

ORIGINAL ARTICLE

Single nut or total nut avoidance in nut allergic children: outcome of nut challenges to guide exclusion diets

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Abstract

Background: Children with diagnosed nut allergy are typically advised by health professionals to exclude all nuts from their diets, irrespective of the outcome of allergy testing, to avoid inadvertent contact through contamination or the possible development of new allergies.

Methods: In our service, as we feel greater diagnostic accuracy prevents dietary risk taking, we provide the facility for children with nut allergy the opportunity of controlled exposure to 'other' nuts irrespective of whether their allergy prick test (PT) results are positive or negative. We performed open food challenges on our paediatric day ward. The challenge food was administered by way of a homemade biscuit containing 8 g of each nut challenged and given in increasing visually measured doses.

Results: Over the 5-year period from 2006, we challenged 145 children diagnosed as peanut allergic or tree nut allergic. In those with peanut allergy challenged to tree nuts, none of the 72 with negative PTs to tree nuts reacted on challenge whilst 7 of 22 (31.2%) with positive PTs did. In patients with tree nut allergy challenged to peanuts and/or other tree nuts, 3 of 38 (7.9%) with negative PT results and 5 of 13 (38.4%) with positive PT results reacted.

Conclusion: Children allergic to peanuts with negative allergy tests to tree nuts had no co-existing allergy, but were at risk of tree nut allergy where PTs were positive. Children with tree nut allergy were at risk of co-existing peanut or other tree nut allergy whether PTs were positive or negative. Oral challenges to clarify allergy status in all nuts show co-existing allergies even in young children and in so doing may reduce anxiety, minimize unnecessary dietary restrictions and prevent later episodes of anaphylaxis through uninformed exposure.

The diagnosis of allergy to foods like nuts is typically made where a clear history of reaction on contact, usually ingestion, of the food in question is confirmed by a positive allergy test, either a PT or serum-specific IgE assay. Currently, children with diagnosed nut allergy are advised to strictly avoid eating the nut allergen and to carry an adrenaline auto-injector as emergency treatment of anaphylactic reactions following inadvertent contact (1). Many clinicians further frequently advise avoidance of all nuts even where there is no clinical or diagnostic evidence of allergy because the rate of cross-reactivity between nuts, particularly tree nuts, is reported as high as 34% (2–4), and because of the potential risk of inadvertent contact from contamination (5). Although theoretically sound, this practice leaves the individual with the situation of not knowing his or her full diagnosis, and thus has two potential effects. It may further increase the already high psychological impact of the diagnosis of nut

allergy as individuals are asked to take care about all nuts rather than focusing on a single nut (6). It may alternatively lead to risk-taking behaviour as individuals feel this advice is unnecessarily restricting (7). A possible solution is to provide the individual with more complete information about all his or her nut allergies. In our service, we offer all children, mostly of school-going age, diagnosed with a nut allergy the opportunity of greater diagnostic clarity through an open food challenge to the nuts of doubtful allergic status. We here present our experience over the past 5 years.

Methods

Data collection

A retrospective audit was carried out on all food challenges from 2005 capturing patient demographic data, challenge

relevant PT results and the challenge undertaken, i.e. the nuts or nuts ingested and its outcome. The indication for the challenge was also recorded, and in this report only those classified as 'allergic to one nut' were considered. Other indications for nut challenges not included were where patients with eczema were screened for potential foods causes of exacerbations or where patients were thought to have outgrown their nut allergy.

Allergy testing

All patients presenting to our Children's Allergy Clinic with a history suggesting an allergic reaction to a nut are allergy tested by prick testing to the six nuts of almond, Brazil nut, cashew nut, hazelnut, walnut and peanut using standardized skin prick test solutions (ALK Abello), where available, or by prick testing to fresh nuts. Patients are not routinely tested for pistachio nut and pecan nut because of their strong cross-reactivity with cashew nut and walnut, respectively, as they come from the same botanical families (8). Prick tests are considered to be positive where the wheal diameter is ≥ 3 mm, and a diagnosis of allergy is made to a specific nut when this PT result confirms a presenting history. Children (predominantly over 5 years old) are then offered an open mixed nut challenge to the other nuts, irrespective of whether PTs are positive or negative, to determine his or her tolerance or otherwise to these nuts. When the presenting history and PTs are inconclusive or contradictory, the patient undergoes

a single nut challenge to the suspected nut to establish whether he or she is indeed allergic.

