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Tolerance of a high-protein baked-egg product in egg-allergic children

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ABSTRACT

Background: Egg allergy is one of the most common immunoglobulin E (IgE)–mediated food allergies. Extensively heating egg has been found to decrease its allergenicity and 55% to 84% of children allergic to egg have been found to tolerate baked-egg products. Because there is no reliable method for predicting baked-egg tolerance, oral food challenges remain the gold standard. Prior studies have reported on baked-egg challenges using up to 2.2 g of egg white (EW) protein.

Objective: To establish whether children with egg allergy would pass a baked-egg challenge to a larger amount of egg protein and the potential criteria for predicting the likelihood of baked-egg tolerance.

Methods: A chart review was conducted of all patients 6 months to 18 years of age with egg allergy who underwent oral baked-egg challenges at Children's Medical Center Dallas over a 2-year period. Challenges were conducted in the clinic with a 3.8-g baked-egg product.

Results: Fifty-nine of 94 patients (63%) tolerated the 3.8-g baked-egg product. The presence of asthma ($P < .01$), EW skin prick test (SPT; $P < .01$) reactive wheal, and EW-specific IgE level ($P = .02$) correlated with baked-egg reactivity, whereas ovomucoid-specific IgE level did not. The positive predictive value approached 66% at an EW SPT reactive wheal of 10 mm and 60% for an EW-specific IgE level of 8 kU_A/L.

Conclusion: Most subjects with egg allergy tolerated baked egg. This study is the first to use 3.8 g of EW protein for the challenges. The EW SPT wheal diameter and EW-specific IgE levels were the best predictors of baked-egg tolerance.

Introduction

Egg allergy, one of the most common immunoglobulin E (IgE)–mediated food allergies, affects 1.6% to 8.9% of the pediatric population.[1–4] Five major egg-allergenic proteins have been identified. Ovomucoid (OM; Gal d 1), a heat-resistant constituent, comprises only 11% of egg white (EW) protein but is the dominant allergen, causing reactions even in miniscule amounts.[3] Ovalbumin (Gal d 2) is the most abundant protein in EW and is sensitive to thermal denaturation. Extensively heating egg decreases its allergenicity by destroying conformational epitopes.[5] In addition, when baked, the interaction of egg proteins with the food matrix, such as wheat, is believed to contribute to decreased recognition of egg proteins by the immune system.[5–7] Prior studies have shown that 55% to 84% of children with egg allergy tolerate baked or baked-egg products.[8–12] There is no current reliable method for predicting baked-egg tolerance based on clinical or immunologic markers; thus, oral food challenges remain the gold standard for determining tolerance to baked egg. It is important to identify patients allergic to egg who tolerate baked egg because regular consumption of baked egg has been shown to promote tolerance to all forms of egg.[13] The ability to incorporate baked-egg products into one's diet also can have psychosocial and nutritional benefits. Baked-egg challenges have been conducted with up to 2.2 g of EW protein (the equivalent of approximately one third of an egg).[8,10–12] This amount has been cited as the typical content in a serving of baked-egg product in the Western diet; however, children with egg allergy might ingest larger amounts of egg protein in baked products, such as sponge cake, which contains approximately 3.8 g of egg protein per serving. The authors' objective was to review their food challenge data to determine the tolerability of a 3.8-g baked-egg challenge and to evaluate potential criteria for predicting the likelihood of tolerating baked egg by associating baseline clinical characteristics and initial diagnostic tests with baked-egg challenge outcomes.

Methods

A retrospective chart review was performed of all patients 6 months to 18 years of age who underwent oral baked-egg

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challenges at The Food Allergy Center at Children's Medical Center Dallas (Dallas, Texas) from November 2010 through December 2012. A history of egg allergy was defined as (1) a recent history (≤6 months) of an IgE-mediated reaction to egg with evidence of IgE sensitization (EW skin prick test [SPT] wheal size >3 mm or EW-specific IgE level >0.35 kU_A/L) or (2) if there was no or a questionable clinical history of egg ingestion and reaction, then an EW SPT wheal of at least 5 mm in those younger than 2 years or at least 7 mm in those at least 2 years old and/or an EW-specific IgE level of at least 2 kU_A/L in those younger than 2 years or at least 7 kU_A/L in those at least 2 years old. Specific IgE levels were measured using ImmunoCAP (Thermo Fischer Scientific, Portage, Michigan) and SPTs were performed with EW extract (ALK-Abello, Round Rock, Texas).

Oral baked-egg challenges were performed openly under physician supervision using sponge cake prepared by the patient's family from a standard sponge cake recipe, which uses 5 eggs per recipe, allowing for a higher concentration of egg protein per serving (Table 1). The cake was baked at 350°F (177°C) for 30 minutes. The entire cake was divided into 8 equal servings, each equivalent to approximately 3.8 g of egg protein (approximately two thirds of an egg). One serving was further subdivided and each dose was administered every 15 minutes in escalating doses of approximately 5% (0.19 g), 10% (0.38 g), 20% (0.76 g), and 25% (0.95 g). A failed challenge was defined as having objective symptoms of an allergic reaction during the challenge or within 2 hours of the last dose and was graded according to the Sampson Anaphylaxis Scale.[14] Variables of age, sex, history of atopic conditions, EW SPT wheal diameter, EW-specific IgE level, and OM-specific IgE level were evaluated for associations with baked-egg challenge outcomes and reaction severity.

