

Labial food challenge in children with food allergy

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The current increase in the prevalence of food allergies appears to have several causes including better screening, improved diagnosis and changes in both the techniques used by food manufacturers and eating habits. Labial food challenge (LFC) is simple, rapid to perform and is associated with only low risks of systemic reaction. It is thus an appealing alternative to the oral food challenge (OFC) for pediatric use.

We report a series of 202 LFC performed over two years in 142 children with food allergy suspected from the case history, positive skin prick tests and specific serum IgE assays: 156 LFC were positive; and 46 negative, followed by positive single-blind, placebo-controlled food challenges (SB-PCFC). The foods provoking reactions were egg white (75 cases), peanut (60 cases), mustard (23 cases), cow's milk (13 cases), cod (8 cases), kiwi fruit, shrimp (4 cases each), chicken, peanut oil (3 cases each), hazel nuts (2 cases), and snails, apple, fennel, garlic, chilli peppers, pepper, and duck (1 case each). LFC positivity was mostly (89.7% of cases) manifested as a labial edema with contiguous urticaria. There were systemic reactions in 4.5% of cases: generalized urticaria, hoarseness and rapid-onset and generalized eczema. The 46 infants with negative LFC results had positive SB-PCFC. The reactions were in 34 cases generalized urticaria, 10 cases asthma attacks, 2 cases early and generalized eczema, and in one case general anaphylactic shock. The sensitivity of the LFC was 77%.

The LFC was easy to perform with children. Positive results indicate the presence of food allergy, but negative results require further investigations preferably double-blind, placebo-controlled food challenge (DBPCFC).

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Food allergy is manifest as a group of clinical symptoms associated with an immuno-allergic response dependent on IgE antibodies directed against food allergens (1). The prevalence is currently increasing. The reasons for this include improved screening, better diagnosis, and developments in eating habits and the techniques used by agro-food manufacturers. The estimated prevalence of food allergy in the general population in 1994 is 1.4 to 1.8% (2), and among children aged under 8 years old between 4 and 8% (1, 3, 4). The prevalence is higher among atopic children (5), a group which accounts for 90% of cases (1). Four foodstuffs are responsible for three quarters of the cases of allergy: egg, peanut, fish and cow's milk (1).

Abbreviations: LFC: labial food challenge; OFC: oral food challenge; SBPCFC: single-blind, placebo controlled food challenge; DBPCFC: double-blind, placebo controlled food challenge; SPT: skin prick test

The diagnosis of food allergy is difficult. It is a stepwise procedure involving rigorous, logical and painstaking methods. The approach used is a decision tree, starting with exhaustive questioning, followed by a survey in involving keeping a log of all the different food ingested during a period of seven days. This allows selection of appropriate skin-prick tests (SPT) to be given to the child. A positive result indicates sensitivity to the food, and this can be followed by assaying specific serum IgE and best confirmed by a recognized challenge procedure for each incriminated food. A new technique, labial food challenge (LFC), is appealing for use with children particularly because of its simplicity. It involves contact between the food and the labial mucosa, to test for local cutaneous manifestations, and this approach tends to avoid systemic reactions. The manifestations result from a local expression of the IgE response to the antigen. This procedure differs from the sublingual test, which is associated with the risk of immediate absorption of antigens

into the circulation via the sublingual veins. However, negative results by LFC require confirmation by OFC.

Materials and methods

Subjects

The study population consisted of 142 children (48 girls, 94 boys) average age 4 years 6 months (range 7 months and 15 years 10 months) admitted between January 1st 1993 and December 31st 1994 with clinical histories suggesting immediate food allergy. The manifestations included: atopic dermatitis (86 children, 61% of cases), recurring rash ($n = 45$, 32%), angio-edema ($n = 36$, 25%), asthma ($n = 34$, 24%), hoarseness ($n = 7$, 5%), anaphylaxis ($n = 6$, 4%) and rhinoconjunctivitis or oral syndrome ($n = 5$, 4%). Sixty-six children presented more than one of these manifestations.