Mixed nut open challenges

Open food challenges are used in which the patient ingests increasing visually measured doses of the challenge food every 20 min (Figure 1). In mixed nut challenges, patients eat a homemade biscuit made by our dietitian containing 8 g of each nut to be challenged (Figures 2 and 3). Peanut challenges are performed resulting in a dose of 8 g of peanuts being ingested either as whole peanuts or in a biscuit. No child refused to eat the challenge biscuit demonstrating that this method is acceptable to children of all ages and thus feasible and practical.

The procedure is conducted in our Children's day ward by an experienced nursing team supported by agreed emergency protocols to manage allergic reactions. Patients are observed during the 20-min intervals between doses for the development of any allergic manifestations. Challenges are considered to be positive when patients develop objective symptoms, i.e. skin rashes (flushing, urticaria or worsening eczema), angioedema, conjunctivitis, rhinitis, wheeze or vomiting. As exception, however, if a patient undergoing a challenge has in addition a positive allergy test, and is thus

Nut biscuit challenge	
Patient's name	
Date of birth	
Food to be challenged: Nut containing biscuit (<i>Nuts identified</i>)	
Procedure	
Step	Dose
1	Small crumb of biscuit to be eaten 15-min observation
2	Large crumb of biscuit to be eaten 15-min observation
3	Two large crumbs of biscuit to be eaten 15-min observation
4	1/32 of a biscuit to be eaten 15-min observation
5	1/16 of a biscuit to be eaten 20-min observation
6	1/8 of a biscuit to be eaten 20-min observation
7	1/4 of a biscuit to be eaten 20-min observation
8	Remainder of biscuit to eaten 60-min observation

Figure 1 Open food challenge protocol for ingesting nut-containing biscuits

Ingredients	Approximate weight (g)
1 level tablespoon of self raising flour	20
1 level teaspoon of margarine	5
1½ teaspoons of Castor sugar	6
½ teaspoon of Golden syrup	3
2 Brazil nuts	8
5 Almonds	8
7 Hazelnuts	8
7 Cashew nuts	8
3 small Walnut halves	8
1–2 flat teaspoons of water to mix	

Method

Ensure all equipment is clean and free from contamination

1. Grind nuts to a coarse powder by using an electric coffee bean grinder or Manually grinding with a pestle and mortar or cheese grater. Remove and regrind any chunks
2. Place flour in a bowl, add margarine and rub into flour
3. Add sugar, syrup and nut powder and mix well
4. Add water and mix into stiff dough. Roll into a ball, place on a greased tray and flatten into a biscuit
5. Bake in a hot oven at 200°C for 12 min until lightly brown

Notes:

For milk allergic patients, use dairy-free margarine.

For fussy eaters or blind challenges, substitute 10 g flour with 10 g or cocoa powder.

For wheat allergic patients, substitute flour with wheat-free baking mix.

Figure 2 Recipe for mixed tree nut biscuit

Step	Dose	Approximate weight (in grams) in dose	
		Of each nut	Of biscuit
1	Small crumb of biscuit	0.02	0.1–0.2
2	Large crumb of biscuit	0.05	0.3–0.5
3	Two large crumbs of biscuit	0.12	0.75
4	1/32 of a biscuit	0.25	1.5
5	1/16 of a biscuit	0.5	3.0
6	1/8 of a biscuit	1.0	6.0
7	1/4 of a biscuit	2.0	12.0
8	Remainder of biscuit	4.0	25.0

Figure 3 Approximate weight of challenge doses for 5 nut biscuit

regarded at higher risk of reacting, subjective symptoms (e.g. mood change, mouth tingling) are considered significant. This individual will subsequently undergo a single-blind challenge, eating two biscuits one with and one without the challenge nut or nuts, to confirm this positive challenge. If allergic symptoms develop, the challenge is aborted and the patient treated with appropriate medication.

Results

During the 5-year 6-month period from January 2006, 145 open nut challenges were performed. Patients were aged

between 28 and 204 months (median 98.5 months); 89 (59.3%) were boys.

Challenge outcomes are shown in Table 1.

Ninety-four patients with diagnosed peanut allergy were challenged to all tree nuts (i.e. almonds, cashew nut, Brazil nut, hazelnut and walnut). In the 72 patients in whom PTs to tree nuts were negative, no patient reacted during challenge, whereas in the 22 patients with positive PT (weal size 3–6 mm) to one or more tree nuts, 7 (31.2%) reacted. The 15 patients with negative challenges tested positive to either one tree nut in 11, two nuts in 3 and 4 nuts in 1, of which 7 were to almonds, 2 to Brazil nuts, 3 to cashew nuts, 7 to hazel nuts and 2 to walnuts. Details of patients with positive challenges are shown in Table 2.