Baseline characteristics were evaluated with χ^2 test for categorical variables and t test for continuous variables with α value equal to 0.05. The EW SPT wheal, EW-specific IgE, and OM-specific IgE values were compared between patients tolerant of baked egg and patients reactive to baked egg. A t test was used to evaluate means with α value equal to 0.05. Receiver operating characteristic curves were made for each value for predicting the baked-egg reactive group. The area under the curve was calculated for each value and sensitivity, specificity, and negative predictive value (NPV) were calculated at certain cutoffs. Spearman correlations with 95% confidence intervals were made to represent the relation between the values and outcome severity.

Results

Ninety-four patients (mean age 4 years, range 1–16 years) with a history of egg allergy underwent a baked-egg challenge to sponge cake (3.8 g of protein). Patient characteristics are listed in Table 2.[15,16] Fifty-nine (63%) tolerated the sponge cake, whereas the remaining 35 (37%) reacted. Asthma, seen in 60% of patients reactive to baked egg and 34% of patients tolerant of baked egg, correlated with reactivity ($P = .01$) alone and in combination with atopic dermatitis ($P < .01$) or allergic rhinitis ($P < .01$). The difference in mean EW SPT wheal size (9 vs 15.53 mm) and mean EW-specific IgE level (9.82 vs 17.96 kU_A/L) in the group tolerant of vs reactive to baked egg was statistically significant ($P < .01$, $P = .02$), whereas OM-specific IgE level did not correlate with baked-egg reactivity ($P = .44$; Figures 1 and 2).

Eighty percent of failed challenges were grade 2 reactions, 17% were grade 3, and 3% were grade 4. Failure of baked-egg challenges resulted in cutaneous symptoms in 77% of patients, respiratory symptoms in 49%, and gastrointestinal symptoms in 40%. Epinephrine, in conjunction with other treatments, was given to 7 of 35 patients (20%) who reacted. Most of those whose challenge failed reacted between the third and fourth dose of the sponge cake (1.3–2.0 g of egg protein). There was no significant correlation between EW- and OM-specific IgE antibody levels or between SPT wheal sizes and reaction severity scored using the Sampson grade.

Receiver operating characteristic curves for EW SPT wheal size, EW-specific IgE level, and OM-specific IgE level showed areas under the curve of 0.79, 0.64, and 0.55, respectively (Figure 3). The EW SPT wheal cutoff of 10 mm had a specificity of 78.0%, sensitivity of 71.4%, and NPV of 82.1% (Table 3). The positive predictive value (PPV) at an EW SPT wheal reaction of 10 mm was 65.8%. An EW-specific IgE cutoff level of 8 kU_A/L had a specificity of 74.6%, sensitivity of 60.0%, NPV of 75.9%, and PPV of 58.3%. An OM-specific IgE cutoff level of 8 kU_A/L had a specificity of 81.4%, sensitivity of 31.4%, NPV of 66.7%, and PPV of 50.0%.

Discussion

A retrospective analysis was conducted of 94 children with egg allergy who completed oral baked-egg challenges to establish tolerability of a 3.8-g baked-egg product, which is a larger amount of EW protein than previously reported, and to determine markers of tolerability. Most patients with egg allergy (63%) tolerated the 3.8-g baked-egg product, consistent with previous studies reporting tolerability of 2.2 g of baked-egg protein. The present study is the first to use 3.8 g of egg protein for challenges compared with the smaller amount of 2.2 g used in previous studies. The reasoning for using a higher egg protein content is based primarily on (1) an

Table 1
Sponge cake recipe[a]

Ingredients
5 eggs, separated
1 cup of white sugar
4 tablespoons of cold water
1 cup of sifted cake flour
1 teaspoon of baking powder
Directions
1. Preheat oven to 350°F (177°C)
2. Grease a tube pan
3. Beat egg yolks and sugar together until very light; add water
4. Sift together flour and baking powder; add to batter
5. Beat egg whites until stiff; fold into batter
6. Pour batter into prepared pan
7. Bake for 30–35 min until brown and pulls away from the edge of the pan
8. Cut into 8 servings

[a]Yields 8 servings (~3.8 g of egg protein per serving).

Table 2
Patient characteristics

	Tolerant to baked egg (n = 59), n (%)	Reactive to baked egg (n = 35), n (%)
Age (y), mean (SD)	4.25 (3.44)	4.63 (2.89)
Girls	38 (64)	18 (51)
History of other food allergies	42 (71)	28 (80)
Asthma	20 (34)	21 (60)
AR	25 (42)	19 (54)
AD	30 (51)	20 (57)
No atopy	10 (17)	4 (11)
AD + asthma ± AR	13 (22)	15 (43)
History of reaction to lightly cooked egg with positive IgE sensitization	20 (34)	20 (57)
EW-specific IgE level and EW SPT wheal size (>95%–100% PPV for age)[a]	26 (44)	22 (63)
EW SPT wheal size only (>100% PPV for age)[b]	44 (75)	33 (94)

Abbreviations: AD, atopic dermatitis; AR, allergic rhinitis; EW, egg white; IgE, immunoglobulin E; PPV, positive predictive value; SPT, skin prick test.

[a]Ninety-five percent of PPVs were established using an age younger than 2 years and EW-specific IgE level higher than 2 kU_A/L and age of at least 2 years and EW-specific IgE level higher than 7 kU_A/L.[15]

[b]One hundred percent of PPVs were established using an age younger than 2 years and an EW SPT wheal of at least 5 mm and an age of at least 2 years and an EW SPT wheal of at least 7 mm.[16]