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Measurement of IgE to pollen allergen components is helpful in selecting patients for immunotherapy

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ABSTRACT

Background: Pollen allergy still represents an important cause of allergic morbidity worldwide. Accurate diagnostic methods are important to determine the disease-causing allergen.

Objectives: To describe the sensitization patterns of patients with spring pollinosis and to make a real-life evaluation of the usefulness of a predetermined IgE molecular profile compared with other sensitization methods for choosing the composition of immunotherapy.

Methods: One hundred seventy-five patients with a diagnosis of spring pollinosis completed a skin prick test study with *Olea europaea*, *Phleum pratense*, palm profilin, and peach peel and an in vitro study of the application of a specific recombinant IgE protocol (nOle e1, rPhl p1-5b, rPhl p12, rPhl p7, and rPru p3). Immunotherapy using the 2 methods was compared.

Results: A high sensitization to nOle e1 and rPhl p1-5b was found. Profilin, polcalcin, and lipid transfer proteins seemed irrelevant for the differential diagnosis of olea and grass pollen sensitization in the most southern area of the Iberian Peninsula. Application of the component resolved the diagnosis, and the choice of immunotherapy was changed in more than 50% of patients.

Conclusion: These results support the necessity of the habitual use of this kind of protocol in routine allergologic practice.

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Introduction

Grass pollen is the most important allergen source that causes spring hay fever worldwide.¹ Because of high pollen counts, olive pollen represents the main allergenic spring pollen in most southern areas in Spain.² In contrast to pharmacologic treatments, allergen-specific immunotherapy has shown disease-modifying capacities in altering the natural history of allergic diseases and decreasing the risk of new sensitization.³ Thus, the identification of the disease-causing allergen is a fundamental requirement to ensure the correct prescription of treatment. Identification is not possible using only the skin prick test (SPT) in cases of parallel pollination, such as grass and olive pollens. For this purpose, in vitro recombinant allergen techniques have provided the opportunity to study principal allergens and the cross-reactive processes involved in allergic reactions.⁴

The aims of the study were to describe the sensitization patterns of patients with spring pollinosis and to make a real-life evaluation of the usefulness of a predetermined IgE molecular profile for olive and grass pollens compared with other sensitization methods.

Methods

Patients

From their daily practice, the authors selected immunotherapy candidates with seasonal pollen-allergic rhinoconjunctivitis and/or asthma diagnosis according to suggestive anamnesis and SPT results. Serum samples were obtained from these patients. The exclusion criterion was receiving immunotherapy in the previous 5 years.

Skin Prick Test

Commercial inhalants consisting of grass (*Phleum pratense*) and olive (*Olea europaea*) were obtained from Bial-Aristegui (Bilbao, Spain); profilin (palm) and Pru p3 (peach peel) were obtained from ALK-Abello (Madrid, Spain). Histamine (10 mg/mL) and a glycerol-saline solution were used as positive and negative controls, respectively. A weal size at least 3 mm larger than the negative control was regarded as positive.

Specific IgE to Molecular Allergens (IgE Assays)

In each serum sample, total IgE and specific IgE antibody levels were compared with those of major allergens from grass (rPhl p1-p5b) and olive (nOle e1) and 3 cross-reactive recombinant allergens (rPhl p12, rPhl p7, and rPru p3) using ImmunoCAP (FEIA; Phadia, Uppsala, Sweden). Results were expressed in kilounits per liter and

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Table 1

Patients' descriptive sensitization results and immunotherapy choices

	Positive SPT result	Positive recombinant/natural specific IgE	Sensitivity/negative predictive value (%)	IT based on SPT	IT based on recombinant IgE
Olive	157	143	96/72	35	51
Grass	143	134	94/75	10	59
Olive + grass	133	110	90/73	130	65
Profilin	53	33	85/96		
Pru p3	22	8	—		
Polcalcin	—	12	—		

Abbreviations: IT, immunotherapy; SPT, skin prick test.

classified as positive or negative according to the cutoff levels required by the analyses.

Choice of Immunotherapy Composition

According to the allergic studies, the initial immunotherapy composition was chosen based on the quantitative SPT results. A second choice based on recombinant IgE values was completed afterward. Then, the 2 choices were compared.

Results

One hundred seventy-five patients (42% female, 58% male) 6 to 62 years old were included in the study. In order of frequency, 157 patients (89%) presented a positive SPT result to olive pollen, 143 patients (81%) to grass pollen, 133 patients (64%) to olive and grass pollens, 53 patients (30%) to profilin, and 22 patients (12.5%) to Pru p3. The median value of total Ig E was 183.5 kU/L (range, 11–2,000 kU/L). One hundred forty-three patients (81%) presented a positive specific IgE result to nOle e1 (median, 4.1 kU/L; range, 0–208 kU/L), 134 patients (76.5%) to rPhl p1-5b (median, 8.1 kU/L; range, 0–100 kU/L), 110 patients (62%) to nOle e1 and rPhl p1-5b, 33 patients (19%) to rPhl p12, 12 patients (6.8%) to rPhl p7, and 8 patients (4.5%) to rPru p3. The sensitivities of the SPT study were 96% to olive, 94% to grass, and 85% to profilin. Its negative predictive values were 72% for the olive SPT, 75% for the grass SPT, and 96% for the profilin SPT. All these results are presented in Table 1. Regarding patients with 2-pollen sensitization, 34 patients presented positive SPT results to the 2 pollens but with negative nOle e1- and rPhl p1-5b-specific IgE results (19% false positive SPT results); of these, only 2 patients showed positivity to rPhl p12 and another 2 patients showed positivity to rPhl p7.

