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RESEARCH REPORT

Skin prick testing to food allergens in breast-fed young infants with moderate to severe atopic dermatitis

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SUMMARY

The role of food allergy in atopic dermatitis is controversial. This study presents results of skin prick tests to 31 different food allergens in a selected population of predominantly breast-fed young infants who had moderate to severe generalized atopic dermatitis. Of the 59 infants (22 female, mean age 26.5 weeks) tested, 54 infants (91.5%) had positive responses to one or more foods, 53 infants (90%) were positive to one or more of the five common food allergens (egg white, cow's milk, peanuts, wheat or soy) and 80% were positive to egg white, which was by far the most common positive test. A total of 37 infants had strongly positive responses to one or more foods, with 33 of these 37 having strongly positive responses to egg white. The significance of these responses is discussed. It is concluded that positive skin prick tests to foods, particularly to egg white, are very common in this selected population of breast-fed infants with moderate to severe atopic dermatitis.

Key words: cashew nut, cow's milk, eczema, egg white, egg, food hypersensitivity, peanut, potato, soy, walnut, wheat.

INTRODUCTION

Atopic dermatitis in the first years of life is common worldwide[1] and a common cause of both infant and parental distress. In infants the possibility of food allergy is a common inquiry of parents who are often keen to determine potential triggers if possible. While food allergy is thought by some to play a pathogenic role in a substantial number of children with AD,[2] the identification of what if any foods are implicated is a process that engenders differences of opinion. Infants and/or their mothers risk being placed on restrictive diets, sometimes inappropriately, in the hope of effecting improvement.

Most previous studies looking at allergies in infants with AD have not discriminated between formula- and breast-fed children. Our aims are to present the results of SPT to food allergens in a group of predominantly breast-fed infants with moderate to severe AD, and to discuss the implications of these findings in the hope of assisting dermatologists that encounter such infants.

METHODS

Infants were recruited from a single dermatology practice with a strong subinterest in paediatric dermatology. All infants had moderate to severe AD, as diagnosed clinically by one of us and a SCORAD[3] value of 40 or greater was an inclusion criterion, most infants having widespread eczema, itch and sleep disturbance. All infants were exclusively breast-fed at the time of first presentation. All had SPT with 31 separate food antigens as listed in Table 1, as well as SPT with a negative (glycerine) and positive (histamine) control. All SPT were performed on the volar aspect of the forearms or anterior thighs. Topical corticosteroids were ceased for 1 day before SPT, antihistamines for 5 days, and no child was taking systemic corticosteroids. Food allergens used were obtained from Hollister-Stier via their Australian agent Richard Thompson Pty Ltd, Alexandria, NSW, and stored and utilized according to the manufacturer's recommendations.

All SPT were performed and read by two of the authors (D.C.O., E.M.). The reaction was read 15 min later and any resultant wheal scored uniformly as per previously

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Abbreviations:

AD	atopic dermatitis
DBPCFC	double-blind placebo controlled food challenges
RAST	radioallergosorbent test
SPT	skin prick tests

Table 1 List of all food allergens tested

Fish	Grain	Nut	Fruit	Vegetable	Meat	Miscellaneous
Codfish	Corn	Almond	Apple	Pea	Chicken	Egg white
Crab	Barley	Brazil nut	Banana	Potato	Beef	Cow's milk
Lobster	Rice	Cashew	Orange	Tomato	Pork	Soy
Salmon	Wheat	Peanut	Peach			Yeast
Shrimp		Pecan	Strawberry			
Tuna		Walnut				

published guidelines.[4] Food allergens eliciting a mean wheal diameter of 4 mm or larger than that produced by the negative control were considered positive. Food allergens eliciting a mean wheal diameter of 10 mm or larger than that produced by the negative control were considered strongly positive.

RESULTS

A total of 59 infants were tested, 22 female, and the average age at the time of testing was 26.5 weeks (range 14–80 weeks). While all infants were exclusively breast-fed at the time of first presentation, 12 (20%) infants had commenced first-line solids by the time SPT were performed.

The most common positive SPT results are shown in Table 2. Only five infants (8.5%) were negative to all foods tested, conversely 54 (91.5%) were positive to at least one food, with a range of positive reactions between one and 12 different foods. A total of 53 (90%) of infants were positive to one or more of the five common food allergens (egg white, cow's milk, peanuts, wheat or soy). Egg white was by far the most common positive SPT with 80% of infants being positive.

All the strongly positive SPT results are shown in Table 3. Strongly positive responses to one or more foods occurred in 37 infants, with seven foods responsible, with strongly positive responses to egg white being present in 33 of these infants. The remaining four infants with strongly positive SPT responses had completely negative responses to egg white, two of these four had strong responses to cow's milk, one had a strong response to peanut, and one had strong responses to both cow's milk and peanut.

