

## Short Communication

# Specific IgE to recombinant allergens (rBetv1 and rBetv2) and apple allergy in patients with pollinosis

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### ABSTRACT

The presence of IgE antibodies to the allergens rBetv1 and rBetv2 was investigated in the sera of 99 patients with specific IgE to apple extract by comparing a group of 43 patients who had oral allergy syndrome (OAS) after ingestion of apple with a group of 56 patients without OAS who had only seasonal respiratory symptoms. The incidence of the presence of IgE antibodies to rBetv1 was 88.1%. All patients had levels of IgE to apple extract greater than 0.35 kU/L. After eating apple, patients allergic to birch pollen with OAS showed significantly higher levels of IgE to apple extract and rBetv1 than patients without OAS ( $P = 0.007$  and  $P = 0.0002$ , respectively). Twenty of 56 patients (35.7%) in the group without OAS who produced specific IgE to apple did not have specific IgE against rBetv1 and rBetv2 and were symptomless after eating apple. In conclusion, patients allergic to birch pollen with specific IgE to rBetv1 showed a significantly elevated frequency of apple allergy. In contrast, our results show that fruit-related symptoms require not only high specific serum IgE levels, but a strong cellular sensitization to birch pollen allergens, together with an increased cellular reactivity to apple allergens.

**Key words:** apple, oral allergy syndrome, rBetv1, rBetv2.

### INTRODUCTION

It is well known that patients with a type I allergy to birch pollen also suffer from intolerance to apple, which gives rise to local symptoms, with or without systemic reactions, on direct contact with the oral mucosa. The term currently

used to describe the complex of clinical features is oral allergy syndrome (OAS). The major birch pollen allergen rBetv1 and a homologous 18 kDa apple protein are responsible for the majority of allergenic cross-reactions between birch pollen and apples.<sup>1</sup>

The purpose of the present study was to determine the frequency of IgE antibodies to rBetv1 and rBetv2 in patients with specific IgE to apple, with and without OAS. In this way, we hoped to establish whether the detection of rBetv1- and rBetv2-specific IgE antibodies could be a helpful tool in the diagnosis of OAS in pollinic patients.

### METHODS

The present retrospective study comprised 99 patients (48 males and 51 females) with a mean age of 37 years (range 9–64 years). All had specific IgE to apple (mean 5.2 kU/L; range, 0.37–53.9 kU/L). The presence of apple-specific IgE was sufficient for inclusion of patients into the study. The clinical symptoms included rhinoconjunctivitis, asthma, urticaria and OAS.

Specific serum IgE antibodies to apple extract and recombinant allergens rBetv1 and rBetv2 were measured by the Immuno CAP System (Pharmacia-Upjohn, Uppsala, Sweden). The results are given in kU/L and CAP classes from 0 to 6. A value greater than 0.35 kU/L (CAP classes 1–6) was regarded as a positive result.

Proportions were compared using a two-tailed Chi-squared test with Yates' correction. The Mann–Whitney *U*-test was used for comparison of two unpaired groups. Results are expressed as the median value.  $P < 0.05$  was considered significant.

### RESULTS

The incidence of the presence of IgE antibodies to rBetv1 was 88.1%. All patients had IgE to apple extract. Of the 43 patients with OAS, 38 (88.3%) had IgE to rBetv1;

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**Table 1** Serologic characteristics of 99 patients with specific IgE to apple and its relationship with specific IgE against rBetv1 and rBetv2

	rBetv1 positive rBetv2 negative		rBetv1 positive rBetv2 positive		rBetv1 negative rBetv2 positive		rBetv1 negative rBetv2 negative	
	n	%	n	%	n	%	n	%
OAS	26	60.4	12	27.9	3	6.98	2	4.4
Non-OAS	11	19.6, $P < 0.0011$	12	21.4, $P < 0.01$	13	23.2, $P < 0.0011$	20	35.7, $P < 0.001$

$P$  values determined using a Chi-squared test with Yates' correction; OAS, oral allergy syndrome.

**Table 2** Levels of IgE to rBetv1, rBetv2 and F49 (apple)

	Patients with OAS ( $n = 43$ )		Patients without OAS ( $n = 56$ )		$P$
F49 (kU/L)	3.4	(1.5–6.9)	1.5	(0.6–4.8)	0.007
rBetv1 (kU/L)	31.9	(8.0–48.4)	0.1	(0.1–8)	0.0002
rBetv2 (kU/L)	0.1	(0.1–2.1)	0.1	(0.1–3.9)	NS
rBetv1:rBetv2*	25.1		1.7		0.0002

Data show the median value with numbers in parentheses indicating the 25th and 75th percentiles. \*The mean value for the ratio rBetv1:rBetv2 is shown. Statistical comparisons were made using the Mann–Whitney  $U$ -test; OAS, oral allergy syndrome.

26 (60.4%) showed IgE binding to rBetv1, but not to rBetv2; 12 (27.9%) had sera containing IgE antibodies to rBetv2 in addition to rBetv1; three (7.0%) had sera that reacted to rBetv2, but not rBetv1; and two (4.7%) did not show specific IgE against either of the recombinant allergens. Interestingly, 20 of 56 patients (35.7%) without OAS but with a positive CAP result for apple (mean 1.9 kU/L, range 0.39–3.28 kU/L) did not report specific IgE against rBetv1 and rBetv2 and did not have symptoms following ingestion of apple. This is a common observation in this geographic area. All these patients showed specific IgE to grass pollen, *Olea europaea* and mugwort, reflecting the high incidence of simultaneous sensitization to these allergens in the region studied.

The serologic features of patients with and without OAS are summarized in Table 1. Median values of IgE levels to apple, rBetv1 and rBetv2 are shown in Table 2. Birch pollen-allergic patients with symptoms after eating apple showed significantly higher IgE levels to apple extract ( $P = 0.007$ ) and rBetv1 ( $P = 0.0002$ ) than patients without OAS.

## DISCUSSION

Our results support the view that the 18 kDa protein represents the major allergen of the apple and that allergenic epitopes of the apple protein are present on rBetv1.<sup>2</sup> However, the finding of the occurrence of IgE to

apple in patients lacking IgE to rBetv1 and rBetv2 shows the complexity of this matter. Recently, a third group of proteins not homologous to rBetv1 and rBetv2, with a molecular weight range of 46–60 kDa and displaying IgE cross-reactivity shared by birch, mugwort pollen and celery, has been identified.<sup>2</sup> According to the literature, these allergens seem to represent homologs of Artv1.<sup>3</sup> Bauer *et al.*<sup>2</sup> showed that the 60 kDa protein seems to represent a non-cross-reacting mugwort-specific allergen. Other mugwort pollen-specific allergens are the 28 kDa allergen and other proteins of 12 kDa and lower. Hence, extracts of birch pollen and celery share three groups of molecules and mugwort pollen and celery have two of these molecules in common.

Our finding of significantly increased levels of IgE against rBetv1 in patients with OAS and specific IgE to apple confirms the results of previous studies.<sup>1–5</sup> The observation that, of 99 patients with specific IgE to apple extract, only 43 patients (43.4%) reported typical symptoms after eating apples suggests that fruit-related symptoms require not only high specific serum IgE levels, but a strong cellular sensitization of birch pollen allergens, together with an increased cellular reactivity to apple allergens, as previously demonstrated.<sup>6,7</sup> Although the present data suggest that there is significant cross-reactivity with rBetv1, the data also suggest that, in more than one-third of patients, sensitivity to rBetv2 or other allergens plays a significant role.<sup>8</sup>

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