

Short communication

Specific IgE to recombinant vegetal panallergen (rBet v 2) and fruit allergy in pollinic patients

Daschner A, Crespo JF, Pascual CY. Specific IgE to recombinant vegetal panallergen (rBet v 2) and fruit allergy in pollinic patients. Allergy 1998; 53: 614–618. © Munksgaard 1998.

The presence of IgE antibodies to the allergens rBet v 1 and rBet v 2 was investigated in patients with known sensitization to ryegrass (*Lolium perenne*) and/or olive (*Olea europaea*) pollen, by comparing a group of 10 patients who had allergic symptoms after ingestion of fruits (A) with a group of 17 patients who had only seasonal respiratory symptoms (B). There was no significant difference between the two groups for total IgE. All patients showed specific IgE to both *L. perenne* and *O. europaea*. No specific IgE binding to rBet v 1 was detected in any patient. The incidence of the presence of IgE antibodies to rBet v 2 was 90% in the group with fruit allergy (A) and 35% in group B. We found a significant association between presence of IgE antibodies to rBet v 2 and fruit allergy ($P=0.007$). Specific IgE values to *O. europaea* pollen were higher in the fruit-allergy group than the group without fruit allergy ($P=0.032$). In conclusion, pollen-allergic patients with specific IgE to birch pollen profilin show a significantly elevated frequency of fruit allergy.

**A. Daschner, J. F. Crespo,
C. Y. Pascual**

Laboratorio de Inmunoalergia, Servicio Alergia
Pediátrica, Hospital "La Paz", Madrid, Spain

Key words: fruit allergy; pollinosis; profilin;
rBet v 1; rBet v 2.

A. Daschner
Laboratorio de Inmunoalergia
Servicio Alergia Pediátrica
Hospital "La Paz"
Castellana 261
Madrid 28046
Spain

Accepted for publication 10 February 1998

Oral allergy syndrome (OAS) is an immediate hypersensitivity reaction that begins within minutes after the contact of oropharyngeal mucosa with a specific food to which the patient is sensitized. OAS is the most common hypersensitivity food reaction in adults (1), but other generalized symptoms can also appear; for instance, erythema, urticaria, angioedema, or systemic anaphylaxis. Allergy to fruits has been described as a major cause of OAS in patients having pollinosis, especially those with hypersensitivity to birch pollen and ragweed. Fruits belonging to the Rosaceae family show cross-reactivity with the major allergen of birch pollen, Bet v 1. Up to 70% of patients with immediate hypersensitivity to birch pollen show intolerance of apple and other fruits. Epitopes have been identified that are shared by birch pollen and apples, leading to IgE cross-reactivities that can explain some of the clinical manifestations (2). Other fruits such as kiwi have been shown to contain a large number of allergens widely cross-reacting with allergens in grass and birch pollen extracts (3).

These studies have been performed mainly in countries with a temperate climate, where birch is a common tree. However, in regions where birch pollen is rare, as in central Spain, there is also a relationship between fruit allergy and allergy to pollen, mainly of grasses. Recently, profilins have been identified as important allergens in these patients (4). Profilins are proteins that are present in almost all eukaryotic organisms, and are thus a panallergen. Important quantities of profilins have been found in various foods and in *Lolium perenne* pollen (5–7).

The availability of the recombinant birch profilin rBet v 2 facilitates cross-reactivity studies. Recombinant (r)Bet v 1 has been shown to induce hypersensitivity reactions equal to those induced by natural Bet v 1 in patients allergic to trees (8). The purpose of this study was to determine the frequency of IgE antibodies to rBet v 1 and to rBet v 2 in pollinic patients with and without OAS. In this way, we hoped to establish whether the determination of rBet v 1- and rBet v 2-specific IgE antibodies

could be a helpful tool in the diagnosis of OAS in pollinic patients.

Material and methods

Patients

Pollinic patients studied in our allergy clinic from 15 July to 30 November 1996 were assigned to either group A or group B.

Group A comprised patients with respiratory symptoms (seasonal rhinoconjunctivitis and/or bronchial asthma) and sensitization to pollen of grasses and/or olive (positivity of prick test and serum specific IgE to *L. perenne* and/or *Olea europaea*) who also presented OAS to at least one fruit and positive specific IgE (>0.35 U/l) to at least one of the fruits in question. Patients with perennial respiratory symptoms, hypersensitivity symptoms in relation to other foods or items such as latex, or unexplained urticaria/angioedema or anaphylaxis were excluded.

Group B comprised patients with seasonal respiratory symptoms and positive skin prick test and specific IgE to *L. perenne* and/or *O. europaea* who did not present any other allergic symptoms.

None of the patients had previously undergone specific immunotherapy. The patients were studied when they were not exposed to their sensitizing inhalant allergens. All patients came from central Spain. Cross-matching of both groups was done according to age.

