading in the negative control were considered as a “marked positive reaction”. Blood was collected from all patients enrolled for the study. Blood was drawn and subjected for Phadiotype testing. Serum was separated and used for immunoassay. Patients with respiratory allergies have increased total IgE (>100 kU/l), which in fact means that 50 % with normal total IgE will not be identified by total IgE testing. The total IgE level is the sum of all IgE in the blood, which can be increased due to other reasons than allergy. Instead Phadiatop is recommended with its superior performance, which only measures allergen-specific IgE antibodies to common allergens and not the total amount where irrelevant IgE could be included. This is a single test that measures IgE antibodies sensitization to common allergens such as grass,

food, tree and weed pollen, animal, mite and mold provoked after normal environmental exposure.

RESULTS

In our study we had a total of 85 cases of which 39 (45.9%) were females and 46 (54.1%) were males. All the 85 patients were subjected to skin prick test and blood test (phadiotype test) after taking due consent. Of the 85 patients we had positive blood test in 57 (67.1%) of patients and positive skin prick test in all the 84 (100%) patients.

Table 1: showing the sex distribution

	Frequency(n=85)	Percent
Sex		
Female	39	45.9
Male	46	54.1
Expectoration	50	58.8
Sneezing	55	64.7
Wheezing	55	64.7
Breathlessness	44	51.8
Chest_pain	26	30.6
Eczema	24	28.2
Contact_with_ tb	6	7.1
Triggering_factors		
1	35	41.2
2	9	10.6
3	3	3.5
4	2	2.4
5	14	16.5
6	22	25.9
Allergy_to_lemon		
0	51	60.0
1	32	37.6
2	2	2.4
Allergy_to_orange		
0	55	64.7
1	27	31.8
2	3	3.5
Allergy_to_grape_fruit		
0	65	76.5
1	6	7.1
2	14	16.5
Allery_to_citrus_fruits		
1	5	5.9
2	25	29.4
3	4	4.7
4	1	1.2
5	50	58.8
Totalallergyposi		
0	50	58.8
1	33	38.8
2 **Totaltriggering_factors**	2	2.4
0	6	7.1
1	78	91.8
2	1	1.2
Weather_changes		
0	1	1.2
1	40	47.1
2	10	11.8
3	2	2.4
4	5	5.9
5	5	5.9

6	22	25.9
Exercise_tolerence		
1	24	28.2
2	10	11.8
3	5	5.9
4	2	2.4
5	44	51.8
Family_ho		
Y	35	41.2
Grades_of_asthma(gina_guidelines)		
1	33	38.8
2	28	32.9
3	20	23.5
4	4	4.7
Age_coded		
5 years	11	12.9
6-10 years	50	58.8
11- 15 years	24	28.2

Table 2

Total PP	Frequency	Percent
0	28	32.9
1	57	67.1
Total	**85**	**100.0**

Table 3

Skin Prick Test	Frequency	Percent
0	1	1.17
1	84	98.8
Total	**85**	**100.0**

Table 4

		TotalPP		
		+	-	Total
SPT	+	57(67.90)	27(32.10)	84
	-	0	1(100)	1
	Total	**57**	**28**	**85**

P <0.001* - Mc nemars test

Number of observed agreements: 58 (68.24% of the observations)
Number of agreements expected by chance: 56.7 (66.66% of the observations)
Kappa= 0.047; SE of kappa = 0.046; 95% confidence interval: From -0.043 to 0.138;
"One way to interpret kappa is with this scale (1): Kappa < 0: No agreement; Kappa between 0.00 and 0.20: Slight agreement; Kappa between 0.21 and 0.40: Fair agreement; Kappa between 0.41 and 0.60: Moderate agreement; Kappa between 0.61 and 0.80: Substantial agreement; Kappa between 0.81 and 1.00: Almost perfect agreement."

DISCUSSION

In our study of the 85 patients, 57 (67%) patients had a positive blood test (phadiotype) for allergy to various citrus fruits. Skin prick test was positive in all the 84 (100%) out of 85 patients. Only one patient was negative which could be due to drugs such as antihistaminic. The inference we can draw from this study is that the blood test is no doubt the most sensitive and specific gold standard test for allergy, the skin prick test is equally sensitive but not very specific. The blood test (phadiotype) and skin prick test results were comparable the p value <0.001 being is significant. Sensitivity and specificity are lower for food allergens, ranging from 30-90% and 20-60%, depending on the type of allergen and methods utilized, i.e. pricking with extracts vs. prick-to-prick techniques described earlier.[17] Double-blind placebo-controlled challenge studies in children demonstrate that SPT possesses a positive predictive value of 76% and 89% for clinical reactions to cow's milk and hen's egg, respectively.[18] The objective value of SPT for drug allergy depends on the

tested drug. In most cases, a positive SPT makes drug allergy very probable; whereas a negative result does not necessarily indicate that the patient will not react on challenge to the drug.[19]

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