Fifty-one patients with tree nut allergy were challenged to peanuts and/or other tree nuts. In 13 who had a positive PT to the nuts being challenged (weal size 3–8 mm), 5 (38.4%) reacted, whilst in the remaining 38 with negative PT to the nuts challenged, 3 (7.9%) reacted. The patients with positive PTs and negative challenges tested positive to peanut only in 5 and hazelnut in 2. The remaining patient, diagnosed unusually with Macadamian nut allergy, tested positive to almond, hazelnut, walnut and peanut. Details on positive challenges for both positive and negative PT to nuts challenged are shown in Table 3.

All 15 patients who reacted had their allergic symptoms successfully treated with oral antihistamines together with oral prednisolone in one and inhaled salbutamol in two. No patient required treatment with intramuscular adrenaline.

Table 1 Outcomes of all nut challenges performed

Diagnosed nut allergy	Pt no.	Nuts challenged	PT result to nuts challenged	No. of positive challenges
Peanut	22	All tree nuts	Positive	7
Peanut	72	All tree nuts	Negative	0
Tree nut	13	Peanuts (9)	Positive	5
		Other tree nuts (1)		
		Peanuts and other tree nuts (3)		
Tree nut	38	Peanuts (15)	Negative	3
		Other tree nuts (1)		
		Peanuts and other tree nuts (22)		

Pt no, patient numbers.

Table 2 Details of positive tree nut challenges in peanut allergic patients with positive PT reactions to one or more tree nuts

PT	Tree nut PT positive (weal size in mm)	Symptoms at challenge
12	Cashew nut (3)	Pruritis, throat symptoms, stomach ache
6	Almond (3), Brazil nut (4), hazelnut (3)	Throat symptoms, nausea
8	Almond (3), cashew nut (5), hazelnut (3)	Mood change, nausea, stomach ache
8	Almond (4), hazelnut (3)	Throat symptoms
5	Almond (3), cashew nut (3)	Lip swelling, pruritis, mouth itch, throat symptoms, nausea
10	Almond (6), Brazil nut (6), cashew nut (6), hazelnut (6), walnut (3)	Lip swelling, mouth itch, throat symptoms, mood change
5	Almond (3)	Lip swelling, throat symptoms

PT – Individual patient peanut PT wheal size in mm.

Table 3 Positive open challenges to other tree nuts and/or peanuts in patients with tree nut allergy

Diagnosed allergy	PT results of challenge nuts	Nuts challenges	Challenge symptoms
Brazil nut (16)	All negative	Other tree nuts and peanuts	Throat symptoms, wheeze (delayed)
Cashew nut (11)	All negative	Other tree nuts	Lip swelling
Cashew nut (3)	All negative	Other tree nuts and peanuts	Wheeze, nausea
Cashew nut (11)	Almond (8), Hazelnut (8) Peanut (8)	Other tree nuts and peanuts	Generalised urticaria, pruritis, sneezing, throat symptoms, cough
Cashew nut (8)	Peanut (6)	Peanuts	Lip swelling, generalized pruritis
Cashew nut (8)	Peanut (6)	Peanuts	Lip swelling, generalized urticaria, pruritis
Cashew nut (15)	Peanut (5)	Peanuts	Throat symptoms, sneezing, wheeze, dyspnoea, vomiting
Almond (4) Cashew nut (4)	Peanut (6)	Peanuts	Lip urticaria

Numbers in brackets are adjacent nut PT weal size in mm.

Discussion

As peanut and tree nut allergy cause most food-related anaphylactic reactions in children, and cross-reactivity between nuts is commonly reported (2–4), it is common practice for paediatric allergy clinics to advise that, even where a single nut allergy is diagnosed, these patients avoid all nuts in their diets. Clark and Ewan (2) further consider that this strict avoidance advice is necessary to prevent the development, with increasing age, of additional clinical nut allergies in sensitized children with exposure to multiple nut types. However, Pumphrey and colleagues (9) demonstrated similar patterns of nut-specific IgE between age quartiles and consequently felt that their study suggests that the apparent mono-allergy in young children and multi-allergy in adults may simply reflect opportunity for exposure rather than an increased range of allergy in the older patients.

