Diagnostic Capacity of Commercial Extracts vs Prick-by-Prick in the Study of Sensitization to Peanut: Which Technique Should We Use?

D'Amelio CM[1]*, García-Moral A[2], Bartra J[2,3]*, Azofra J[4]*, García Blanca E[5]*, Quiñones MD[6], Goikoetxea MJ[1]*, Martínez-Aranguren R[1], Gastaminza G[1]*

[1]*Clínica Universidad de Navarra, Instituto de Investigación Sanitaria de Navarra, Pamplona, Spain*

[2]*Hospital Clínic, Barcelona, Spain*

[3]*Hospital Clínic, Barcelona, IDIBAPS, Universitat de Barcelona, Barcelona, Spain*

[4]*Hospital Universitario Central de Oviedo, Oviedo, Spain*

[5]*Complejo Hospitalario de Navarra, Instituto de Investigación Sanitaria de Navarra (IdiSNA), Pamplona, Spain*

[6]*Hospital Monte Naranco, Oviedo, Spain*

[*]*Member of the Spanish Research Network on Allergy (ARADyAL: Red Nacional de Alergia -Asma, Reacciones Adversas y Alérgicas-) RD 16/0006/0031, RD16/0006/0007, of the Carlos III Health Institute, Madrid, Spain*

J Investig Allergol Clin Immunol 2020; Vol. 30(5): 373-375
doi: 10.18176/jiaci.0555

Key words: Skin prick test. Prick-by-prick. Allergy. Peanut. Commercial extract.

Palabras clave: Prueba cutánea. Prick by prick. Alergia. Cacahuete. Extracto comercial.

Peanut is a well-known allergen that can cause severe reactions. Skin tests are usually the first step when confirming IgE-mediated sensitization owing to their simplicity and reliability [1]. There is currently no consensus on whether the skin prick test (SPT) using commercialized allergen extracts or the prick-by-prick test with fresh food is preferable for detecting allergen sensitization [2-4]. We aimed to compare the diagnostic capacity of SPT with that of prick-by-prick testing in the detection of sensitization to peanut and to investigate the association between the results of these tests and the molecular sensitization profile.

The study population comprised 42 patients (aged >6 years) who were prospectively recruited from 5 allergy departments in Spain. All patients had a history of objective symptoms (digestive, respiratory, urticaria, or anaphylaxis) immediately after ingestion of peanut during the previous 2 years and a positive SPT result with commercial peanut extract (ALK-Abelló, Bial-Aristegui, Diater, or Leti, as used in each allergy service). All patients signed the informed consent document (Investigational Ethics Committee [060-2013]) and filled out the study questionnaire on symptoms presenting with peanut and the frequency of consumption of other foods.

SPTs were performed with 4 commercial peanut extracts (ALK-Abelló, Bial-Aristegui, Diater, Leti), peach extract (30 mg/mL of Pru p 3, ALK-Abelló), profilin (ALK-Abelló), peanut lipid fraction extract (Diater), and apple extract

(quantified Mal d 1, 10 µg/mL); prick-by-prick tests were performed with roasted peanut and crunchy peanut butter (Varma Foods SL). Sodium chloride (0.9%) and histamine hydrochloride (10 mg/mL) served as negative and positive controls, respectively. Wheals of ≥3 mm in diameter were considered positive, as recommended by EAACI guidelines [5].

Determination of serum specific IgE (sIgE) was performed in all cases (ImmunoCAP, Thermo Fisher Scientific) against peanut (whole extract), recombinant (r) peanut allergens (rAra h 1, rAra h 2, rAra h 3, rAra h 9), and rPru p 3. Following the manufacturer's recommendations, sIgE was considered positive when its value was ≥0.10 kU_A/L. The statistical analysis was performed using STATA/IC 12.0. Variables were tested for normality using the Shapiro-Wilk test. Values for nonnormally distributed quantitative variables were expressed as median (IQR), and comparative analyses were conducted using the Mann-Whitney test. Analysis of variance was used to compare the wheal sizes of the commercial extracts, and the Tukey test was applied for the pairwise comparison. The proportion of positive or negative results was compared between the different SPT results using the Cochran test.

The median age of the study population was 28.3 (6-69) years (26 [62%] females); 9 (21%) were aged <18 years (median, 11.3 [6-17] years). Fourteen patients (33.3%) presented with angioedema, 12 (28.5%) urticaria, 7 (16.7%) anaphylaxis, 5 (11.9%) respiratory symptoms, and 4 (9.5%) gastrointestinal symptoms.

The results of the skin tests are shown in the Table. Differences between the commercial extracts were not statistically significant. Interestingly, all the commercial extracts showed better diagnostic accuracy than the prick-by-prick approach, both with roasted peanut (P<.001) and with peanut butter (P<.001). Statistically significant differences were also detected in the SPT wheal size between the 4 commercial extracts and the prick-by-prick approach (P<.0001).

Twenty-seven patients (64%) were exclusively sensitized to lipid transfer protein (LTP), ie, not sensitized to storage proteins, 6 (14%) were sensitized to LTPs and storage proteins, and 4 (10%) were exclusively sensitized to storage proteins. Four patients (9.5%) were sensitized to rAra h 1, 10 (23.8%) to Ara h 2, and 1 (2.4%) to Ara h 3; 3 patients (7.1%) were sensitized to Ara h 8 and 31 (73.8%) to Ara h 9. Thirty-two patients (76.2%) were sensitized to Pru p 3 (4 patients did not have sIgE to any of these allergens).