Table 2 Most common positive skin prick test results (59 infants tested)

Food	Number positive (%)
Egg white	47 (80)
Cow's milk	30 (51)
Peanut	26 (44)
Wheat	12 (20)
Potato	12 (20)
Cashew nut	8 (14)
Soy	7 (12)
Walnut	6 (10)

Table 3 All strongly positive skin prick test results (59 infants tested)

Food allergen	Number strongly positive (%)
Egg white	33 (56)
Peanut	6 (10)
Cow's milk	5 (8.5)
Beef	1 (1.7)
Pork	1 (1.7)
Potato	1 (1.7)
Walnut	1 (1.7)

DISCUSSION

Food allergy as a contributing factor to childhood AD is an area of controversy. The evaluation of food allergy in children has been the subject of several recent reviews.[2,5–7] There is immense community interest in food allergy as a cause of symptoms, and clinicians are commonly directly asked by parents to evaluate the possibility of food allergy. A population study in the UK showed that prevalence rates of self-reported food allergy are approximately 10 times greater than the actual rates.[8] With regard to AD specifically, food allergy is thought to play a role in 30–40% of infants with at least moderate severity AD.[2,7,9] In general, studies have suggested[7,10,11] that the younger the child and the worse the skin, the more likely it is that foods will be implicated in contributing to the AD. It is generally agreed useful to consider food allergy in AD of moderate to severe degree rather than intermittent or mild degree.[7]

Our study is one of few studies to look at young infants only, most include older children as well. We found a high rate of positive SPT responses overall (90%), with about three-quarters showing positive response to egg white, and about half showing positive responses to cow's milk and peanut. Strongly positive responses were seen predominantly with egg white. Other papers report comparable findings. One group found 70% of children under 12 months of age with AD had a positive RAST to egg, and that 60% of children aged 12–24 months also had a positive RAST to egg.[6] Another group reported positive SPT to foods in 93% of children aged under 2 years with severe AD.[11]

Our study looked at a predominantly breast-fed population, and the high rate of positive skin responses found suggest that breast-feeding does not protect against sensitization, which is presumed to have occurred *in utero* or by transfer through breast milk from the maternal diet.

Our study can be criticized for not having a control group and not determining the significance of the positive screening test, specifically the lack of any form of food challenges to determine whether the SPT results obtained were clinically relevant. We did not follow up positive SPT results with RAST testing. We also did not formally evaluate the response of the AD after the results of the testing was reported to the parents and dietary exclusion suggested.

Previous studies assist in providing control data. One study from Sweden[12] followed prospectively a sample of 86 female infants until 4 years of age, with measurement of IgE to some (egg, cow's milk) foods at 3 and 8 months of age. They found transient development of low levels of IgE to egg and cow's milk can be a normal finding in a small percentage (5–10%) of healthy infants, unassociated with any atopic symptoms. In another study from Japan[13] of 82 infants under 12 months of age (representing a sample of the normal infant population), only one had positive IgE antibodies to cow's milk, while none had positive IgE antibody to egg. In comparison in our group of infants with moderate to severe AD, we found positive SPT to food allergens in the majority of infants studied.

The relevance of the positive SPT as a potential screening test in our study is problematic. The study of food allergy generally, including food allergy in children with AD, has relied on the use of SPT or RAST or RAST-like tests as screening tests of IgE-based reactions, and comparing them to the gold standard of DBPCFC. The method of performing DBPCFC is outlined in detail elsewhere.[14] In Australia, government funding for RAST is limited to four allergens, with resulting more common use of SPT, whereas in the USA, where much of the literature originates, RAST is the preferred screening test.

There are a number of possible skin reactions in a food-allergic infant. Skin reactions observed with DBPCFC include urticaria/angioedema, itch and AD. Most studies report skin redness and itch having onset a short period of time after oral challenge with the implicated food. Most studies do not evaluate children days later to assess the presence of the typical lesions of AD. Hypothetically, it is proposed that foods cause release of mediators in the skin causing itch, leading to scratching and eventual flare of AD days later.[9] Overall, very little of the published literature to date has involved dermatologists. It is possible that many of the reactions reported in the literature as flares of AD may have represented food-related urticaria.

It is imperative to understand that both SPT and RAST or RAST-like tests are screening tests, and that a positive SPT or RAST may not be of any clinical relevance to a given individual. Screening tests such as SPT and RAST may be most useful if negative as they have a very high negative predictive value.[9] Conversely, the positive predictive value of a positive SPT or RAST in isolation of predicting a clinically relevant reaction is only 30–50%,[9] that is overall only about 40% of children with positive SPT or RAST and suspected food allergy react with clinical symptoms to a food when exposed.[7] However, the size of the reaction does matter, so the greater the size of the wheal in the SPT or the titre in a semi-quantitative RAST, the greater the likelihood of clinical relevance. Ideally, a positive screening test should be supported by a suggestive history of worsening on exposure to the implicated food or improvement with elimination of the implicated food.

