Ann Allergy Asthma Immunol xxx (2016) 1–5

Contents lists available at ScienceDirect

The economic effect and outcome of delaying oral food challenges

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ARTICLE INFO

Article history:
Received for publication January 13, 2016.
Received in revised form February 22, 2016.
Accepted for publication February 24, 2016.

ABSTRACT

Background: Food specific IgE (sIgE) is a useful marker to assess predictability of oral food challenge (OFC) outcome. A threshold of less than 2 kUA/L for peanut, egg, and milk has been proposed as a 50% negative predictive value at which patients may pass an OFC.
Objective: To assess the economic effect and outcome of delaying OFCs.
Methods: A retrospective analysis was performed for peanut, egg, and milk OFCs conducted between 2001 and 2012 at a tertiary food allergy referral center. Delayed OFC was defined as greater than 12 months from the time the sIgE level became less than 2 kUA/L. Time to OFC was explored in association with skin prick test result (wheal size), OFC outcome, and the economic effect of delay.
Results: Of 319 challenges, 173 OFCs were delayed (54.2%) by a mean time of 35.5 months (range, 13–123 months) vs a mean time of 4.2 months in the 146 challenges that were not delayed ($P < .001$). The overall OFC passage rate was 89.9%. There was no association between delayed OFC and history of anaphylaxis, type of allergen, age at OFC, or challenge outcome. Delay in OFC was associated with an estimated mean economic cost of $12,203 per patient ($4,184 per 12 months) and $1,951,487 total (total delay, 5,597 months) in this population.
Conclusions: Despite a 50% negative predictive value, more than 50% of OFCs were delayed in this population by a mean time of nearly 3 years. Delaying OFC is associated with increased costs, and quality improvement is needed to help decrease time to OFC and reduce the economic burden of food allergy on families and the health care system.

Introduction

Food allergy affects 8% of children in the United States based on self-report survey.[1] Several studies report an overall increase in food allergy prevalence, although exact US prevalence data and trend interpretation are limited based on use of indirect methods and not oral food challenge (OFC) to confirm allergy.[2–4] However, according to most available estimates, there appears to be an increase in children with a diagnosis of food allergy.[5] Inappropriate testing, especially using food specific IgE (sIgE) alone, in patients without a convincing history of suspected food-induced allergic reaction may be contributing to misdiagnosis, unnecessary food avoidance, and inflated estimates of food allergy prevalence.[6,7]

The gold standard diagnostic procedure for suspected IgE-mediated food allergies is the double-blind, placebo-controlled food challenge.[5] In clinical practice, open (nonmasked) challenges are well accepted as an alternative and are preferentially used because they are less labor intensive, more time efficient, and more practical.[8] Skin prick testing (SPT) and sIgE have been identified as useful markers to predict OFC outcome. An sIgE threshold of less than 2 kUA/L to peanut, egg, and milk has been proposed as a 50% negative predictive value (NPV) at which patients can be expected to pass an OFC and a challenge procedure can be safely offered.[9]

There is sparse literature exploring why OFC may not be offered or if offered why it may be deferred. Reasons may include conflicting allergy testing data, the patient has a history of severe anaphylaxis or poor asthma control, or deferral may simply be due to patient, caregiver, or clinician preference.[10] On the basis of survey

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Disclosures: Authors have nothing to disclose.
Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
Funding Sources: This study was supported in part by a gift from an anonymous foundation and by grant 2UL1TR000433 from the National Center for Advancing Translational Sciences. Dr Greenhawt also received support from grant 2KL2TR000434 from the National Center for Advancing Translational Sciences.

http://dx.doi.org/10.1016/j.anai.2016.02.016
1081-1206/

report, allergists may decide to delay or defer an OFC due to concerns that the patient may react, time limitations to perform the OFC, poor reimbursement, inadequate training, lack of comfort in performing the challenge, or lack of resources (staff, space) to perform the OFC.[11] The most common reasons for deferring OFC according to a recent caregiver survey were "no interest in adding the food into the diet" and "fear of not passing the challenge."[12]

Food allergy was recently estimated to have a direct annual medical cost of $4,184 per year per child (inclusive of direct medical, out-of-pocket, lost labor productivity, and related opportunity costs), with nearly 80% of these costs being borne by the family and just 20% being related to direct medical care.[13] It is possible that delaying or deferring the OFC, despite the patient being an appropriate OFC candidate, may lead to additional unnecessary financial costs (eg, opportunity costs, lost-labor productivity costs), as well as the opportunity cost of not potentially being able to reintroduce the food.[13] Although the reasons for delaying an OFC procedure are complex and dependent on the allergist's assessment and the caregiver and patient or family preference for the procedure, the costs associated with OFC delay should be considered. No study to date has explored the health or economic effect of delaying the decision to perform OFC. The objectives of this study were therefore to investigate the timing of OFC administration in relation to testing results, the OFC outcome, and the economic cost of delaying the OFC.

