

Can Allergen-Specific IgE Antibodies Diagnose Egg Allergy Accurately?

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Diagnosis of food allergy requires thorough history and physical examination, and/or skin prick tests or serum immunoassays to determine food-specific IgE (sIgE) antibodies for IgE-mediated food allergy.¹ Double-blind placebo-controlled food challenges (DBPCFC) are actually still the gold standard for diagnosis.² Many researchers endeavored to find solutions on diagnosing food allergies without food challenge tests. The traditional DBPCFC tests are time-consuming, expensive and troublesome for physician and patients. Serum immunoassays of food-sIgE has become a widely used modality to evaluate IgE-mediated food allergies.³ Higher concentrations of food-sIgE levels are correlated with an increasing likelihood of clinical allergic reactions but not generally associated with the severity.⁴⁻⁶ However, different predictive values are being suggested from recent studies, which might be influenced by diet, age, disease, and challenge protocol.⁵⁻⁷ Ethnicity or geographic location can also affect the difference in predictive values because they influence prevalence and causes of food allergies.^{8,9} Moreover, the absence of food-sIgE does not indicate absence of clinical reactions to food.¹⁰

The current international guidelines recommend using oral food challenges (OFC) for diagnosing food allergies.¹¹ A single-blind or an open-food challenge can be considered diagnostic under careful medical history and physical examination, instead of DBPCFC. Recently, Atopic Dermatitis Study Group in the Korean Academy of Pediatric Allergy and Respiratory Diseases introduced an adjusted guideline for the OFC for Korean children.¹² If a patient has food allergy-suspected symptoms, food-sIgE antibodies would be determined to support the diagnosis. And then, if food-sIgE levels are below the diagnostic values, we can use OFC for diagnosing specific food allergy.

In Korea, egg allergy is known as the most frequent food allergy in children,^{13,14} however, large well-designed epidemiological studies are lacking. We still use diagnostic decision points for egg-sIgE levels based on US studies. Namely, we diagnose

patients with egg allergies based on egg-sIgE levels exceeding the diagnostic values with 95% of certainty.¹ Nevertheless, we often meet patients with high egg-sIgE and no clinical symptoms and vice versa. In the current issue of *Allergy, Asthma & Immunology Research*, Min et al.¹⁵ reported that the sensitivity and specificity of the predictive decision point values for egg white-sIgE antibodies by ImmunoCAP were relatively low in Korean children. This study started a new challenge for Korean allergists. However, the important thing we have to remember is that sIgE tests for identifying foods can potentially provoke IgE-mediated food allergy, but alone these tests are not diagnostics of food allergies, especially in patients without clinical allergic reactions.¹¹ So we cannot exclude the possibility that the inclusion criteria, which are infants with no experience of egg intake or with a non-specific clinical response to egg intake, may cause low sensitivity and specificity. The measurement of food-sIgE levels in patients without history of clinical symptoms related to food ingestion is discouraged. Further study will be needed to determine the predictive decision point values for food allergies, especially egg allergy.

It is known that the natural history of egg allergy has a good tolerance prognosis. Kim et al.¹⁶ reported that 41% of children had developed tolerance to egg allergy by 3 years of age and 60% by 5 years of age in Korean toddlers with atopic dermatitis. However, another study suggested a worse prognosis that 4% of children will outgrow egg allergy by 4 years of age, 12% by 6 years of age, and 37% by 10 years of age.¹⁷ These recent studies implicate that egg allergy is more persistent than the conven-

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tional wisdom and it is important to predict the prognosis of egg allergy. So some predictors have been suggested to indicate the persistence in egg allergy. Egg-sIgE of >50 kIU(A)/L can be used as a predictor for persistent egg allergy.¹⁷ High ovomucoid-sIgE (Gal d1), which is one of most important allergens in egg protein, also can be used as a predictor for persistence in egg allergy.¹⁸ On the contrary, low ovomucoid-sIgE could indicate a good prognosis of egg allergy.¹⁹ Likewise, component allergen-sIgE can be used as a prognostic marker in patients with egg allergy, not as a diagnostic marker. In this issue, Min et al.¹⁵ concludes that egg white component sIgE cannot predict the clinical reactions. Prospective studies should be determined to implicate component sIgE as a prognostic marker in Korea.

Moreover, large epidemiological cohort studies for food allergy, especially in infants, are necessary to understand the current situation and natural history immediately. Prospective clinical studies are also needed to diagnose and manage food allergies and predict their prognosis more accurately.

