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Original article

Usefulness of antigen-specific IgE probability curves derived from the 3gAllergy assay in diagnosing egg, cow's milk, and wheat allergies

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3gAllergy	IMMULITE 3gAllergy
EW	egg white
OFC	oral food challenge
sIgE	specific IgE

ABSTRACT

Background: Specific IgE (sIgE) antibody detection using the Siemens IMMULITE® 3gAllergy™ (3gAllergy) assay have not been sufficiently examined for the diagnosis of food allergy. The aim of this study was to evaluate the utility of measuring sIgE levels using the 3gAllergy assay to diagnose allergic reactions to egg, milk, and wheat.

Methods: This retrospective study was conducted on patients with diagnosed or suspected allergies to egg, milk and wheat. Patients were divided into two groups according to their clinical reactivity to these allergens based on oral food challenge outcomes and/or convincing histories of immediate reaction to causative food(s). The sIgE levels were measured using 3gAllergy and ImmunoCAP. Predicted probability curves were estimated using logistic regression analysis.

Results: We analyzed 1561 patients, ages 0–19 y (egg = 436, milk = 499, wheat = 626). The sIgE levels determined using 3gAllergy correlated with those of ImmunoCAP, classifying 355 patients as symptomatic: egg = 149, milk = 123, wheat = 83. 3gAllergy sIgE levels were significantly higher in symptomatic than in asymptomatic patients ($P < 0.0001$). Predictive probability for positive food allergy was significantly increased and correlated with increased sIgE levels. The cut-offs for allergic reaction with 95% predictive probability as determined by the 3gAllergy probability curves were different from those of ImmunoCAP.

Conclusions: Measurements of sIgE against egg, milk, and wheat as determined by 3gAllergy may be used as a tool to facilitate the diagnosis of food allergy in subjects with suspected food allergies. However, these probability curves should not be applied interchangeably between different assays.

Introduction

Egg, milk, and wheat are common causative foods in food allergy,[1] accounting for the top three causes of food allergies in Japan.[2] The levels of allergen-specific IgEs (sIgEs) produced in response to food are useful predictors of clinical reactions caused by food allergens.[3–9] Previously, we found that egg white (EW)-, milk-, and wheat-sIgE levels were associated with positive symptoms in children suspected of having a food allergy, and obtained decision points (cutoff values) for each of these food allergens using the ImmunoCAP system (Thermo Fisher Scientific, Uppsala, Sweden).[10,11] These sIgE decision points can be used to help clinicians decide when oral food challenges (OFCs) are appropriate.[12–14]

Currently, several assays for measuring sIgE antibodies are used by commercial laboratories. The Siemens IMMULITE® 3gAllergy™ (3gAllergy) assay (Siemens Healthcare Diagnostics Inc., Tarrytown, NY, USA) is one such assay; however, limited publications are available regarding its clinical usefulness for the diagnosis of food allergy in comparison to those for ImmunoCAP. The 3gAllergy readout is reported as IU_A/mL, whereas that of ImmunoCAP is reported as kU_A/L. However, even though the results reported using the same sIgE level measures, the sIgE levels are not considered diagnostically interchangeable because some studies have shown discrepancies among results obtained with different assays.[15,16]

Therefore, to determine whether the 3gAllergy assay represents a valid measure of sIgE levels in food allergy, this study aimed to

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evaluate the utility of measuring sIgE levels using the 3gAllergy assay to diagnose allergic reactions to egg, milk, and wheat.

Methods

Study design

This retrospective study was conducted on patients with suspected allergies to egg, milk, and wheat who visited the Department of Pediatrics of Sagamihara National Hospital from December 2009 to May 2012 and were tested within six months of the first visit for sIgE to EW, milk, and wheat (Fig. 1).

Inclusion criteria consisted of patients who had been confirmed as symptomatic or asymptomatic after ingesting egg, milk, or wheat. Patients were defined as symptomatic if they displayed a positive reaction to OFC in the hospital, or by convincing history of immediate allergic reaction (urticaria, pruritus, wheals, eyelid or lip swelling, oral cavity irritation, coughing, wheezing, dyspnea, abdominal pain, vomiting, and diarrhea) owing to intake of the causative food(s) within 1 year before and after blood sampling. Patients were defined as asymptomatic if they could ingest half of a cooked egg (3.1 g egg protein), 100 mL milk (3.4 g milk protein), or 100 g boiled udon noodles (Japanese wheat noodles composed of 2.6 g wheat protein) without exhibiting an immediate allergic reaction within 6 months after blood sampling.

For the exclusion criteria, patients were excluded if they had never consumed the causative food(s) because of only positive sIgE levels, if they only ingest the causative food(s) less than the above-mentioned doses within 6 months after blood sampling, if they kept avoiding the causative food(s) with no immediate allergic reaction within 1 year before and after blood sampling, or if data were missing.