Based on the SPT results, the immunotherapy prescription was grass in 10 patients, olive in 35 patients, and grass and olive in 130 patients; in contrast, based on molecular IgE results, the immunotherapy prescription changed to grass in 59 patients, olive in 51 patients, and grass and olive in 65 patients (Table 1). In the 175 patients, after application of the molecular profile, the immunotherapy composition changed in 97 patients (55%); the most frequent prescription change was from to grass and olive pollens to only grass pollen (35 patients); of this group, 11 patients showed positivity to rPhl p12 and 2 patients showed positivity to rPhl p7. In 27 patients, the prescription changed from grass and olive pollens to only olive pollen; of these, only 2 patients presented positivity to rPhl p12 and rPhl p7, respectively.

Discussion

The present study describes how molecular diagnosis can improve the accuracy of a diagnosis of parallel pollen allergy compared with traditional methods. The area in which the authors live is the most southern on the Iberian Peninsula and it has 2 clearly defined botanical provinces: one corresponds to the coast and the other corresponds to the inner countryside, representing olive and grass as the 2 main allergenic pollens. The flowering period is continuous and rising, with total pollen counts up to 100 grains/m³ from week 6 to

26 (February to June) and spring counts of 500 and 1,400 grains/m³ for grass and olive pollens, respectively.⁵

Concerning individual sensitizations, the present patients expressed a predominant SPT result for olive vs grass pollen sensitization (157 vs 143 patients) with high ratios of sensitivity (>90%). In addition, the sensitization results were high for nOle e1 and rPhl p1-5b, with data for specific IgE being comparable to a similar descriptive study reported by Barber et al.⁶ In the southernmost area of the Iberian Peninsula, they estimated very high (>76%) nOle e1 sensitization and high (51% to 75%) rPhl p1 sensitization, whereas the authors obtained 81% using nOle e1 and 76.5% using rPhl p1-5b in the present patients. Barber et al also estimated low (0% to 10%) profilin (using apple profilin, rMal d 4) and lipid transfer protein (using peel peach, rPru p3) sensitizations, whereas the present patients showed similar results to serum rPru p3 sensitization (4.5%) and somewhat higher sensitization to *P pratense* profilin (19%). Other descriptive studies have been published, but none corresponded to the authors' geographic zone; actual research has shown that the relevance of lipid transfer protein is mostly limited to the Mediterranean basin.⁷ In 2009 Casquete-Román et al⁴ described rPhl p7 plus rPhl p12 sensitization in 46% of 162 pediatric patients with pollinosis; this study concerned patients from the northern area of Spain. Recently, an Italian study of grass pollen allergy in children reported that 20% had rPhl p12 sensitization.⁸ Remarkably, in the present positive profilin group, noteworthy rates for sensitivity (81%) and negative predictive value (96%) were obtained with the profilin SPT, a useful tool in the differential diagnosis of pollinosis when the result is negative.

In the initial group of 133 patients with 2-pollen SPT sensitization, sensitization was corroborated, by blood-specific recombinant IgE testing, in only 110 patients (false positive ratio, 19%). In the present group, only 2 sensitizations to rPhl p12, another 2 to rPhl p7, and none to Pru p3 were detected. These results strengthen the use of the protocol and require future research to clarify it.

Applications of recombinant allergens in the authors' daily clinical practice allowed the possibility of improving and perfecting the procedure to detect the real disease-eliciting allergen. After evaluating only 2 pollens, the immunotherapy composition was changed in 55% of patients, showing similar results to those recently published in a complex pollen area (center of the Iberian Peninsula) by Sastre et al.⁹ The use of a molecular protocol in the present patients meant not considering a positive olive SPT result when it was also positive for the grass SPT in 35 patients and profilin sensitization was present in almost half of them; sensitization was not present in the patients whose initial positive grass SPT result was not considered for final immunotherapy composition.

According to these results, the authors support the necessity of the regular use of this kind of protocol in their routine allergologic practice. Because the southernmost region of Spain is not a rich pollen area compared with other Spanish areas and only 2 pollens were investigated, immunotherapy prescription failures were corroborated in more than 50% of initial immunotherapy composition choices. In conclusion, component-resolved diagnostics

improved the selection of suitable patients for immunotherapy by establishing individual sensitization patterns in an area with overlapping pollen seasons.

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