Skin prick tests

Commercial food extracts (Stallergens, France) were used diluted 1:10 (wt/vol) for skin prick tests (SPT). SPT involved placing a drop of extract suspension on the volar side of the forearm and pricking through the drop with a lancet (Dome Hollister-Stier, Slough UK) with a 1 mm tip. The results were assessed by comparison with the wheal induced by histamine (10 mg/ml histamine base) and/or codeine (9%) if histamine was negative. Dermographic reactions were excluded by testing with a negative control solution (50% glycerosaline solution). Wheals with diameters equal or greater than 3 mm and more than half the average diameter of positive controls were scored as positive. The foods used for skin prick test were as follows: egg yolk, egg white, peanut, cow's milk, cod, wheat, corn, soy, beef, shrimp, pork, chicken, duck, snails, peas, tomato, banana, apple, kiwi fruit, walnut, hazelnut, almond, celery, carrot, potato, vanilla, and various spices including mustard, cumin, paprika, coriander, chilli pepper, pepper, fennel and garlic. These foods were also tested as fresh foods by the prick + prick technique (6). The food was bought locally, frozen in 1 mm³ cubes, and thawed on the day of the test. Solid foods, for example peanuts, were crushed and diluted 1:3 (wt/vol) in phosphate buffered saline.

Specific IgE assays

An ELISA kit was used (DPC-Behring Diagnostic, France). A score in class two or above, that is, greater than or equal to 1.5 IU/ml, was considered to be positive.

Challenge procedures

The technique described by Moneret-Vautrin (7) was used for labial food challenges (LFC). This technique can use both commercial food extracts and crushed fresh food resuspended in physiological salt solution. Foods scoring positive in skin prick tests were tested. A drop was placed on the lower lip and left for 10 seconds to 2 minutes with the mouth slightly opened with a cotton swab between the lip and gum (7). The result was read 15 minutes later, and a photograph taken as a permanent record. A subject can take two LFC in a half day.

Three types of symptoms were taken as positive results in LFC: smoothing of the lip with disappearance of the fine physiological transversal wrinkles; edema, presenting as local discoloration or a swelling of one or both lips; a contiguous rash, spreading in some cases as far as the neck. Positive reactions in LFC can be divided into five types: (1) smoothing of the lower lip; (2) erythema under the lip; (3) contiguous rash of the cheek and chin; (4) edema of the cheek associated with rhinitis and watering eyes; and (5) systemic reaction associated with itching of the areas affected by eczema and coughing (7).

All negative LFC were followed by single-blind, placebo-controlled food challenge (SBPCFC). This test was performed after a recommended 5 to 7 days of an elimination diet of the suspected foods. Opaque capsules or lyophilized food was used (8, 9, 10, 11, 12). The initial dose was 1 mg and increasing doses were given every twenty minutes up to the daily dose for the age of the subject (13, 14, 15, 16, 17). We used Dextrose in capsules as placebo, and apple sauce as the vehicle. Children were observed for at least 24 hours after the challenge. A challenge was considered positive when there was an objective systemic, respiratory (asthma), nasal (rhinitis), cutaneous (rash, pruritus, urticaria, angio-edema, eczema) or digestive (abdominal pain, vomiting, diarrhea) symptom which occurred within 2 hours of the oral challenge (15, 16). Respiratory symptoms appear within 20 minutes following the administration of any dose. The only late (between 2 and 24 hours) manifestation was generalized eczema.

The diagnosis of food allergy was made if skin tests were positive, specific IgE above 1.5 IU/ml and LFC and/or oral food challenge were positive.

Data analysis

Sensitivity was calculated by the method of Goldman (18): sensitivity of the LFC was defined as the number of positive test results among allergic children divided by the number of allergic children. As there was no negative control group (no allergic

children) in the study specificity and predictive value could not be determined.

Results

A total of 202 LFC were performed, 156 of which were positive and 46 negative. The 46 negative results were re-tested by single-blind, placebo-controlled food challenge (SBPCFC). The positive LFC results were mostly type 3 reactions (91% of cases) (Table 1). There were seven systemic reactions (5% of cases) to LFC, all of which were moderate: four cases of generalized urticaria, two cases of rapid and generalized eczema and one of hoarseness. The actual classification of food allergens triggering food allergy among children are reported in Table 2. The foods which scored negative by LFC and subsequently positive by SBPCFC were peanut (eleven cases), milk (ten cases), egg (eight cases), mustard (seven cases), peanut oil (three cases), shrimp, chicken and kiwi fruit (two cases each) and cod (one case) (Table 3). The minimum dose causing a reaction was between 1 mg and 5 g, and 1 ml to 100 ml for milk. Among the reactions there were 34 cases of urticaria (74%), ten asthma attacks (22%) which responded satisfactorily to treatment with an aerosol of β -agonists, two rapid (within 6 hours) generalized eczema outbreaks (4%) and one case of anaphylaxis (2%) which required intravenous epinephrine, corticosteroids and antihistamines (Table 4). The sensitivity of the LFC was 77% and thus the incidence of false negatives 23% among the children defined as allergic by SBPFC. No child without a food allergy was reported in this study. Thus, we cannot define the specificity nor the predictive value of the LFC.