Interestingly, the wheal size was greater in patients sensitized to storage proteins than in those who were not sensitized to these allergens (see online repository Figure 1). The SPT with the commercial extracts yielded a greater wheal size than the prick-by-prick test, independently of the molecular sensitization profile (P<.001).

Regarding the size of the resulting wheal, a good correlation was observed for the prick-by-prick results between peanut butter and roasted peanut (0.80), the lipid fraction and roasted peanut (0.72), the DIATER commercial extracts and roasted peanut (0.70), and the DIATER commercial extracts and peanut butter (0.75). Interestingly, all patients who were sensitized to storage proteins had positive prick-by-prick results.

The mean value of specific sIgE against peanut was 5.57 kU_A/L. Higher concentrations were found in patients sensitized exclusively to storage proteins than in those who were sensitized exclusively to LTP (median sIgE, 14.89 vs 2.94 kU_A/L, respectively; Mann-Whitney, P=.034).

According to our results, the commercial extracts studied were better able to detect sensitization to peanut than the prick-by-prick technique, in contrast to the findings of Rancé et al [6], who found superior diagnostic capacity with raw extracts than commercial extracts and hypothesized that this difference may be due to the loss of peanut oil and hydrophobic agents in the commercial extracts. However, we only found positive SPT results with the lipid fraction—the isolated oily fraction—in 19% of the population, and neither monosensitization nor negative SPT results with commercial extracts were observed in these patients.

Although the allergenic composition of commercial food extracts may be highly variable [6,7], we hypothesize that mechanical or chemical procedures during the preparation of the extracts may favor the availability of the different allergenic components, especially LTP, to which most of the patients were sensitized. Moreover, we consider that the presence of other components may be affected by cooking or presentation of the food in prick-by-prick testing, which is often used because of its simplicity and low cost but is not standardized [8]. Therefore, it is important to consider the possibility of obtaining false-negative results. Additionally,

Table. Skin Test Results in the Studied Population

	Commercial Extract/Allergen							
	Diater CE SPT	Leti CE SPT	ALK-Abelló SPT	Bial SPT	Roasted Peanut PBP	Peanut Butter PBP	Lipid Fraction (Diater) SPT	Peach Extract (30 mg/mL of Pru p 3, ALK) SPT
No. (%) of positives	30 (90.5)	37 (88)	36 (85.7)	33 (78.6)	22 (52.4)	26 (61.9)	8 (19)	29 (96)
Mean wheal size, mm (min;max)	32 (8;77)	38.1 (8;103)	35.6 (7;161)	26.6 (7;95)	33.7 (7;143)	31.5 (7;88)	33.7 (7;143)	43.8 (8;102)

Abbreviations: CE, commercial extract; PBP, prick-by-prick; SPT, skin prick test.

performance of prick-by-prick testing may vary according to the total amount of allergen tested, its state of preservation, and its exposure to the skin. However, the skin tests were performed by allergology nurses to minimize these factors. The commercial extracts we used demonstrated better diagnostic performance in detecting sensitization to peanut than the prick-by-prick approach, although these results varied according to the molecular sensitization profile.

A potential limitation of the present study was the impossibility of determining specific sIgE against all the available peanut allergens and the fact that not all the patients underwent oral food challenge. Our data point to the usefulness of performing SPT to peanut using commercial extracts. However, commercial peanut extracts must be standardized in order to guarantee the presence of all allergenic components and thus improve diagnostic accuracy.

Funding

This work was supported by Instituto de Salud Carlos III (ISCIII) and cofunded by Fondo Europeo de Desarrollo Regional – FEDER for the Thematic Networks and Co-operative Research Centers: ARADyAL (RD16/0006/0031 and RD16/0006/0007). MJ Goikoetxea was the recipient of a grant from Fundación Jesús de Gangoiti Barrera.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

1. Keet CA, Wood RA. Food allergy and anaphylaxis. Immunol Allergy Clin North Am. 2007;27:193-212.
2. Sicherer SH, Sampson HA. Food allergy: a review and update of epidemiology, pathogenesis, diagnosis, prevention and management. J Allergy Clin Immunol. 2018;141:41-58.
3. Valcour A, Jones JE, Lidholm J, Borres MP, Hamilton RG. Sensitization profiles to peanut allergens across the United States. Ann Allergy Asthma Immunol. 2017;119:262-6.
4. Heizerling L, Mari A, Bergmann KC, Bresciani M, Burbach G, Darsow U, et al. The skin prick test – European standards. Clin Transl Allergy. 2013;3:3.
5. Muraro A, Wefel T, Hoffmann-Sommergruber K, Roberts G, Beyer K, Bindslev-Jensen C, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. Allergy. 2014;69:1008-25.
6. Rancé F, Abbal M, Lauwers-Cancés V. Improved screening for peanut allergy by the combined use of skin prick tests and specific IgE assays. J Allergy Clin Immunol. 2002;109:1027-33.
7. Asero R, Scala E, Villalta D, Pravettoni V, Arena A, Billeri L, et al. Shrimp Allergy: Analysis of Commercially Available Extracts for In Vivo Diagnosis. J Investig Allergol Clin Immnol. 2017;27:175-82.
8. Elizur A, Appel MY, Nachshon L, Levy MB, Epstein-Rigbi N, Golobov K, et al. NUT Co Reactivity Acquiring Knowledge for elimination recommendations (NUT CRACKER) study. Allergy. 2018;73:593-601.

Manuscript received March 4, 2020; accepted for publication April 21, 2020.

Carmen M D'Amelio
Departamento de Alergología
Clínica Universidad de Navarra
Avenida Pio XII, 36
31008 Pamplona, Spain
E-mail: cdamelio@unav.es