Furthermore, a diagnosis of nut allergy in a child can have a considerable psychological burden on the individual and his or her family because of its continuing potential risk of anaphylaxis (6) and because it enforces many food choices and lifestyle restrictions; a burden which is likely to be increased by the belief that that all nuts and nut traces have the potential to cause anaphylaxis. Accurate diagnosis of nut allergy *per se* and of the nuts to which an individual with the diagnosis is allergic is therefore essential.

This greater diagnostic clarity is also of potential benefit to families where their culture dictates that nuts are widely used in the home environment. Our hospital serves a population predominantly of either Caucasian or southern Asian (Indian or Pakistani) origin. Nuts are a common part of the Asian diet. Whilst as professionals we may believe total nut avoidance is preferable, we have found that being able to provide specific nut avoidance advice, for example allowing children with single peanut allergy to eat cashew or almond within home cooking, to our Asian vegetarian families, is welcomed and thereby improves their quality of life. As nuts are an important source of protein in vegetarian diets, allowing a more inclusive diet will improve its nutritional value.

In 2006, we adopted the practice of offering all patients diagnosed with nut allergy the opportunity to undergo an open mixed nut challenge to the other nuts, to enable us to give evidence-based advice on whether the child has a single or multiple nut allergy. As this was our aim, for our mixed nut challenges, all the nuts of uncertain allergenicity were placed in a single biscuit. We regard this a sensible approach as it eliminates the need for multiple single nut challenges in individual patients, allowing us to offer our service within a 6-week waiting period, and does not change the outcome of advice as individual tree nuts are rarely listed on ingredients lists, whereas peanuts and tree nuts are commonly distinguished. Further specific individual nut challenges are only carried out at patients' requests. The practice of using a homemade biscuit rather than whole nut ingestion was well accepted. It also allowed us to incorporate the recommended 8 g dose (10) of each nut into a smaller volume of food that had to be ingested.

Where patients with clinically suspected peanut allergy prick tested positive to peanuts (confirming peanut allergy) and negative to all tree nuts, all were able to ingest tree nuts at challenge without reacting. We advise this group to continue with strict peanut avoidance, including peanut trace warnings, but allow them to ingest tree nuts and foods with tree nut warnings, if they wish to, within the home environment. Indeed the absence of any challenge reactions to tree nuts in patients with peanut allergy and negative PT to tree nuts suggests that this group may not need supervised challenge to allow tree nut contact. We would, however, recommend that as a precaution individuals undergo repeat PT say 6 months after the first negative test to confirm these findings before allowing them tree nut exposure.

The distinction in patients with tree nut allergy is not so clear-cut and needs confirmation with oral challenges whether the PT results to the other tree nuts or peanuts are positive or negative. Reactions occurred in patients confirmed as tree nut allergic to both peanuts and other tree nuts when PTs were positive or negative. Similarly, patients with diagnosed peanut allergy and positive PTs to tree nuts also need

confirmatory challenges. Without challenge, this co-reactivity remains undiagnosed, potentially increasing the risk of an unexpected anaphylaxis later in life (9). Here too patients received dietetic advice on safely broadening their diets appropriate with the outcome of their challenges if they wish to, and when PTs are positive are actively encouraged to do so to avoid clinical reactivity developing (11). All patients reacting on challenge are advised to continue avoiding all nuts and nut traces.

Whilst we acknowledge that with this approach there remains the potential risk of allergic reactions through contamination where nuts are mixed together, we have not had reports of adverse reactions from patients. We further feel that this negative aspect is outweighed by patient feedback that anxiety is greatly reduced, that it reduces the number of food restrictions as manufactured products containing a named nut or nut warning no longer needs to be avoided and that confirming single nut allergy may also improve compliance and decrease risk taking behaviour as patients are

able to concentrate more on total exclusion of that nut rather than taking chances because of an inability to conform to the more stringent dietary restrictions of total nut avoidance. Many patients may continue to choose avoidance of all nuts following a negative challenge but feel less anxious about the possibility of anaphylaxis.

Conclusion

The practice of supervised exposure in patients with diagnosed nut allergy to other nuts of uncertain allergic status provides an improved understanding of an individual's nut allergies and aims to decrease some of the psychological burden, food restrictions and risk taking behaviour that occurs in these patients. In patients with peanut allergy who PT negative to tree nuts, confirmatory PT rather than oral challenge may suffice to exclude other nut allergies, whilst in patients either with tree nut allergy or with positive PT to tree nuts, confirmatory challenges are needed.

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