REFERENCES

1. Sicherer SH, Sampson HA. Food allergy. *J Allergy Clin Immunol* 2010;125:S116-25.
2. Hasan SA, Wells RD, Davis CM. Egg hypersensitivity in review. *Allergy Asthma Proc* 2013;34:26-32.
3. Hamilton RG, Franklin Adkinson N Jr. In vitro assays for the diagnosis of IgE-mediated disorders. *J Allergy Clin Immunol* 2004;114:213-25; quiz 226.
4. Sampson HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. *J Allergy Clin Immunol* 2001;107:891-6.
5. Osterballe M, Bindslev-Jensen C. Threshold levels in food challenge and specific IgE in patients with egg allergy: is there a relationship? *J Allergy Clin Immunol* 2003;112:196-201.
6. Celik-Bilgili S, Mehl A, Verstege A, Staden U, Nocon M, Beyer K, Niggemann B. The predictive value of specific immunoglobulin E levels in serum for the outcome of oral food challenges. *Clin Exp Allergy* 2005;35:268-73.
7. Komata T, Soderstrom L, Borres MP, Tachimoto H, Ebisawa M. The predictive relationship of food-specific serum IgE concentrations to challenge outcomes for egg and milk varies by patient age. *J Allergy Clin Immunol* 2007;119:1272-4.
8. Lee AJ, Thalayasingam M, Lee BW. Food allergy in Asia: how does it compare? *Asia Pac Allergy* 2013;3:3-14.
9. Han Y, Kim J, Ahn K. Food allergy. *Korean J Pediatr* 2012;55:153-8.
10. Perry TT, Matsui EC, Kay Conover-Walker M, Wood RA. The relationship of allergen-specific IgE levels and oral food challenge outcome. *J Allergy Clin Immunol* 2004;114:144-9.
11. NIAID-Sponsored Expert Panel, Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, Plaut M, Cooper SF, Fenton MJ, Arshad SH, Bahna SL, Beck LA, Byrd-Bredbenner C, Camargo CA Jr, Eichenfield L, Furuta GT, Hanifin JM, Jones C, Kraft M, Levy BD, Lieberman P, Lucciolli S, McCall KM, Schneider LC, Simon RA, Simons FE, Teach SJ, Yawn BP, Schwaninger JM. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol* 2010;126:S1-58.
12. Song TW, Kim KW, Kim WK, Kim JH, Kim HH, Park YM, Ahn K, Yang HJ, Yum HY, Lee SY, Jeon YH, Pyun BY. Guidelines for the oral food challenges in children. *Pediatr Allergy Respir Dis* 2012;22:4-20.
13. Ahn K, Kim J, Hahm MI, Lee SY, Kim WK, Chae Y, Park YM, Han MY, Lee KJ, Kim JK, Yang ES, Kwon HJ. Prevalence of immediate-type food allergy in Korean schoolchildren: a population-based study. *Allergy Asthma Proc* 2012;33:481-7.
14. Han DK, Kim MK, Yoo JE, Choi SY, Kwon BC, Sohn MH, Kim KE, Lee SY. Food sensitization in infants and young children with atopic dermatitis. *Yonsei Med J* 2004;45:803-9.
15. Min TK, Jeon YH, Yang HJ, Pyun BY. The clinical usefulness of IgE antibodies against egg white and its components in Korean children. *Allergy Asthma Immunol Res.* 2013;5:138-42.
16. Kim J, Chung Y, Han Y, Ahn K, Lee SI. The natural history and prognostic factors of egg allergy in Korean infants with atopic dermatitis. *Asian Pac J Allergy Immunol* 2009;27:107-14.
17. Savage JH, Matsui EC, Skripak JM, Wood RA. The natural history of egg allergy. *J Allergy Clin Immunol* 2007;120:1413-7.
18. Benhamou AH, Caubet JC, Eigenmann PA, Nowak-Wegrzyn A, Marcos CP, Reche M, Urisu A. State of the art and new horizons in the diagnosis and management of egg allergy. *Allergy* 2010;65:283-9.
19. Montesinos E, Martorell A, Felix R, Cerda JC. Egg white specific IgE levels in serum as clinical reactivity predictors in the course of egg allergy follow-up. *Pediatr Allergy Immunol* 2010;21:634-9.