

## Allergy to Strawberry in Children of the Mediterranean Area: Is It Really Allergy?

Cabrera-Freitag P<sup>1,2</sup>, Bermejo Becerro A<sup>1</sup>, Abreu Ramírez MG<sup>1</sup>, Álvarez-Perea A<sup>1,2</sup>, Infante Herrero S<sup>1,2</sup>, Fuentes-Aparicio V<sup>1,2</sup>, Zapatero Remón L<sup>1,2</sup>

<sup>1</sup>Paediatric Allergy Unit, Hospital General Universitario Gregorio Marañón, Madrid, Spain.

<sup>2</sup>Gregorio Marañón Health Research Institute (IiSGM), Madrid, Spain.

### Corresponding author:

Paula Cabrera Freitag

E-mail: [paula.cabrera@salud.madrid.org](mailto:paula.cabrera@salud.madrid.org)

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Fruits from the *Rosaceae* family are the most frequent cause of allergic reactions to fruits in the mediterranean area [1]. Among them, strawberry, belonging to the *Rosoideae* subfamily, has an apparently unjustified reputation among the general population as self-reported symptoms with strawberry are very common [2,3] but few cases of true allergic patients are listed in the literature [4-7].

The aim of our study was to make a descriptive analysis of pediatric patients with a self-reported clinical history of strawberry allergy and to analyze true allergy. Patients from our Pediatric Allergy Section of the Hospital General Universitario Gregorio Marañón (Madrid, Spain) were retrospectively approached on the basis of a clinical history of strawberry allergy, having a specific IgE (sIgE) to strawberry performed and being under 17 years of age.

The following data were analyzed: demographic and clinical characteristics of the patients, specific IgE (sIgE) values to strawberry [ImmunoCAP 250 (Thermo Fisher®)], skin prick test (SPT) results with a commercial strawberry extract (Leti®), sensitization to profilin by prick and peach non-specific lipid transfer protein (nsLTP) by prick (Peach extract enriched with Pru p 3, ALK-Abelló®) or ImmunoCAP (Pru p 3) and tolerance to strawberry by oral food challenge (OFC). sIgE values to birch PR-10 (Bet v 1) were not analyzed as birch pollen sensitization is not common in our area. SPT weals of  $\geq 3$ mm and sIgE values  $\geq 0,35$ ku/l were considered positive.

Qualitative variables are expressed as frequency and quantitative variables as median and interquartile range (IQR). Categorical variables were compared using the chi-square test and Fisher exact test; quantitative variables were compared using the Mann-Whitney U test.

Forty-three children with a clinical history of strawberry allergy were included in the study, 29 (67%) with positive SPT and/or sIgE to strawberry (group 1) and 14 (33%) with both negative results (group 2).

Median time between self-reported symptoms related to strawberry intake and the allergological study was 4 (3-6) months and 6 (4-9) months for tolerance assessment. Cofactors as concomitant exercise, infectious disease and nonsteroidal anti-inflammatory drugs intake were excluded in all patients.

Among patients belonging to group 1 (58.6% male, median age 9 (6-12) years), the most frequent reported symptoms were pruritus of the oral mucosa [oral allergy syndrome (OAS)] and cutaneous symptoms (48.3% and 37.9%, respectively). Three patients (10.3%) reported gastrointestinal symptoms and one anaphylaxis (3.4%). All patients had coexistence of other atopic diseases: 23 patients (79.3%) were allergic to other foods [mostly other fruits (n=20), being peach the fruit most frequently involved (39,3% of fruit allergic patients)], 16 (55.1%) had rhinoconjunctivitis and/or bronchial asthma related to aeroallergens other than birch and 13 (44.8 %) atopic dermatitis. Symptoms at onset in patients belonging to group 2 (57.1% male, median age 4.5 (2-12) years), were OAS (50%) and cutaneous symptoms (50%). All but one patient had at least another atopic disease: 7 (50%) atopic dermatitis, 6 (42.8%) had at least one other food allergy [being fruits the food most frequently involved (n=4)] and 5 (35.7%) rhinoconjunctivitis and/or bronchial asthma related to aeroallergens but not birch.

No statistical differences were observed regarding gender, age and type of symptoms between groups. Patients in group 1 were most frequently allergic to other foods as well as to other fruits

compared to those in group 2 ( $p=0.03$  and  $0.01$  respectively) but no differences were observed for other atopic diseases.