Immunologic studies

Skin prick tests with *O. europaea* and *L. perenne* as well as with fruits (banana, fig, kiwi, muskmelon, orange, peach, pineapple, and watermelon) were performed with commercial extracts (ALK-Abelló, Spain). The prick test was considered positive when the size of the wheal induced by the allergen was 3 mm larger than that induced by the negative control. Isotonic glycerol saline was used as negative control and 0.1 mg/ml histamine hydrochloride as positive control. The tests were also performed by prick by prick with ripe natural fruit.

Serum specific IgE to *L. perenne*, *O. europaea*, rBet v 1, and rBet v 2 was assessed by CAP-FEIA (Pharmacia, Uppsala, Sweden) for all selected patients. The total serum IgE was assessed by IMx-Method (Abbot Diagnostics, Chicago, IL, USA).

Statistics

Bivariate comparison of the means of specific IgE (after logarithmic transformation) to rBet v 1 and rBet v 2, *L. perenne*, and *O. europaea* was performed

between groups A and B. Correlation between rBet v 2 and age of patients, and specific serum IgE to *L. perenne* and *O. europaea* was assessed. Statistical analysis was done with the SPSSV-Program (SpSS For Windows Student Version 6.0.1, SPSS, Inc., 1989–93). The chi-square test and Fisher's exact test for independent samples were used. Correlation was calculated with the Pearson correlation coefficient.

Results

The mean age in group A was 18 years (range 10–35). There were 10 patients (six male, four female). The mean age in group B was 17 years (range 8–30). There were 17 patients (10 male and seven female). The fruits mostly implicated in immediate hypersensitivity symptoms in group A were peach (5), muskmelon (4), kiwi (4), banana (4), and watermelon (2) (Table 1). Patients in the fruit allergy group had positive skin prick tests, "prick by prick", and specific IgE with the implicated fruits.

The values of specific IgE to the tested allergens are shown in Table 1. Specific IgE binding to rBet v 1 was not detected in any serum sample from either group. All patients were sensitized to *L. perenne* and *O. europaea*.

Specific IgE binding to rBet v 2 was detected in 9 out of 10 patients of group A (90%) and in six out of 17 patients of group B (35.3%). Significant differences in number of positive results were found in comparing both groups ($P=0.007$).

The mean value of specific IgE to rBet v 2 was 6.62 kU/l (SD 3.64) in group A, compared with 1.42 kU/l (SD 3.28) in group B, but there were no significant differences ($P=0.123$). The mean value of specific IgE to *L. perenne* was 233 kU/l (SD 260) in group A, compared with 117 kU/l (SD 115) in group B, without significant differences ($P=0.12$). There were significant differences ($P=0.032$) between the mean values of specific serum IgE to olive pollen (*O. europaea*) in both groups, these being 13.8 ± 10.2 kU/l in group A and 5.7 ± 9.2 kU/l in group B.

rBet v 2 was extremely positively correlated with total IgE ($r=0.68$, $P<0.001$) and with olive pollen ($r=0.82$, $P<0.001$), but less so with *L. perenne* ($r=0.49$, $P=0.009$) (Table 2). Otherwise, specific IgE values to *L. perenne* and *O. europaea*, as well as total serum IgE, were highly correlated.

Discussion

All patients showed specific IgE to *L. perenne* and *O. europaea*, reflecting the high incidence of simultaneous sensitization to both allergens in the region

Table 1. Values for total and specific IgE (*Lolium perenne*, *Olea europaea*, rBet v 1, and rBet v 2)

Patient no.	Group	Implicated fruits	Total IgE	<i>L. perenne</i>	<i>O. europaea</i>	rBet v 1	rBet v 2
1	A	B, K, M	992	860	29	0	3
2	A	K	538	289	0.8	0	1.8
3	A	P	132	30	3.5	0	0
4	A	M, O, P, W	493	230	23.2	0	6.8
5	A	B	369	94	10.3	0	3.4
6	A	P	941	310	24.1	0	1.6
7	A	B, F, K, M, Pa	185	35	10.6	0	2.5
8	A	M, P	96	30	3.6	0	0.4
9	A	P	338	93	5.6	0	2.7
10	A	W	322	69	15	0	6.7
11	B	—	88	41	1.3	0	0.9
12	B	—	149	84	5.2	0	0
13	B	—	154	32	1.3	0	0
14	B	—	487	92	1.6	0	0
15	B	—	300	223	3.5	0	0
16	B	—	93	47	4.2	0	0.6
17	B	—	482	210	1.7	0	0
18	B	—	32	16	4.6	0	0
19	B	—	76	29	2.4	0	0.5
20	B	—	605	74	2.3	0	0
21	B	—	171	73	1.5	0	0
22	B	—	284	219	8.6	0	6.8
23	B	—	1274	410	40	0	14
24	B	—	592	313	4.8	0	0
25	B	—	65	11	0.9	0	0
26	B	—	104	56	0.9	0	0
27	B	—	365	68	6.3	0	2.1