Various authors have attempted development of thresholds for SPT diameters or RAST titres at which DBPCFC will almost always be positive and thus unnecessary.[15–19] The various thresholds determined vary with the age of the child and the food tested, and may also vary for the type of clinical manifestations elicited (for example, cutaneous manifestations versus respiratory manifestations). One group[19] found that for children older than 2 years with food allergy symptoms, SPT greater than 8 mm for cow's milk, 7 mm for egg and 8 mm for peanut where always associated with a positive food challenge, but for under 2 years of age, the thresholds were 6 mm, 5 mm and 4 mm, respectively. Wider application of such data is limited unless one ensures use of the same commercial RAST or SPT allergens as described in individual studies. Also to date such studies have only been carried out for the broader food-allergic population, not specifically in the subset of food-allergic children whose main manifestation is AD. The take-home messages, however, remain that the size of the response (wheal diameter or IgE titre) does matter in terms of predicting clinical relevance, and a smaller size of response needed for clinical relevance in the younger child.

When interpreting the results of our study in light of the above information, the following generalizations can be made. While 80% of our infants reacted with positive SPT to egg white, the clinical relevance of this positive SPT is unclear. However, we believe the strongly positive reactions to egg white found in 56% of our infants are more likely to be of clinical relevance. Further work needs to be carried out in this area to determine the thresholds at which SPT are likely clinically important in this patient population.

In most infants with food allergy (not just AD), it is clear from the combination of IgE screening test (SPT or RAST) followed by DBPCFC that very few foods are implicated, variously referred to as the 5[6], 6 or 7[7,9] most common food allergens, namely, egg, cow's milk, peanut, wheat, soy, tree nuts and fish. Our findings indirectly support the notion that essentially the same few foods are potentially implicated in contributing to AD, with egg white the most likely food allergen to elicit a positive SPT in the population we studied. As the infants were predominantly breast-fed, it is presumed sensitization has occurred by passage of allergens across the placenta or through breast milk. Others have shown that early sensitization to cow's milk or egg is associated with a worse clinical outcome in young children with AD.[20]

The role of dietary elimination for the prevention or treatment of AD is also an area of controversy. Exclusion or elimination diets for preventing AD are not felt to have a role during pregnancy, though they may have a role for breast-feeding mothers or for the infants themselves.[6] Exclusive breast-feeding in the first 3 months of life is associated with a lower risk of AD during childhood in children with a family history of atopy.[21] There is also some evidence

for improvement in extent and severity of AD with elimination diets.[22] Involvement of a dietician experienced in evaluating the needs of young infants is important, as nutritional deficiencies have been reported from overzealous restriction.[23] Also the foods most commonly eliminated are ubiquitous in the food supply, food labelling is complex and hidden sources may be missed without some professional guidance. It is also important to be aware that with time many food allergies in young children resolve, although resolution is less likely in cases of severe allergy to nuts.[24]

Our study shows that a group of predominantly breast-fed infants with moderate to severe AD has very high rates of positive SPT to the common food allergens, with egg white the most likely food allergen implicated. Although we have not determined the clinical relevance of this screening test in our population, our reading of the literature suggests the larger the reaction the more likely this is to be relevant to an individual patient. It is our practice to screen for food allergy using SPT and to eliminate foods with strong positive responses, provided these are of limited number. Ideally, such foods are eliminated for at least a 12-month period. Our clinical impression of those infants with strongly positive responses is that dietary elimination appears to help the AD in some but not all infants.

In our experience, it is a common wish of the parents of infants with AD to seek out allergy testing from the medical profession, or alternatively pseudoallergy testing if this is not easily available. Current evidence suggests that it is reasonable to screen for food allergy in infants with moderate to severe AD. Breast-feeding may reduce the overall rate and severity of AD but does not obviate the need for allergy testing in the infant with moderate to severe AD. We propose that this could be conceptualized like patch testing for allergic contact dermatitis, that is a 'standard series' of the common food allergens (milk, egg white, peanuts, soy, wheat, fish and tree nuts) should be conducted with all patients with extra allergens added based on history. This standard series could be performed with either SPT or RAST, though in this country SPT may be the cheaper option and the main contraindication is suspicion of anaphylactic reactions to foods. As with patch testing, false positive responses occur with SPT, but the larger the wheal diameter, the less likely it is the response is a false positive and the more likely it is the response is clinically relevant. As it is imperative firstly to do no harm, before food exclusion consultation with a dietician experienced with children is recommended to ensure adequate exclusion and that nutrition is maintained.

The role of food allergy in AD remains an area of controversy. We encourage the wider dermatology community to become involved in this work in the future.

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