

Peanut Allergy – A Tough Nut to Crack

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Although caution is required in comparing surveys, peanut allergy, tree nut allergy or both continue to be reported by >1% of the US population (e.g. >3 million subjects) and appear to be increasing in children over the past decade [1]. Along with the potential for anaphylactic reactions [2], this makes it a growing health problem in developed countries. Double-blind placebo-controlled food challenges (DBPCFCs) are still the golden standard for the diagnosis of peanut allergy, but this is an expensive and not always accessible method. Several studies have been performed to investigate the relationship between peanut-specific IgE (sIgE) levels and the outcome of DBPCFCs [3–8], resulting in significantly different cutoff levels to produce a 100% positive predictive value. The pros and cons of these studies are discussed in a report along with a recent investigation performed in 103 children in the Netherlands [9]. However, these studies all focused on comparing DBPCFC outcomes with sIgE to peanut. In current diagnostics, natural peanut extract is used, which is highly sensitive but lacks specificity when pollen-allergic patients are assessed, due to cross-reactivity between major pollen allergens Bet v 1 and profilin and their homologues in peanut. Moreover, cross-reactive carbohydrate determinants can give rise to false-positive results.

Codreanu et al. [10] sought to develop a new set of in vitro blood tests to diagnose peanut allergy using a panel

of recombinant peanut allergens (Ara h 1, 2, 3, 6, 7 and 8), coupled to ImmunoCAPs, to measure sIgE. A sizeable number of challenged peanut-allergic patients (n = 166) were included, sampled in two different centers. Center 1 (n = 91), a referral center at national level, recruited both adults and children and performed DBPCFC, and center 2 (n = 75) mainly recruited children at a regional level and performed open food challenges. Although center 1 thus received patients with more severe symptoms, the detection of sIgE to peanut allergens and the sensitization profiles were similar, indicating that the outcome of the in vitro tests was not affected by patient age and sex, symptom severity or by the eliciting dose. In addition, 61 pollen-allergic patients without peanut allergy were included to determine specificity of the tests. Indeed, in the latter group, 79% had sIgE to peanut extract above the cutoff level (0.10 kU/l) despite their tolerance to peanut, confirming the low specificity of this extract. As stated above, elevated cutoff levels have been proposed (up to 15 kU/l [6–8]), but in this study, 29 (center 1) and 63% (center 2) of the patients had lower peanut sIgE levels, leading to an unacceptable risk of accidental ingestion for these patients.

Previous reports indicating that peanut-allergic patients are most frequently sensitized to Ara h 2, followed by Ara h 1, 6, 3 and 7, respectively, were confirmed in this study. Ara h 2 and 6 showed sensitivities of 96 and 92%,

respectively, while sensitivities to Ara h 1 (75%), Ara h 3 (61%) and Ara h 7 (43%) were lower. The positive sIgE to peanut in the atopic patients (79%) was found to be primarily caused by sensitization to Ara h 8 (69%), indeed the only known homologue to a pollen-associated allergen (Bet v 1) included in the study. Few patients were also positive to the other allergens tested.

Seven of 166 patients (4%) could not be diagnosed by sIgE to Ara h 2, 6 of them could be diagnosed by either Ara h 6, 1 or 3, but 1 patient with a previous reaction to accidental peanut intake remained undiagnosed. As this patient had undetectable sIgE to Ara h 8 and 9, and cross-reactive carbohydrate determinant, other peanut allergens may exist in this patient. One possible candidate may be oleosin, previously described by Pons et al. [11] as an IgE-binding protein in peanut.

This is the first time the specificity of detection of IgE to main peanut allergens is determined in such a large group of patients. It is interesting to note that while in a previous study 47% of the patients were monosensitized (sIgE) to Ara h 2 [12], here the number of monosensitized patients was significantly lower (6%). This may be partly due to the higher number of patients included (166 vs. 30) but also to the fact that all patients were challenged in this study (vs. 17 in the previous study). The results presented suggest that in most cases, peanut allergy can be diagnosed by measuring sIgE to Ara h 2 and/or Ara h 6. Although the DBPCFC should no longer be considered a mandatory diagnostic procedure, it has to be used in those rare events where the patient has a clinical history of peanut allergy, but no measurable sIgE. Additionally, the DBPCFC will remain useful for determining eliciting doses for oral immunotherapy.

References

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