Values in kU/l. Group A: pollen-allergic patients with fruit allergy (positive skin prick tests to implicated fruits). Group B: pollen-allergic patients without fruit allergy. Implicated fruits: B: banana, F: fig, K: kiwi, M: muskmelon, O: orange, P: peach, PA: pineapple, W: watermelon.

studied. The patients were studied in summer and autumn, at a time when they were not exposed to these inhalant allergens, because it is known that exposure can augment values of specific IgE (9, 10). Whereas in countries with a temperate climate, fruit allergy is associated with birch pollen allergy and entities such as birch–apple syndrome are well known (11, 12), in central Spain, where our patients were studied, fruit allergy is associated with sensitization to grass pollen (4). In the birch–apple syndrome, the presence of IgE antibodies to Bet v 1 determines the cross-reactivity (2, 13). In Spain, this sensitization to the major birch pollen allergen seems not to be so important in the cross-reactivity between pollen and fruits. Otherwise, van Ree et al. had previously suspected that profilin is one of the responsible allergens of cross-sensitization, besides CCD (carbohydrate cross-reactive determinant) and other still unidentified structures (14). Recently, a major allergen was isolated in *L. perenne* pollen (Lol p XI) that shows a high degree of homology with the major olive pollen allergen Ole e 1. In this allergen, IgE binds to the carbohydrate determinant (15). Another study detected an epitope in the major allergen Ole e 1, in which xylose is involved in recognition of specific IgE (and IgG) (16).

We confirm that in central Spain the major allergen Bet v 1 is not implicated in pollen-allergic patients with fruit allergy. No serum sample demonstrated specific IgE-binding to rBet v 1. In animal models, it has recently been shown that rBet v 1 induces substantially higher levels of IgE than rBet v 2 with a much lesser dose (17). This underlines that the major birch pollen allergen does not reach sufficient airborne levels to induce IgE antibodies in allergic patients living in central Spain. Bet v 1 belongs to the family of pathogenesis-related proteins (PRP) (18). This pan-allergen can be detected in various plants and fruits; however, no homologue to Bet v 1 could be detected in olive pollen or grass pollen (4, 19). In our selected patients, no IgE antibodies to Bet v 1 could be found in any patient, but specific IgE to Bet v 2 is detected in 57% of all patients, reaching 90% in the group of patients with fruit allergy. The presence of IgE antibodies to Bet v 2 is only an indicator of primary sensitization to a profilin related to the pollen of olive or grasses.

We tried to correlate sensitization to profilin with the presence of fruit allergy. We included patients with allergy symptoms associated with any fruit. Birch pollen-related fruits (BPRF) have been

Table 2. Pearson correlation coefficient and level of significance for variables age, total IgE, and specific IgE binding to *Lolium perenne*, *Olea europaea*, and rBet v 2

	Total IgE	<i>L. perenne</i>	<i>O. europaea</i>	rBet v 2
Age	0.06 P=0.77	-0.03 P=0.90	0.09 P=0.66	0.20 P=0.30
Total IgE		0.82 P<0.001	0.80 P<0.001	0.68 P<0.001
<i>L. perenne</i>			0.71 P<0.001	0.49 P<0.01
<i>O. europaea</i>				0.82 P<0.001

described (12) that include not only fruits of the Rosaceae family, but also dried fruits, carrot, potato, etc. As the relationship between fruit allergy and pollen allergy is not the same in central Spain as in regions where birch is a common tree, and as we did not know initially which fruits would be implicated in cross-reactivity between foods and pollen of grasses or olive, we also included in the fruit allergy group, patients with allergy to fruits such as banana or kiwi. The relationship between banana, avocado, kiwi, chestnut, and fig with latex is well known (20); therefore, we excluded patients who presented immediate hypersensitivity symptoms to latex.

Prognostic factors that could predict the appearance of fruit allergy in (birch) pollen-allergic patients have been previously sought. Fruit allergy could be associated not only with more severe respiratory symptoms but also with higher levels of total and specific IgE (21, 22). High and significant correlation was found between rBet v 2 and fruit allergy. It is worth noting the very high correlation between specific IgE to rBet v 2 and specific IgE to olive pollen allergen, and the smaller correlation between specific IgE to profilin and total IgE and specific IgE to *L. perenne*. It seems that the sensitization with elevated specific IgE to olive pollen is an indicator of specific IgE to Bet v 2.

In this study, a high incidence of IgE antibodies to profilin Bet v 2 was detected in patients with allergy to *L. perenne* and *O. europaea*, particularly in the group of patients with fruit allergy. Further studies must consider the role of sensitization to olive pollen in relation to sensitization to profilin and/or onset of fruit allergy in grass pollen-allergic patients.