Patient's allergological study results are shown in the table.

Tolerance was assessed in 28 (65.1%) children (16 belonging to group 1 and 12 to group 2) with a dose proportion according to their age and all but one tolerated strawberry (96.4%).

There were no significant differences between patients belonging to group 1 in which tolerance to strawberry was assessed and those who not, regarding age, clinical symptoms, coexistence of other atopic diseases, sIgE values to strawberry and SPT results with strawberry, profilin and nsLTP.

These data were not analyzed for patients belonging to group 2 owing to the small sample (12/14 tested for tolerance vs 2/14 not tested).

All but one child in group 1 (16/29 tested) tolerated strawberry (93.7%): 3 were not allergic to other fruits, 7 were allergic to peach, 3 to other *Rosacea* fruits distinct from peach and two to fruits other than *Rosacea*. The one who did not tolerate strawberry, had a clinical history of anaphylaxis with strawberry, a positive SPT and CAP to strawberry (2.47kU/ L) as well as a positive SPT to profilin (sensitization to LTP not tested). This boy was also allergic to apple, house dust mite and plane tree pollen.

All tested children in group 2 tolerated strawberry.

As previously described in other studies carried out in southern Europe, most of the patients in our study self-reporting symptoms after strawberry consumption suffered mild symptoms (OAS and cutaneous symptoms) and were allergic to other fruits, mostly peach [4,5,7].

Moreover, 96% of the children in our study with symptoms after strawberry intake tolerated the fruit in a subsequent OFC, supporting the idea that true allergy to strawberry is not as frequent as it seems. This was independent of whether or not they were sensitized to strawberry, so neither SPT nor CAP seem to have a good sensitivity, but a good specificity as all patients with both negative diagnostic tests tolerated strawberry.

Probably, the high percentage of patients sensitized to peach LTP [61.3% (19/31 tested)] and profilin [41.4% (12/29 tested)], could partly explain patient's sensitization to strawberry due to cross-reactivity [4].

Our study suggests that true allergy to strawberry in our Mediterranean area is rare.

Therefore we believe that, in our region, an OFC should be considered in those children referring mild symptoms (OAS and/or cutaneous symptoms) after strawberry intake, regardless of whether or not they are sensitized to strawberry and even in those sensitized to LTP. Nevertheless in those patients with more severe symptoms, true allergy to strawberry might be considered.

Further studies involving more patients are needed in order to analyze if the severity of the symptoms and strawberry allergens sensitization profile is associated to true strawberry allergy.

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## **Conflicts of Interest**

The authors declare that they have no conflict of interest.

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**Table.** Allergological study results of the patients

	Group 1 (n=29)	Group 2 (n=14)	p-value
Strawberry sIgE ≥0.35 kU/L [n (%)] sIgE value [m (p25-p75) kU/L] <0.35 kU/L [n (%)]	26 (89.7) 2.53 (1.05-8) 3 (10.3)	0 (0) NA 14 (100)	<0.0001
Strawberry SPT [n (%)] Positive Negative ND	9 (31) 9 (31) 11 (37.9)	0 (0) 14 (100) 0 (0)	0.003
Peach LTP Positive [n (%)] n positive by SPT/n tested by SPT n with Pru p 3 ≥0.35 kU/L/n tested for Pru p 3 sIgE value [m (p25-p75) kU/L] Negative [n (%)] ND [n (%)]	17 (58.6) 13/20 11/15 7.35 (2,04-15,6) 6 (20.7) 6 (20.7)	2 (14.3) 2/8 0/2 NA 6 (42.9) 6 (42.9)	0.03
Profilin by SPT [n (%)] Positive Negative ND	12 (41.4) 9 (31) 8 (27.6)	0 (0) 8 (57.1) 6 (42.8)	0.21
OFC with strawberry [n (%)] Positive Negative ND	1 (3.4) 15 (51.7) 13 (44.8)	0 (0) 12 (85.7) 2 (14.3)	0.98

n, number of patients; %, percentage; m (p25–p75), median (25th and 75th percentile); sIgE, specific IgE; SPT, skin prick test; ND, not done; NA, not applicable; OFC, oral food challenge.