Methods

Study Design

This was a retrospective analysis of peanut, egg, and milk open OFCs conducted at clinics at the Division of Allergy and Clinical Immunology, University of Michigan, between 2001 and 2012. These 3 foods were chosen based on prior divisional study identifying them as the most common OFCs offered and because these items have previously been evaluated and proposed as having a 50% NPV for reactivity.[9,14] Patients who underwent OFCs were identified from the Division of Allergy and Clinical Immunology database using *International Classification Diseases, Ninth Revision* (*ICD-9*), coding, *Current Procedural Terminology* (*CPT*) coding for ingestion challenge, and medical record review for OFC procedures performed. Patients who had peanut, egg, and milk SPTs and corresponding food sIgE tests before challenge were included in the analysis. Patients with a history of non–IgE-mediated food allergy were excluded.

Delayed OFC was defined as an OFC that occurred more than 12 months from the time when the patient's sIgE level was less than 2 kUA/L (50% NPV) for peanut, milk, or egg. Variables that were investigated include time (months) to OFC, number of visits with allergy testing once the sIgE level decreased to less than 2 kUA/L, SPT result (wheal size), and OFC outcome. Total costs associated with delay were calculated according to recently published data quantifying the direct and indirect economic effect of food allergy.[13] The study was approved by the University of Michigan Institutional Review Board.

Statistical Analysis

The primary outcome was to investigate the proportion of delayed OFCs and compare elapsed time between the delayed group and the nondelayed group. Secondary outcome measurements included differences in OFC outcome, SPT result (wheal size), age at OFC, number of additional visits, history of anaphylaxis, and allergen type between the 2 groups. Descriptive statistics were determined through frequency analysis. Mean differences between groups were assessed using independent sample *t* tests and proportional differences by Fisher exact tests. Predictive associations were determined through both logistic regression and linear regression. An α of .05 was used for significance. The study had 80% power to detect a 20% difference in all primary and secondary outcomes between the groups with 62 patients per arm. All analyses were performed using STATA SE, version 13 (StataCorp, College Station, Texas).

Results

There were 270 patients identified who underwent 319 OFCs to peanut, milk, or egg between 2001 and 2012. Forty-five patients underwent 2 or more challenges. Patient characteristics are listed in Table 1. The mean age at food allergy diagnosis was 27 months, and the mean age at initial OFC was 80 months. OFC to egg was performed most frequently, followed by OFC to peanut and milk. Table 2 lists the presenting symptoms of food allergy within this population. Hives were the most commonly reported symptoms of presenting illness. There were 229 challenges (71.8%) performed in patients who had a prior history of at least a single presenting symptom to the challenged food, whereas 73 (22.9%) were performed in patients avoiding the food item due to sensitization (eg, a high sIgE level or large wheal on skin testing), and 17 (5.3%) were performed in patients avoiding the food secondary to potential cross-reactivity with another food allergen. Overall, 56 (17.6%) of 319 challenges were to foods in patients with medical record–verified symptoms that were consistent with anaphylaxis, according to the 2006 National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network criteria. There was no association noted between the OFC item and a reported history of anaphylaxis.

Of 319 OFCs, 173 (54.2%) were delayed, defined as occurring more than 12 months from the time that the food sIgE level decreased to less than 2 kUA/L (Table 2). Mean age at the time of the OFC was 88 months in the delayed group vs 72 months in nondelayed group ($P \leq .001$). The mean time to OFC was 35.5 months (range, 13–123 months) in the delayed group vs 4.2 months in the nondelayed group ($P < .001$). Peanut was the most frequently delayed type of OFC (n = 74) (Fig 1) and was delayed the most number of months (mean of 37 months in the delayed group) (Fig 2). These patients were also the oldest at the time of the OFC (mean age, 88 months). The mean number of additional visits with testing after the sIgE level decreased to less than 2 kUA/L in the delayed group was 2.13 (range, 1–7). Egg OFC was associated with the most number of visits with testing in the delayed group (mean, 2.29). Combined OFC passage rate for all items was 89.9%, with 83.7% passing peanut OFC, 93.1% egg OFC, and 95.4% milk OFC. The odds of passing either a milk (odds ratio] [OR], 4.01; 95% confidence interval [CI, 1.1–14.1; $P = .03$) or egg (OR, 2.9; 95% CI, 1.25–7; $P = .01$) OFC were significantly higher than passing a peanut OFC. The passage rate for delayed OFC was 92.5% vs 87.6% for nondelayed OFC, which was not significant. Peanut OFC had the lowest pass rates in both the delayed and nondelayed OFC groups compared with egg and milk.

Table 1
Study Population Characteristics

Characteristic	Finding (N = 270)
Male, No. (%)	174 (64)
Multiple food allergies, No. (%)	180 (67)
Comorbid atopic disease, No. (%)	
Atopic dermatitis	147 (54)
Allergic rhinitis	132 (49)
Asthma	93 (34)
Mean age at initial food allergy diagnosis, mo	27
Mean age at initial oral food challenge, mo	80