References

1. Pastorello EA, Incorvaia C, Ortolani C. The mouth and

- pharynx. In: Ortolani C, editor. Atlas on mechanisms in adverse reactions to food. Allergy 1995;50 Suppl 20:41-4.
2. Ebner C, Birkner T, Valenta R, et al. Common epitopes of birch pollen and apples – studies by Western and Northern blot. J Allergy Clin Immunol 1991;88:588-94.
3. Pastorello EA, Pravettoni V, Ispano M, et al. Identification of the allergen components of kiwi fruit and evaluation of their cross-reactivity with timothy and birch pollens. J Allergy Clin Immunol 1996;98:601-10.
4. van Ree R, Fernández-Rivas M, Cuevas M, van Wijngaarden M, Aalberse RC. Pollen-related allergy to peach and apple: an important role for profilin. J Allergy Clin Immunol 1995;95:726-34.
5. Valenta R, Duchêne M, Ebner C, et al. Profilins constitute a novel family of functional plant pan-allergens. J Exp Med 1992;175:377-85.
6. Valenta R, Duchêne M, Pettenburger K, et al. Identification of profilin as novel pollen allergen; IgE auto-reactivity in sensitized individuals. Science 1991;25: 557-60.
7. van Ree R, Voitenko V, van Leeuwen WA, Aalberse RC. Profilin is a cross-reactive allergen in pollen and vegetable foods. Int Arch Allergy Immunol 1992;98:97-104.
8. Godnic-Cvar J, Susani M, Breiteneder H, et al. Recombinant Bet v 1, the major birch pollen allergen, induces hypersensitivity reactions equal to those induced by natural Bet v 1 in the airways of patients allergic to tree pollen. J Allergy Clin Immunol 1997;99:354-9.
9. Crimi E, Voltolini S, Gianiorio P, et al. Effect of seasonal exposure to pollen on specific bronchial sensitivity in allergic patients. J Allergy Clin Immunol 1990;85: 1014-19.
10. Yunginger JW, Gleich GJ. Seasonal changes in serum and nasal IgE concentrations. J Allergy Clin Immunol 1973;51: 174-81.
11. Dreborg S, Foucard T. Allergy to apple, carrot and potato in children with birch pollen allergy. Allergy 1993;48: 167-72.
12. Eriksson NE, Formgren H, Svenonius E. Food hypersensitivity in patients with pollen allergy. Allergy 1982;37: 437-43.
13. Pauli G, Oster JP, Deviller P, et al. Skin testing with recombinant allergens rBet v 1 and birch profilin, rBet v 2: diagnostic value for birch pollen and associated allergies. J Allergy Clin Immunol 1996;97:1100-9.
14. van Ree R, Aalberse RC. Pollen-vegetable food cross-reactivity: serological and clinical relevance of crossreactive IgE. J Clin Immunoassay 1993;16:124-30.
15. van Ree R, Hoffman DR, van Dijk W, et al. Lol p XI, a new major grass pollen allergen, is a member of a family of soybean trypsin inhibitor-related proteins. J Allergy Clin Immunol 1995;95:970-8.
16. Batanero E, Villalba M, Monsalve RI, Rodríguez R. Cross-reactivity between the major allergen from olive pollen and unrelated glycoproteins: evidence of an epitope in the glycan moiety of the allergen. J Allergy Clin Immunol 1996;97:1264-71.
17. Vrtala S, Mayer P, Ferreira F, et al. Induction of IgE antibodies in mice and rhesus monkeys with recombinant birch pollen allergens: different allergenicity of Bet v 1 and Bet v 2. J Allergy Clin Immunol 1996;98:913-21.
18. Breiteneder H, Pettenburger K, Bito A, et al. The gene coding for the major birch pollen allergen, Bet v 1, is highly homologous to a pea disease resistance response gene. EMBO J 1989;8:1935-8.
19. Ebner C, Hirschwehr R, Bauer L, et al. Identification of allergens in fruits and vegetables: IgE cross-reactivities with the important birch pollen allergens Bet v 1 and

- Bet v 2 (birch profilin). *J Allergy Clin Immunol* 1995;95:962-9.
20. Blanco C, Carrillo T, Castillo R, Quiralte J, Cuevas M. Latex allergy: clinical features and cross-reactivity with fruits. *Ann Allergy* 1994;73:309-14.
21. Foglé-Hansson M, Bende M. The significance of hypersensitivity to nuts in patients with birch pollen allergy. *Allergy* 1993;48:282-4.
22. Asero R, Massironi F, Velati C. Detection of prognostic factors for oral allergy syndrome in patients with birch pollen hypersensitivity. *J Allergy Clin Immunol* 1996;97:611-16.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.