Oral food challenge

OFC was performed by either a single-blinded test or an open test, according to the Japanese Pediatric Guideline for Food Allergy 2012.[17] Egg was given as a pumpkin-flavored cupcake using either an egg yolk or half of a whole egg mixed with 40 g pumpkin and 5 g sugar, and cooked in a 1000 watt microwave for 90 s. Milk was administered either as 48 g yogurt or prepared as a pumpkin-flavored cupcake (25 mL milk mixed with 40 g pumpkin and 5 g sugar, cooked in a 1000 watt microwave for 90 s). Wheat was consumed as 15–100 g boiled udon noodles cooked in 100 °C water for 1 min (Tablemark, Tokyo, Japan).[18] Each challenge food was given in gradually increasing amounts in three meals, with 30 min between each administration. The challenge was terminated either when the entire challenge dose had been consumed, or when indications of a hypersensitivity reaction occurred. If an allergic reaction was induced, patients were treated according to severity using medications, fluid resuscitation, histamine H1 receptor antagonists, steroids, inhalation of β 2 stimulants, or intramuscular injection of adrenaline.

Measurement of serum-specific IgE

Blood samples were drawn during the course of regular clinic visits and were stored at −84 °C in the hospital refrigerator. Allergen-sIgE levels were measured using the 3gAllergy and ImmunoCAP assays. Both assays used sera from blood sampled at the same time. ImmunoCAP assay was measured on the same day of blood sampling. The 3gAllergy assay was performed using frozen sera. The 3gAllergy assay uses biotinylated allergen extracts in liquid format to capture sIgE antibodies. These sIgE antibodies form antibody-antigen complexes on streptavidin coated beads via avidin-biotin binding. The captured sIgE antibodies are then detected by an enzyme-labeled anti-IgE antibody.[19] The 3gAllergy readout is reported as IU_A/mL according to the CLSI, Clinical Laboratory Standards Institute, guideline.[20] The range of 3gAllergy readouts was 0.10–500 IU_A/mL. In this study, to simplify calculations, 0.05 IU_A/mL was substituted for all values <0.1 IU_A/mL and 501 IU_A/mL was used for all values >500 IU_A/mL.

In the ImmunoCAP assay, allergen extracts are absorbed into a cellulose sponge and detected following the addition of an enzyme-labeled antibody. The assay range available in Japan at the time of the study was 0.35–100 kU_A/L; however for the purposes of this study, 0.15 kU_A/L was used in calculations for all values <0.35 kU_A/L, and 101 kU_A/L was used in place of all values >100 kU_A/L.

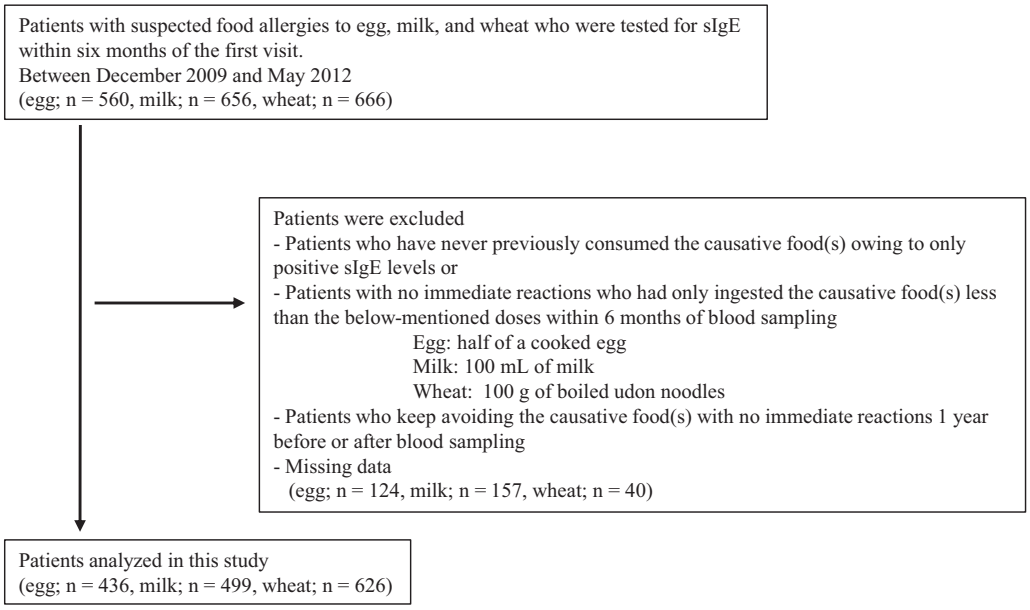

Fig. 1. Schematic of this study.