Discussion

Challenge tests are essential to the medical analysis of food allergy. Such tests can be used to reproduce the clinical history, respecting the time, quantity of food and the symptoms. Double blind oral challenges are positive in 20% to 70% of cases suspected from the case history, skin prick tests and serum IgE assays (3, 8, 9, 11, 17). However, oral food challenge does not give any information about pathogenesis. It is potentially dangerous and contra-indicated where the food allergy takes the form of acute anaphylaxis (19). It may also give false negative results if the dose used is insufficient, and the placebo effect, although minor in children, requires the use of a double blind protocol (12, 13, 14, 16).

We are unaware of any previous comparative study of the labial and oral challenge tests. The lip is necessarily in contact with all foods ingested in everyday life such that it may become sensitized,

Table 1. Manifestations observed in 156 positive labial food challenges in 142 children

Type I	4	3%	smoothing of the lip
Type II	2	1%	erythema under the lip
Type III	142	91%	contiguous urticaria
Type IV	1	1%	edema of the cheek, rhinitis and eye watering
Type V	7	5%	systemic reaction
Total	156		

Table 2. Food allergens identified (by skin prick tests, specific serum IgE assays, and labial and/or single-blind, oral food challenge) for 142 children aged between 7 months and 15 years old. Other foods positive: kiwi fruit, shrimp (4 cases each), chicken, peanut oil (3 cases each), hazel nuts (2 cases), and snails, apple, fennel, garlic, chilli peppers, pepper, and duck (1 case each)

	Total challenges (n)	%	LFC n	SBPCFC n
Egg	75	37%	67	8
Peanut	60	30%	49	11
Mustard	23	11%	16	7
Cow's milk	13	6%	3	10
Fish	8	4%	7	1
Other	23	11%	14	9
Total	202			

LFC: labial food challenge; SBFC: single-blind, placebo-controlled food challenge

Table 3. Manifestations observed in patients with positive single-blind, placebo-controlled (SBPCFC) following a negative labial food challenge (LFC)

Manifestations	n	%
Urticaria	34	73.9%
Asthma	10	21.7%
Atopic dermatitis	2	4.3%
Anaphylaxis	1	2.1%
Total SBPCFC	47	

and is a target organ. The anatomic characteristics of the lip make it suitable for allergy testing. The labial epithelium differs on different parts of the lip, and there is little keratinization outside the mouth and none inside and thus permeability is slight. The lip is red because of the rich vascularization of the chorion, which leads to even minor histamine type vasodilatation causing visible edema. Finally, the labial mucosa contains mastocytes, which in the presence of even small amounts of allergen, are able to degranulate and release histamine and inflammatory mediators.

The LFC has several advantages. It is straightforward and takes less than 30 minutes. Only a single dose is required. Outpatients can be tested, at the same time as undergoing skin prick tests. The risk of systemic reaction is lower than that associated with the OFC, such that is suitable for patients who suffer

anaphylactic shock or asthma. Among the eight cases in our series, challenge procedures were not performed for three (milk, peanut and shrimp) and the LFC was positive in the five (milk and egg) others manifest as labial edema and contiguous urticaria. The test is also cheap, an advantage over other allergy tests.

The major drawback of the LFC is the difficulty in detecting weak reactions. Photographs can be taken and subsequently be used to search for minor signs of positivity. The relatively poor sensitivity of the method justifies systematic single-, or better, double-blind, placebo-controlled food challenge for all negative results.

The frequency of allergy to various foods in our series differed slightly from that reported by Moneret-Vautrin (1): in our series, as previously, egg and peanut are the two most common food allergens (1, 15) but mustard was the third most common allergen. Possibly, this reflects differences in local diet.

Challenge procedures are the cornerstone for the diagnosis of food allergy (1, 14, 16). Labial food challenge is appealing for pediatric use as it is rapid and associated with a relatively small risk of systemic reaction. The sensitivity is poor, such that double-blind, placebo-controlled food challenge is required after negative LFC results. Further comparative analyses of the LFC and OFC will better determine the value of the LFC for the exploration of cases of food allergy.

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